Total solution for the HPLC method development process by ChromSword software

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Summary

- HPLC method development is a repetitive and time-consuming process of method planning, development, execution and interpretation.
- ChromSword software combined with Agilent HPLC and UHPLC systems provides fully automatic and straightforward method development.
- ① Lamotrigine with impurities and ②API with three pairs of isomers, were used as test samples for the method development.
- The HPLC various conditions were easily and quickly screened by ChromSword Auto to determine the best columns, solvents and buffer combinations.
- The result of fine optimization could be tested for its robustness by AutoRobust in accordance with Quality by Design (QbD) principles.

Back Ground

- The method development by using HPLC and LC/MS is one of important steps for various research and development processes in pharmaceutical, chemical, food, agricultural and environmental fields.
- Especially for the process chemistry in pharmaceutical industries, the HPLC method development is a critical step to increase productivity and to improve chemical quality under regulations as QC and QA requirement.
- Recently, since the preparation and synthesis of active pharmaceutical ingredients (API) are shifting to the Asian countries, more strict regulations should be applied to API.
- Therefore, from the point of pharmaceutical QC and QA, the importance of the exact and repaid method development could be increased in the pharmaceutical industries.

Method

【Software】
- ChromSword Auto 4.0 >> Automated method development
- ReportViewer 5.0 >> Data fast browsing, Analyzing and Design space
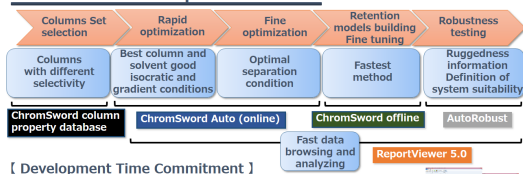- AutoRobust 2.1 >> Automated robustness test

【General Condition】
- HPLC : Agilent 1200 method development system (Binary pump) 8 Column switching valve, Multi Wavelength Detector
- Column : Reverse Phase Columns(50 mm, 4.6 mm)
- Mobile Phase : MeOH or ACN/H3PO4 buffer or H2O
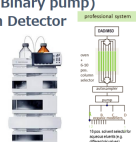
【Samples】
①Lamotrigine and impurities
②API＋3 Pair isomers

## Automated Development Process

[Development Time Commitment]
- Optimization of separation of target compounds: 1-48 h/sample
- Screening columns and solvents/pH: 5 min– 1 h/column/solvent/pH
- Impurities profiling, separation of the max. number of compounds: 6-48 h/sample
- Robustness test: 10-36 h
- Analytical development report: 1-5 min/project

## Rapid Optimization in 3-5 Runs

[Lamotrigine and impurities]
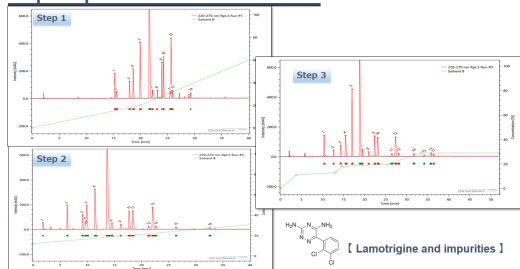
Fast Importing and Fast Browsing

- HPLC data was able to be quickly imported directly from not only Agilent's chromatography data system (CDS) folder but also other HPLC data system.
- Several λmaxs of each peak's were able to be showed on peak top.


[API＋3 Pair isomers]
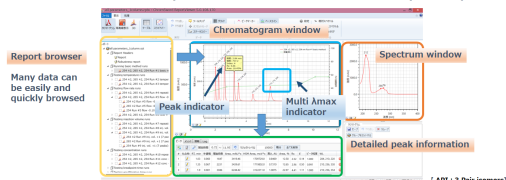
Overlay comparing

- Each chromatogram data was able to be quickly and easily compared by overlay with different colors.
- Spectrums of each peak was easily overlayed to understand the peak characterization with different colors.

[API＋3 Pair isomers]
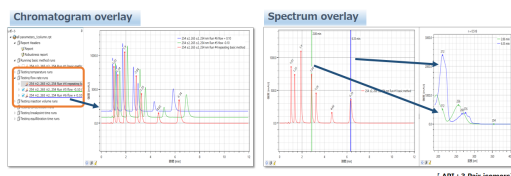
2D, 3D Chromatograms

- Chromatograms were able to be visually and intuitively browsed by 2D and 3D data browsing functions.
- Chromatograms and spectrums on the 2D and 3D windows are also compared by overlay function with double click on peak tops.

[API＋3 Pair isomers]
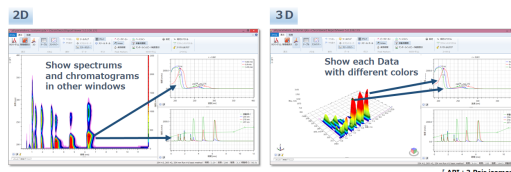
Automated Robustness Test

- The robustness of HPLC methods was fully automatically carried out by AutoRobust to study the influence of variations in method parameters on the results.
- AutoRobust set up robustness condition in approx. 10 min. much shorter than about 1h by manual set up.

3 columns x 6 variables x 3 steps 2(+/-)
= 108 runs (+basic method)<<10 min.

☐ Temperature
☐ Flow rate
☐ Concentration (%B)
☐ Gradient break point positions
☐ Injection volume
☐ Equilibration time
☐ Wavelength
☐ Column batch
☐ Buffer concentration/pH

Robustness Test/Design Space

- The result of fine optimization was tested for its robustness by AutoRobust in accordance with Quality by Design (QbD) principles.
- The expected chromatogram could be easily simulated for building up the next experiment conditions by the new design space.

[API＋3 Pair isomers]