

Development of a High Performance Autosampler for Front-end UHPLC to Improve LC/MS and LC/MS/MS Analysis Efficiency

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Introduction

To speed up R&D in such areas as pharmacokinetics and synthesis in drug discovery, it has become increasingly necessary to analyze large numbers of samples at high speed and with high precision. Recently, a new high-throughput autosampler, SIL-30AC_{MP}, was introduced in response to these demands. With an ultrafast injection performance and a pressure range up to 130 MPa, the SIL-30AC_{MP} autosampler enables ultra-fast LC/MS/MS analysis when combined with the LCMS-8000 series that features ultrafast positive/negative ionization switching and high-speed scanning. The minimum cycle time of analysis with LC/MS/MS by combining the SIL-30AC_{MP} autosampler was 14 seconds for three pharmaceutical mixes. The

autosampler provided an ultralow level of carryover of chlorhexidine with an improved rinsing mechanism. In this presentation we will show results of carryover evaluation of some pharmaceutical compounds and an applicability evaluation of the SIL-30AC_{MP} for synthetic studies in drug discovery and pharmacokinetics.



Nexera MP with LCMS-8040 system



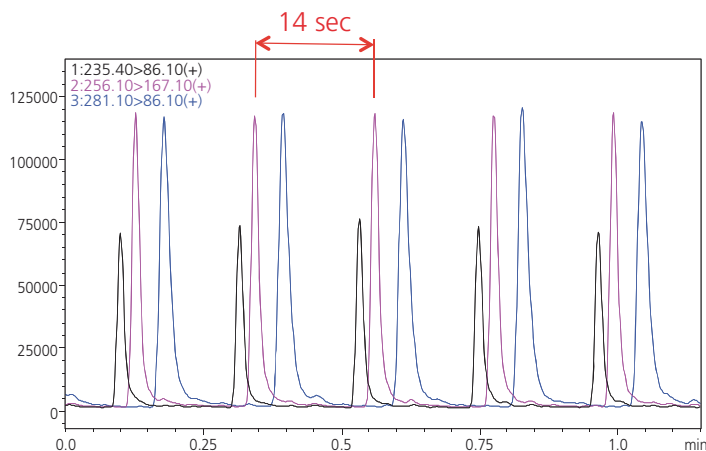
Nexera MP with LCMS-8080 system

Ultra Fast Injection Cycle

High-speed injection of 7 seconds enables ultrafast LC/MS/MS analysis

Achieve ultrafast LC/MS/MS analysis by combining the SIL-30AC_{MP}, featuring the fastest injection operating time of just 7 seconds and an analysis cycle of 14 seconds, with the ultrafast positive/negative ionization switching (15

msec) and high-speed scanning (15,000 u/sec) of the Shimadzu LCMS-8030/8040 Triple Quadrupole Mass Spectrometer.



Event #	Compound	Q1 m/z	Q3 m/z
1	Lidocaine	235.4	86.1
2	Diphenhydramine	256.1	167.1
3	Imipramine	281.1	86.1

Column : Shim-pack XR-ODS II 1.5 mmID × 30 mm, 2.2 μm
 MP : acetonitrile / water =25/75
 containing 0.1% formic acid
 Flow rate : 1.2 mL/min
 Ionization : ESI (+)

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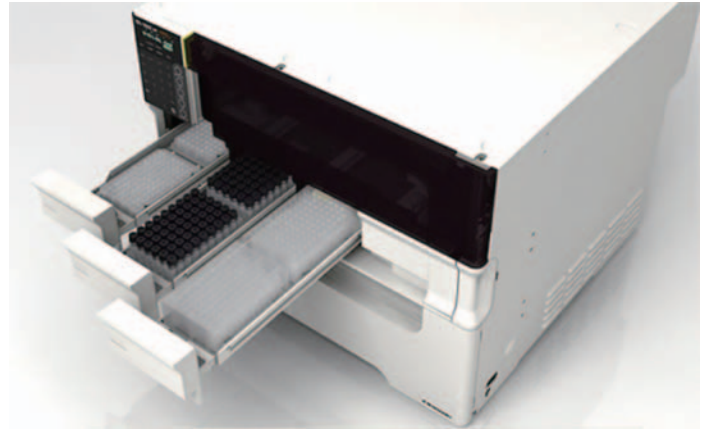
Large Sample Capacity

Mixture of 3 Plates Possible

The SIL-30AC_{MP} accommodates 6 microtiter plates (96/384MTP, DWP) or plates for 1.5 mL vials. With 384-well plates, up to 2304 samples can be loaded at a time. Even with 1.5 mL vials, 324 samples can be loaded, which means that a large amount of samples can be handled with sufficient margin even as a standalone unit.

