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Application News

Software for Efficient Method Development "LabSolutions™ MD"

Automatic Optimization of Gradient Conditions by AI Algorithm for Impurity Analysis

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User Benefits

- The AI algorithm of LabSolutions MD can automatically optimize gradient conditions to greatly reduce labor of LC method development.
- Anyone can optimize gradient conditions, regardless of their experience in chromatography.
- Gradient conditions that meet the resolution criteria for specified peaks are automatically searched (e.g., principal component and its related impurities).

■ Introduction

In the typical LC method development, the process begins with "preparation" which includes mobile phase preparation, column installation, and creation of analysis schedules, then the analysis is started. After that, the acquired data is analyzed and "preparation" for the subsequent analysis is carried out, followed by starting the next analysis again. The method development progresses by repeating these processes, but in addition to the significant time required to repeatedly create analysis schedules, expertise in chromatography is necessary to explore optimal conditions based on data analysis. In other words, typical method development requires "human intervention". Therefore, eliminating human involvement and automating such method development processes would be desirable to improve labor efficiency. This article introduces an example of automatic optimization of gradient conditions to separate montelukast (a small molecule drug) and its related impurities using LabSolutions MD (Technical Report C190-E309), a dedicated software for supporting method development.

■ Analytical Conditions and Target Compounds

The analytical conditions and target compounds are shown in Table 1. In this article, the criteria for resolution and elution time of the last peak were set for montelukast and related impurity (Imp1). LabSolutions MD automatically explored the gradient conditions to meet these criteria.

Table 1 Analytical Conditions and Target Compounds

System : Nexera™ X3	
Sample : montelukast	
Mobile phase:	
Pump A : 0.15% formic acid in water	
Pump B : 0.1% formic acid in acetonitrile	
Column : Shim-pack Scepter™ Phenyl-120 (100 mm × 3.0 mmI.D., 1.9 µm) *1	
Analytical conditions	
B Conc.	: 5% (0 min)→95% (X*2 ~X+2 min) →5%(X+2~X+7 min) *2 : X = 8, 9, 10, 11, 12 (5 patterns)
Column Temp.	: 30 °C
Flow rate	: 0.5 mL/min
Injection Vol.	: 10 µL
Detection	: 238 nm (SPD-M40, UHPLC cell)
Criteria of automatic optimization of gradient conditions	
Resolution	: > 3.0 (montelukast and Impurities)
Elution time of last peak	: < 15 min

*1 : 227-31064-03 (Shimadzu GLC product number)

■ Automatic Optimization of Gradient Conditions

Fig. 1 shows the workflow of automatic optimization of gradient conditions using LabSolutions MD. This software has a unique AI algorithm to automatically explore gradient conditions that satisfy resolution criteria by alternately repeating "improvement of gradient conditions by AI (condition search)" and "analysis under improved conditions (correction analysis). For the criteria, "resolution" and "elution time of the last peak" can be set. In this article, automatic optimization of gradient conditions was applied to montelukast (specified as the principal peak) and related impurity (Imp1) to meet the criteria of resolution (> 3.0) and maximum elution time of 15 minutes for the last peak (Fig. 2), considering the reduction of analysis time.

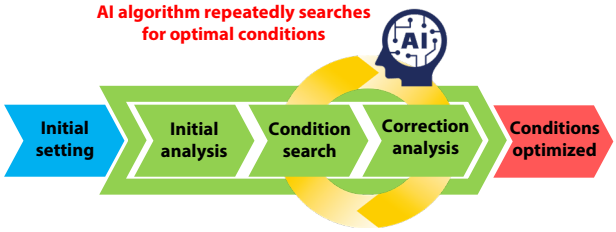

Fig. 1 Workflow for Automatic Optimization of Gradient Conditions by LabSolutions MD

