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The efficiency of multi-sample analysis using a dual gradient LCMS system

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Satoru Watanabe, Daisuke Nakayama, Yusuke Inohana,
Tadayuki Yamaguchi
Shimadzu Corporation, Kyoto, Japan

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Introduction

Higher throughput is of the utmost importance to laboratory efficiency and profitability. Conventional analysis requires performing various processes such as column washing, equilibration at initial mobile phase concentrations, and the next sample injection by the autosampler during the analysis.

We developed and evaluated the dual gradient LCMS system "Nexera MX" which incorporates a special flow line structure and instrument control system, and performs overlap control of sample injection by alternately using two analysis systems (streams).

Fig. 1 Nexera MX system

Experimental

The dual gradient LCMS system has two analytical streams which contain pump units and analytical columns. By using these, after one stream completes data acquisition, the other stream starts data acquisition immediately without a time delay. The flow diagram is shown in Fig.2

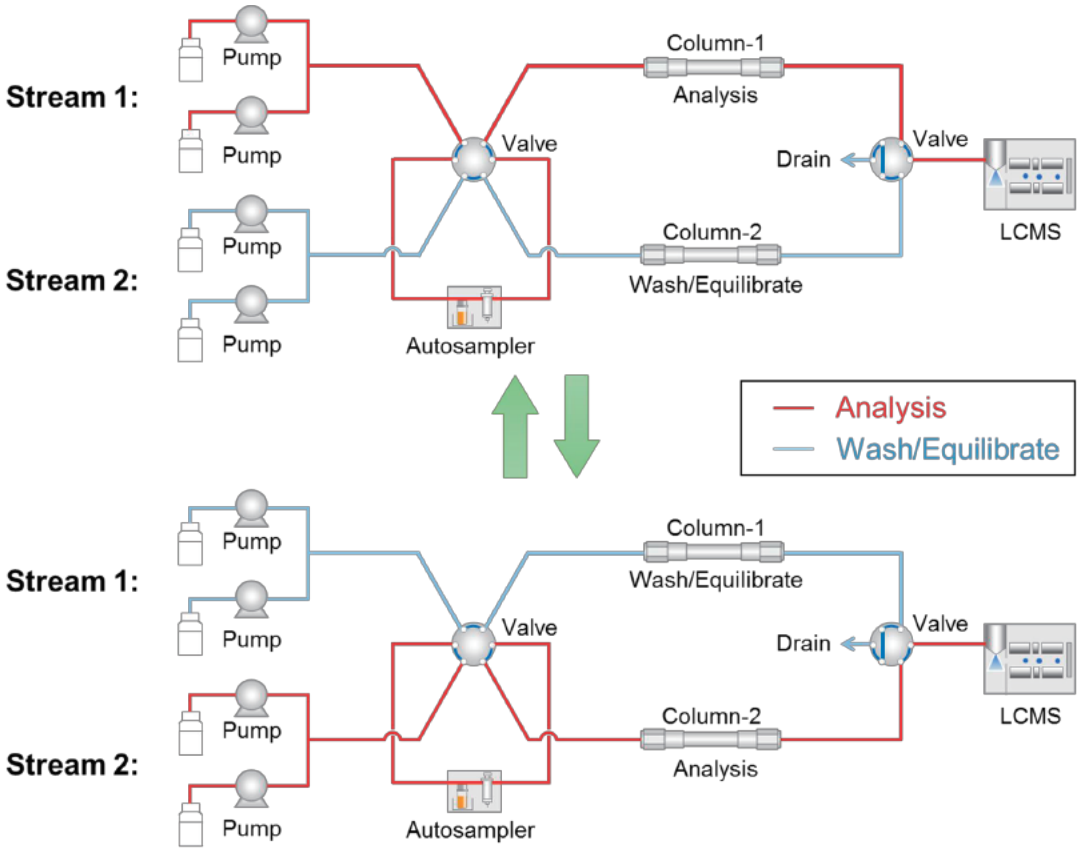

Fig. 2 Flow diagram

An analytical time chart comparing a conventional LCMS System and a dual gradient LCMS system is shown in Fig 3. The conventional LCMS System operates [Load sample]-[Data Acquisition]-[Wash/Equilibrate] in a serial manner. The dual gradient LCMS system operates in parallel and nearly the entire LCMS time can be used for data acquisition.