Open access design

Offers an open access environment, in which two or more researchers share one system. For example, one person can be performing on-time analysis with 1.5 mL vials while another is loading a microtiter plate analysis. Vials or plates can be replaced even while analysis is in progress.

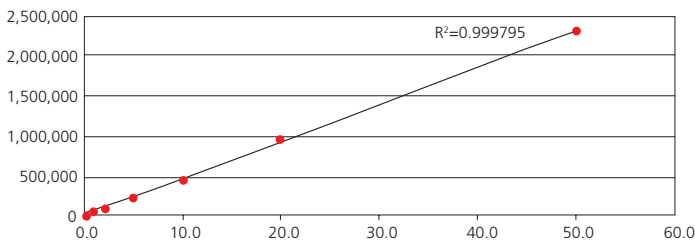


Linearity and Repeatability Evaluation

Wide linearity from 0.1 µL to 50 µL

The SIL-30AC_{MP} supports an injection volume range of 0.1 µL to 50 µL. Linearity is achieved within a broad injection range from injection of trace amounts required on a UHPLC

up to the order of several tens of µL used on conventional models. The SIL-30AC_{MP} provides excellent repeatability even in the injection of trace amounts of 1 µL or less.



injection Volume (µL)	Repeatability (N=6)	injection Volume (µL)	Repeatability (N=6)
0.1	0.67%	2	0.09%
0.2	0.32%	5	0.05%
0.5	0.26%	10	0.05%
0.7	0.14%	20	0.04%
1	0.11%	50	0.03%

Injection Repeatability (Actual Values)

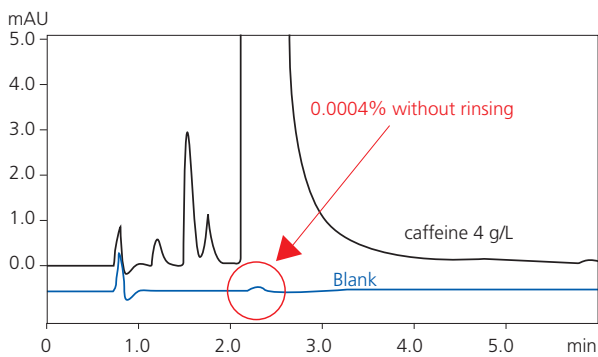
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Carryover Evaluation

Ultralow (near-zero) carryover

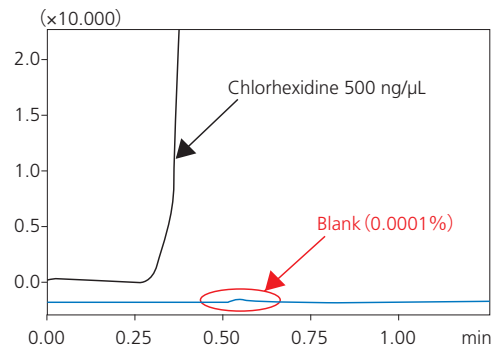
Ultralow carryover achieved without the need for rinsing

When rinsing is performed to keep carryover low, the total analysis time sometimes increases as the number of analyses increases. Nexera autosamplers excel in suppressing carryover even without rinsing.



Ultralow carryover even on a high-sensitivity LC/MS/MS

Ultralow carryover performance is required with LC/MS/MS systems. The SIL-30ACMP demonstrates exceptional carryover performance even on compounds such as chlorhexidine that are very prone to adsorption. Moreover, the SIL-30ACMP features an improved rinsing mechanism to achieve even lower carryover.