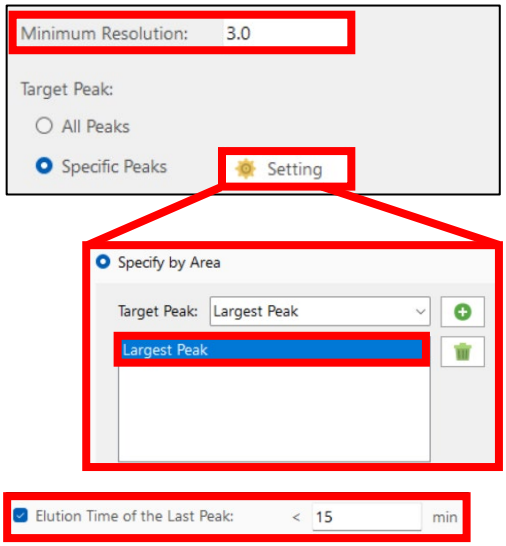

Fig. 2 Setting for Automatic Optimization

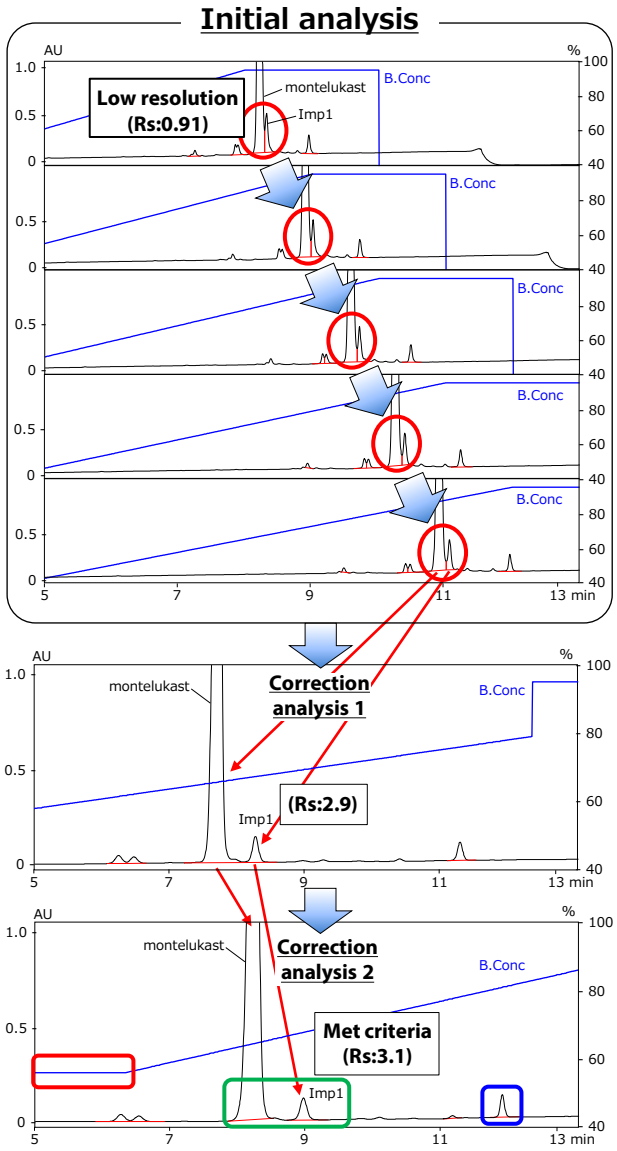

Fig. 3 Result of Automatic Optimization of Gradient Conditions
* blue line shows gradient conditions

The result of automatic optimization of gradient conditions is shown in Fig. 3. After the initial analyses were performed with the five different patterns of gradient curves (conditions are shown table 1), the resolution of montelukast and Imp1 was automatically optimized through two correction analyses. The result of initial analyses shows that the resolution of montelukast and Imp1 was not sufficient (red circles in the initial analyses in Fig. 3). After repeated correction analyses by the AI algorithm, the gradient conditions that finally met the criteria was automatically explored (correction analysis 2). In correction analysis 2, the resolution criteria (> 3.0) was achieved (green box) by inserting an isocratic elution (red box). The elution time of the last peak (blue box) also met the criteria (< 15 minutes).

■ Conclusion

Automatic optimization of gradient conditions using AI algorithm of LabSolutions MD was applied to montelukast and its related impurity. As a result, gradient conditions that met the criteria ("resolution for montelukast and related impurity > 3.0" and "elution time of the last peak < 15 minutes") were successfully explored. This result indicates that significant labor saving in method development can be expected by LabSolutions MD. This article introduces an automatic optimization of gradient conditions in method development while LabSolutions MD also supports a series of workflow of method development, including the screening phase and robustness evaluation phase. For details, please refer to the Technical Report "Efficient Method Development Based on Analytical Quality by Design with LabSolutions MD Software (C190-E284)".

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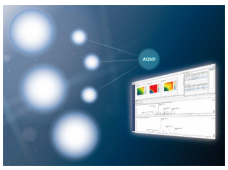

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