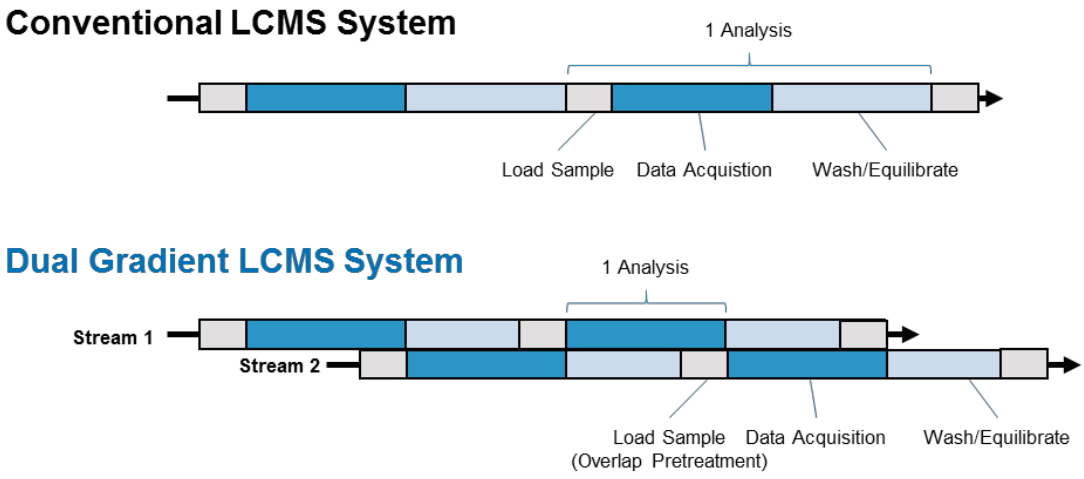

Fig. 3 Analytical Time Chart

Methods

Samples:

We evaluated the analytical cycle time and the repeatability in the analysis of four biomarker compounds for the four major molecular species in the Cytochrome P450 family, using an ultra-high speed reversed phase column and LCMS-8060 triple quadrupole mass spectrometer.

Analytical Conditions:

Analytical conditions are shown in Table 1. Stock solutions (100ng/mL) were prepared by dissolving standard samples in 10% acetonitrile.

Table 1 Analytical Conditions

Column	: ODS Column 2.0×20 mm, 2.2 µm		
Mobile Phase	: A : 0.1% Formic Acid in Water		
	: B : 0.1% Formic Acid in Acetonitrile		
Flow Rate	: 0.4 mL/min		
Time Program	: B: 5% (0 min) – 95 % (0.3 – 0.5 min) – 5% (0.51 – 1.0min)		
Column Temperature	: 40 ℃		
Injection Volume	: 1 µL		
Compound/MRM	: (±)-4'-Hydroxybufuralol	(CYP2D6)	/ 287.10 -> 186.20
	(±)-4'-Hydroxymephenitoin	(CYP2C19)	/ 235.05 -> 150.10
	1'-Hydroxymidazolam	(CYP3A4)	/ 342.00 -> 203.10
	4'-Hydroxydicrofenac	(CYP2C9)	/ 311.90 -> 230.05

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Software:

Shimadzu LabSolutions software supported various processes from method setting to data analysis. The special user interface allows for quick method development and graphical batch queue management (Fig.4).