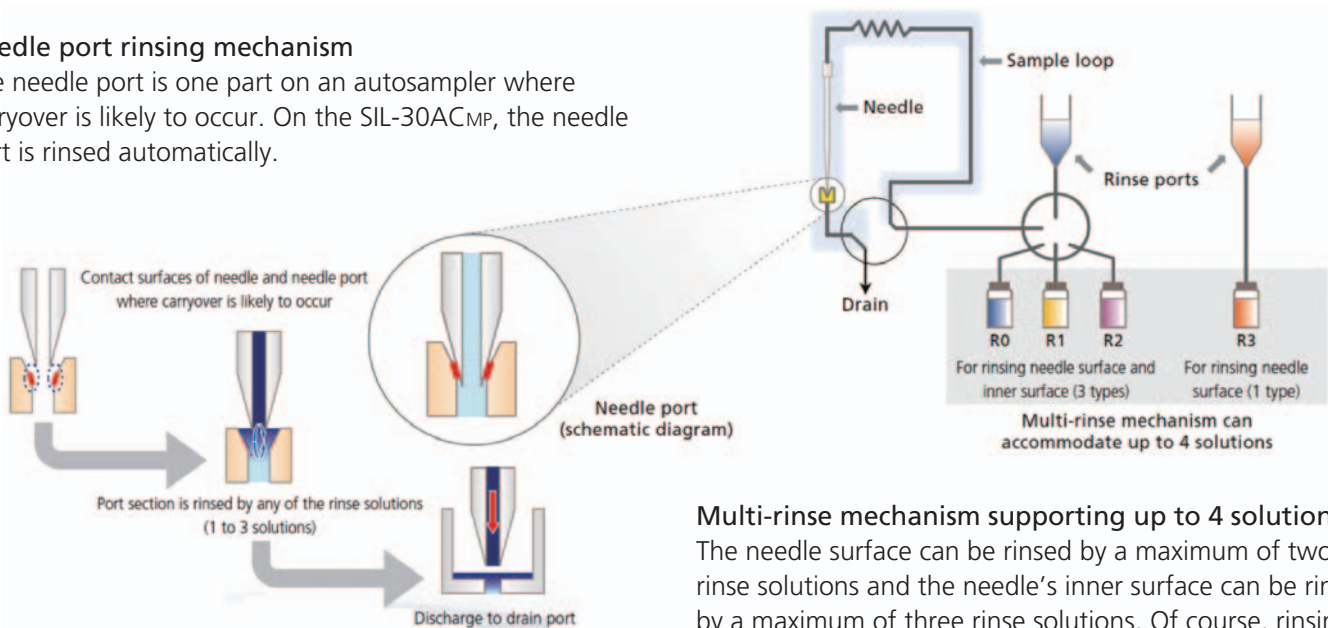
Improvements in high-sensitivity analysis and quantitative precision achieved by ultralow carryover

In the batch analysis of multiple components, components with greatly differing polarities are frequently analyzed together. In cases such as this, sufficient rinsing may not be achieved using one type of rinse solution. To combat this,

the SIL-30ACMP has not only been designed with a hardware structure to which components are less likely to adsorb, but also has a modified rinse mechanism designed to achieve even lower carryover.

Needle port rinsing mechanism

The needle port is one part on an autosampler where carryover is likely to occur. On the SIL-30ACMP, the needle port is rinsed automatically.



Multi-rinse mechanism supporting up to 4 solutions

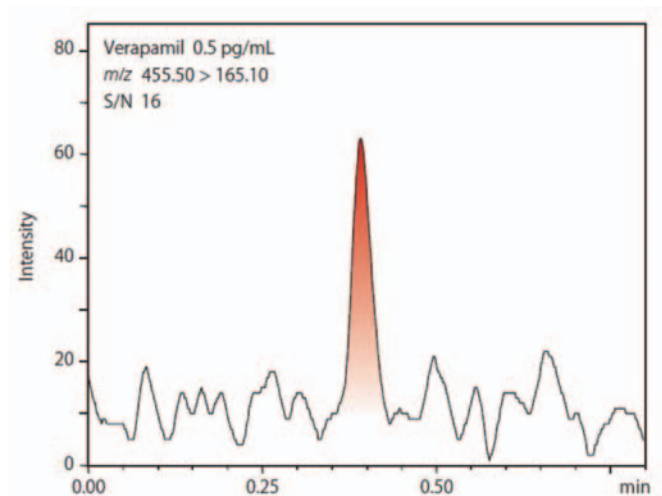
The needle surface can be rinsed by a maximum of two rinse solutions and the needle's inner surface can be rinsed by a maximum of three rinse solutions. Of course, rinsing with just one solution in the usual way is also possible. The rinsing order can also be set as desired.

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Femtogram detection with LC/MS/MS

Superior performance as MS front-end UHPLC system

500 fg/mL of Verapamil was injected and analyzed with the LCMS-8080. The data indicates sensitive analysis in the low femtogram area can be achieved.



Column : Shim-pack XR-ODS III
 Mobile phase: 5 mmol/L Ammonium acetate - Water / Acetonitrile = 10 / 90
 Flow rate : 0.5 mL/min

Conclusion

The Nexera MP including the SIL-30AC_{MP} Multi-plate Autosampler is ideally suited as a front-end LC for LC/MS and LC/MS/MS systems.

1. High-speed injection significantly improves throughput in multi-sample processing
2. Outstanding injection mechanism assures precision when injecting small volumes
3. Ultralow carryover even on a high-sensitivity LC/MS/MS
4. Open access design enables the loading of samples, even during analysis

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