

平成 29 年度「日本薬局方の試験法等に関する研究」研究報告  
グラジエント HPLC のシステム適合性試験における  
精度評価の省力化に関する研究<sup>\*3</sup>

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Repeatability Assessment of Gradient HPLC Systems with Complex Elution Programs  
for the Analysis of Japanese Pharmacopoeia Drugs by ISO 11843-7

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#### Summary

In the Japanese Pharmacopoeia, 17th edition (JP17), each HPLC system used for purity test and assay must be confirmed to comply with the system suitability tests, including tests for required detection, system performance, and system repeatability, before being used to perform the specification tests. For the system repeatability test, standard solution or test solution for the system suitability test is injected several times (generally 6 injections are recommended) and the relative standard deviation (RSD) of the peak height or peak area of the analyte is evaluated. As an alternative way to evaluate repeatability, previous studies have shown that ISO 11843-7 can be applied for the evaluation of the system repeatability in isocratic HPLC or simple gradient HPLC. However, 26 drug substances and drug products in JP17 require more complicated gradient HPLC for their specification tests. It is still unclear whether ISO 11843-7 can be applied to these complicated gradient elution programs, because significant changes of the mobile phase composition have an impact on the baseline noise in HPLC analysis. In this study, the gradient conditions employed for the 26 drugs were classified into 3 patterns, and the purity tests for cefotaxime sodium, simvastatin, and cefaclor, as representatives of the three gradient patterns, were investigated. Then the stochastic RSD obtained by ISO 11843-7 and the statistical RSD obtained from six replicate injections of standard solutions were compared in each case. The stochastically estimated RSDs were all within the 95% confidence intervals of the corresponding statistically estimated RSDs. Thus, it was found that ISO 11843-7 can be applied to the evaluation of repeatability in complicated gradient HPLC systems. This information will be helpful to reduce the required resources for the specification tests.

#### Key words

System suitability test, Gradient elution, High performance liquid chromatography, Repeatability, ISO 11843-7