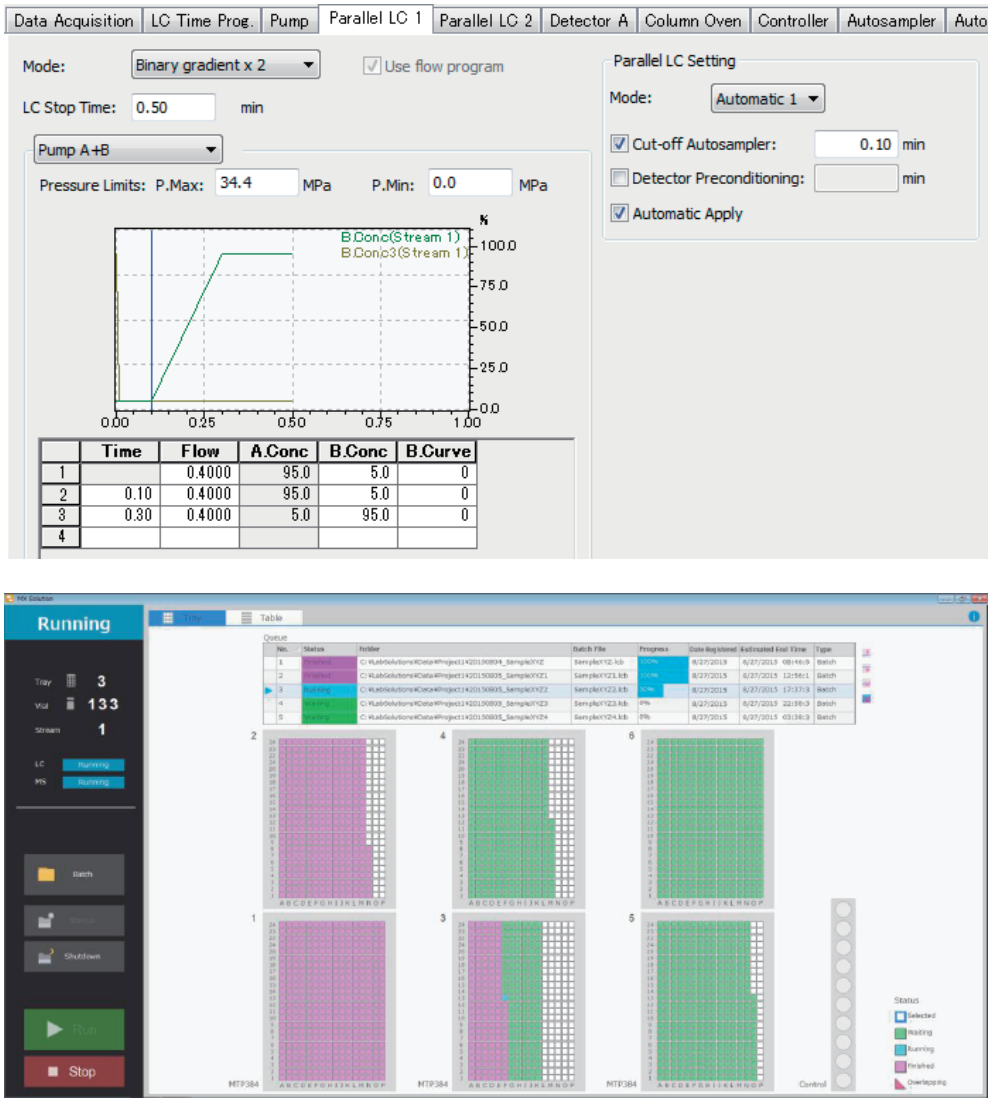

Fig. 4 Software Screen
(Top: LC gradient Method, Bottom: Batch Queue Management)

Results

The dual gradient LCMS system was evaluated for four compounds. This system provided a cycle time that is at least twice as fast compared with the conventional LCMS system in Fig.5.
The repeatability results (N=6) were shown in Table 2. When using dual streams, the repeatability of the retention time is reduced slightly. This result would seem to reflect the difference between the two columns. However the standard deviation is a max of 0.3 sec and the identification precision is not affected. The repeatability of the peak area results are good for all compounds.

Table 2 Repeatability Comparison

Compound	Conventional LCMS System		Dual Gradient LCMS System	
	RT (%RSD)	Area (%RSD)	RT (%RSD)	Area (%RSD)
(±)-4′-Hydroxybufuralol	0.54	3.37	0.52	2.97
(±)-4′-Hydroxymephenitoin	0.48	4.54	1.14	3.54
1′-Hydroxymidazolam	0.46	3.68	1.40	2.07
4′-Hydroxydicrofenac	0.43	1.32	1.41	3.62

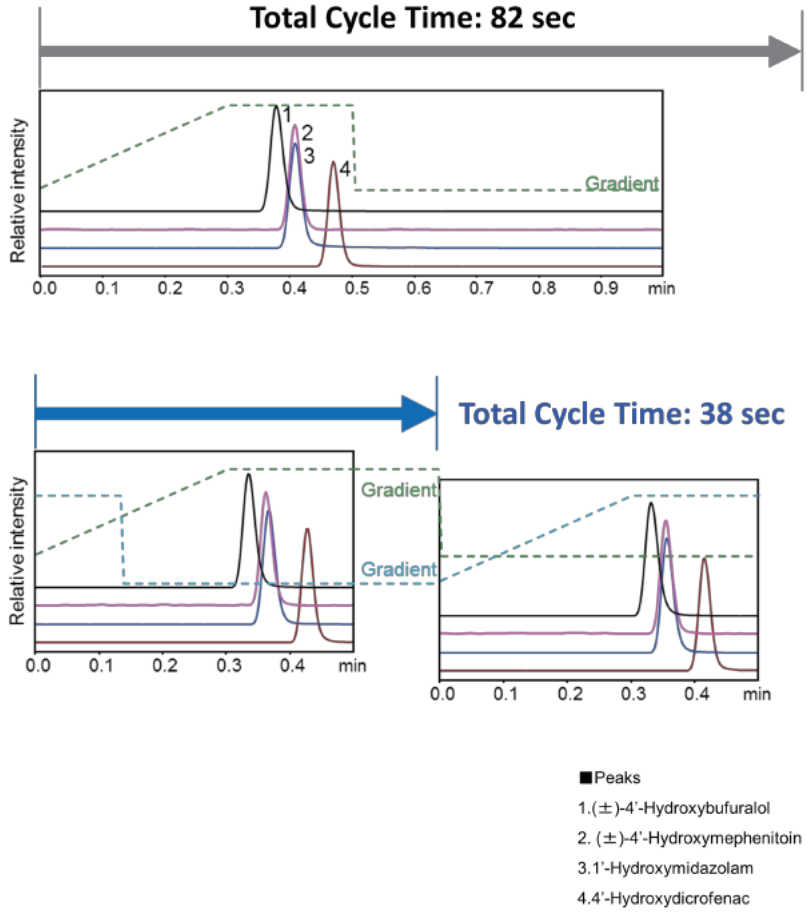

Fig. 5 Chromatogram
(Top: Conventional LCMS System, Bottom: Dual Gradient LCMS System)

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Conclusions

The evaluation results showed that the dual gradient LCMS system "Nexera MX" shortens total cycle time considerably. This system can increase the number of samples analyzed and maximize throughput. It is quite effective to laboratory efficiency and profitability in pharmacokinetic studies of pharmaceuticals or clinical laboratories.

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