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Application News

Preparative Purification Liquid Chromatograph – Nexera™ Prep

Workflow Enhancement for Purification of New Synthetic Compounds in Drug Discovery Process

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User Benefits

- Automatic screening against synthetic crude compounds provides a labor-saving operation.
- The easy scale-up algorithm achieves smooth transfer from a screening step to a purification step.

■ 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 a novel automation for target screening and preparative purification by LC/MS using a dedicated, designed software.

■ Conventional Workflow

Fig. 1 shows a conventional workflow of target compound screening and purification in drug discovery. First, crude compounds from the synthesis step are analyzed by LC-MS, and the operator checks each result. Then, the preparative method is developed manually through the conventional scale-up method. Finally, the crude compounds are purified by preparative LC.

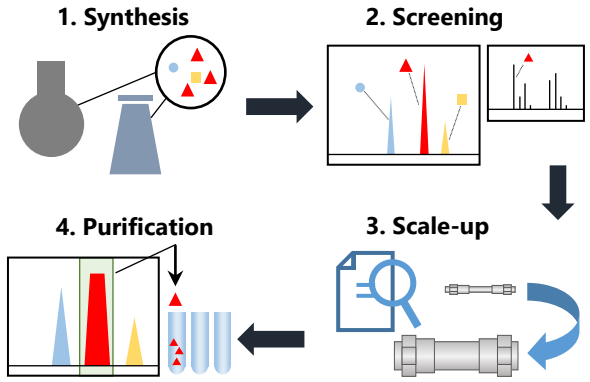


Fig. 1 Conventional workflow of target screening and purification

■ Advanced Workflow

► Automatic Screening by Open Solution

Typical screening steps require manual checking for each crude sample. Open Solution™ is an open-access software that assists the whole drug discovery workflow from screening to purification. The software automatically classifies crude samples into three situations using target *m/z* information and MS spectrometry (Fig. 2).

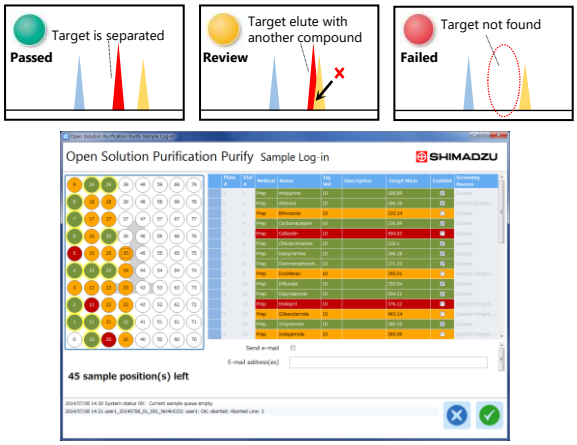


Fig. 2 Open Solution classify crude compounds to three situations

► Automatic Scale-up by ASAPrep

Open Solution creates a scale-up method using ASAPrep™ algorithm (Auto Scale-up from Analytical to Preparative). This algorithm creates the focused gradient profile for preparative scale utilizing information from screening results. (Fig. 3) The only need for the user is to choose passing samples (green colored) and start the purification step by just one click.

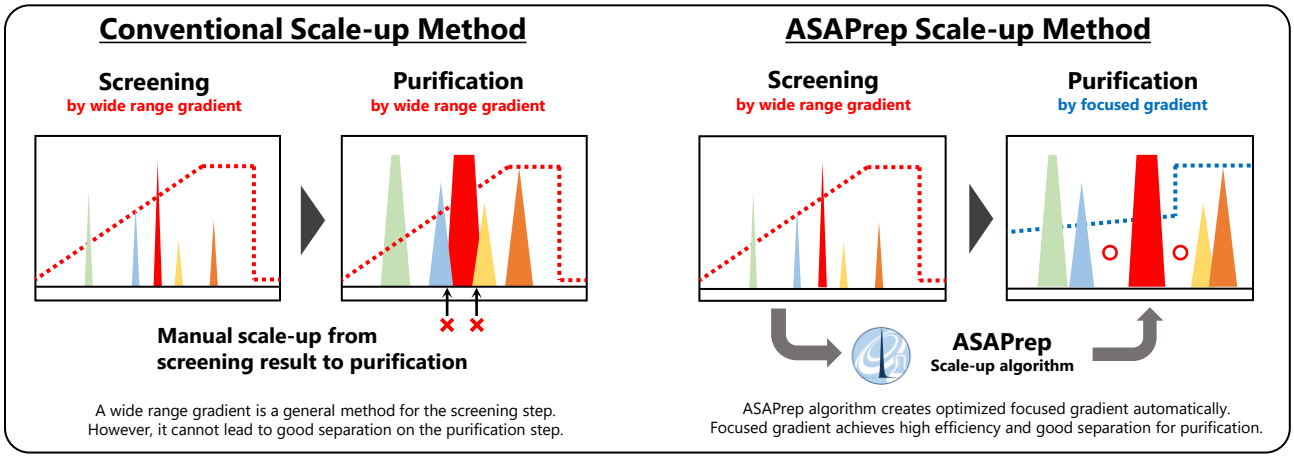


Fig. 3 Comparison of workflow between conventional and ASAPrep algorithm

■ Screening and Purification of Crude Medical Compounds

We performed screening, scale-up, and purification against three types of medical compounds, containing impurities. Table 1 shows the analytical conditions for the screening step, and Table 2 shows the analytical conditions for the purification step. All these results are shown in Table 3. LC-MS analysis (LCMS-2020) finds three target compounds at the screening step. Then, the ASAPrep algorithm calculated the dedicated, focused gradient profile by the retention time of each target compound through the screening result. The focused gradient that followed the ASAPrep algorithm showed good separation at the purification step and identified each compound by LCMS-2020.

■ Conclusion

This article introduces workflow enhancement for drug discovery from screening to purification. Open Solution software and ASAPrep algorithm provide easy and labor-saving operations to check screening results and preparative method development. Automatic workflow for purification is expected to increase productivity and reduce labor costs.

Table 1 Analytical conditions for screening step

Column	: Shim-pack GISS C18 *1 (100 mm × 2.1 mm I.D., 1.9 µm)
Mobile phase	: A) 0.1 % formic acid in water B) 0.1 % formic acid in acetonitrile
Flow rate	: 0.5 mL/min
Time program	: B conc. 5 % (0 min)→ 95 % (3-4 min) →5 % (4.01-5 min)
Column temp.	: 40 ℃
Injection volume	: 1 µL
Vial	: SHIMADZU LabTotal™ for LC 1.5 mL, Glass*2
Analytes	: Target compound 2 mg/mL in DMSO
Detection	: 254 nm (SPD-M20A) Pos./Neg., Scan *m/z*: 50-1000 (LCMS-2020)

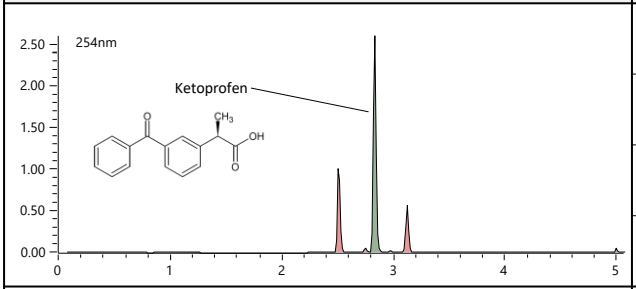
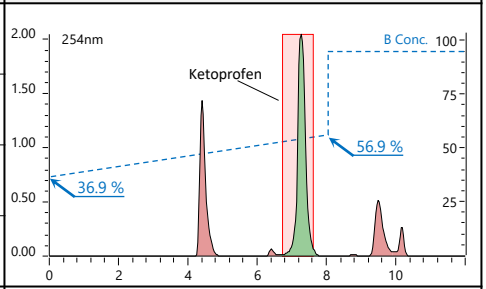
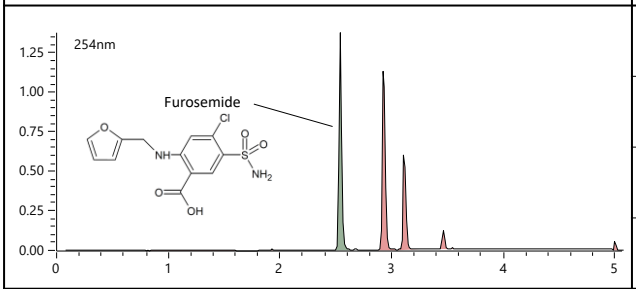
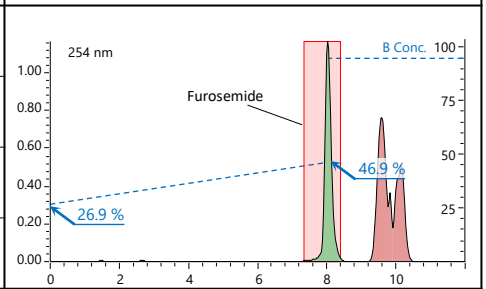
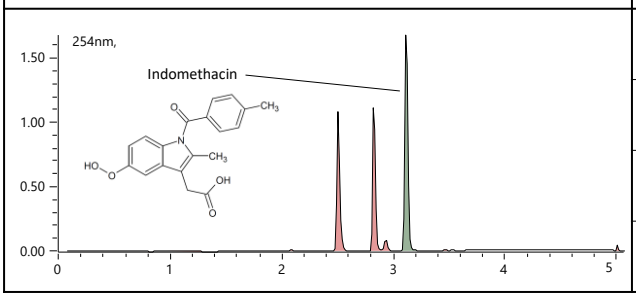
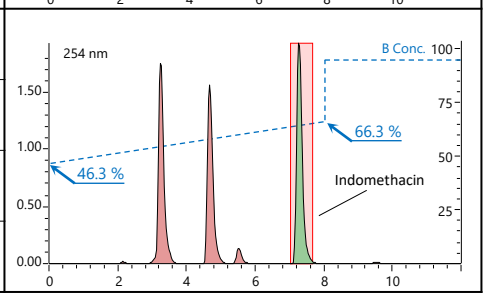
*1 P/N: 227-30048-02 *2 P/N: 227-34001-01

Table 2 Analytical conditions for purification 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
Time program	: B conc. XX*4 % (0 min)→ XX+20 % (8-12 min)
Column temp.	: Ambient
Injection volume	: 400 µL
Vial	: 10 mL screw vial *5
Analytes	: Target compound 20 mg/mL in DMSO
Detection	: 254 nm (SPD-20AV) Pos./Neg., Scan *m/z* 50-1000 (LCMS-2020)

*3 P/N: 227-30066-02 *5 P/N: 220-97331-09
*4 XX: Initial B conc. of focused gradient

Table 3 Results of screening and purification steps

Screening Chromatogram	ASAPrep Algorithm	Purification Chromatogram
	Target mass 254.28 Retention time 2.83 min Focused gradient Int. B Conc. 36.9 % Screening result PASS	
	Target mass 330.74 Retention time 2.53 min Focused gradient Int. B Conc. 26.9 % Screening result PASS	
	Target mass 357.79 Retention time 3.11 min Focused gradient Int. B Conc. 46.3 % Screening result PASS	

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