SHIMADZU
Excellence in Science

Ultra High Performance Liquid Chromatograph

Nexera X4

EXPERIENCE NEW SEPARATION

Expanding on technologies cultivated with previous Nexera series models, the next-generation Nexera X4 ultra high performance liquid chromatograph (UHPLC) achieves an incomparable level of analytical performance. The lowest degree of peak broadening* in the industry results in ultra-sharp peaks and outstanding separation performance while cutting-edge fluid control technology provides exceptional solvent delivery consistency, even for fast analysis under ultra-high-pressure conditions, and highly reliable results. Engineered with precision, the high-end Nexera X4 UHPLC offers new value for all laboratories that demand maximum performance.

* ECBB value or 7 µL

Ultra-Sharp Peaks

Reduces peak dispersion to achieve excellent chromatographic separation.

Ultra-Fast Analysis

Increases productivity by ensuring consistent ultra-fast gradients.

Ultra-Low Solvent Consumption

In combination with narrow-bore columns, it significantly reduces the quantity of solvent consumed.

Nexera X4

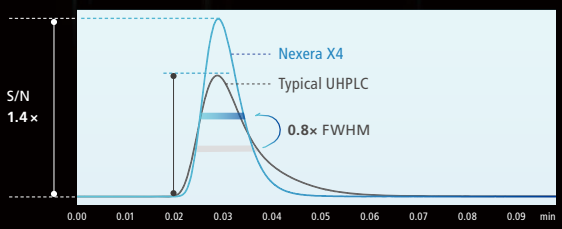
ULTRA HIGH PERFORMANCE LIQUID CHROMATOGRAPH

Engineering Excellence

Innovative design pursuing maximum performance

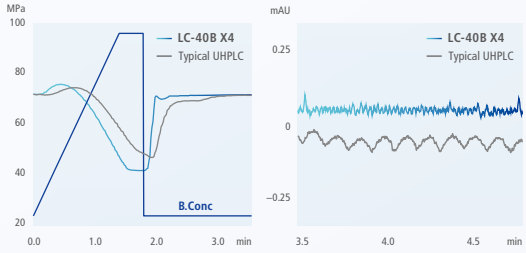
Exhibiting Maximum Performance while Maintaining Instrument Robustness

Nexera X4 systems incorporate proprietary Nexflow technology that minimizes extra-column band broadening without changing the tube's internal diameter or length. By reducing the risk of blockages and minimizing peak broadening, the Nexera X4 delivers outstanding separation performance.



Solvent Delivery Unit Achieves High-Speed High-Precision Gradients

The LC-40B X4 is a binary gradient pump featuring four independently actuated plungers and a pressure feedback mechanism. Independent plunger actuation greatly reduces pump-derived pulsation and improves gradient responsiveness. These advanced fluid control technologies deliver stable baselines for ultra-fast gradients and consistent, reliable performance under high-pressure conditions.

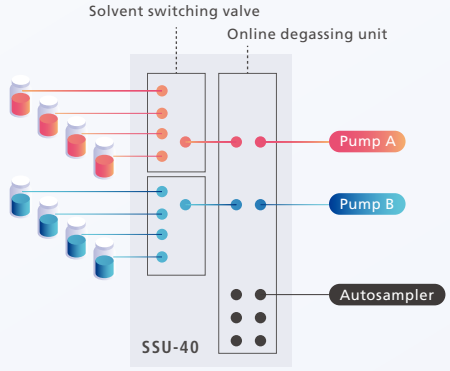


High Responsiveness During Gradient Elution

Reduced Baseline Pulsation

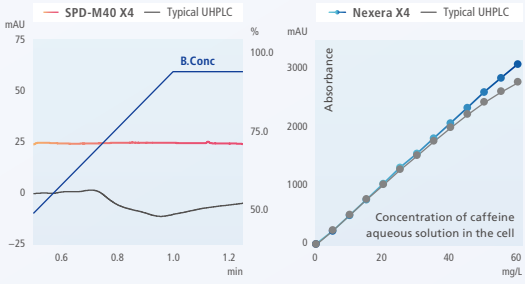
Mobile Phase Switching and Degassing Unit Broadens the Analysis Width

The SSU-40 is a solvent switching and online degassing unit for binary pumps that can switch between up to 4 solutions per pump. Automatic mobile phase switching helps improve the efficiency of method screening.



Newly Designed Low-Dispersion, High-Sensitivity PDA Detector

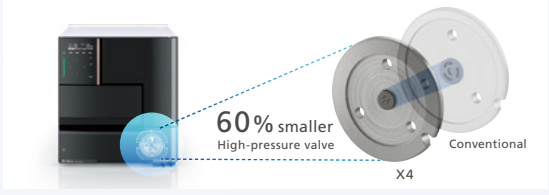
The SPD-M40 X4 is a photodiode array detector that uses a capillary cell to reduce peak broadening. This design minimizes solvent-derived refractive index effects, leading to stable baselines and higher sensitivity. In addition, the broader dynamic range enables analysis of a wider range of low to high-concentration samples.



Improved Baseline Stability

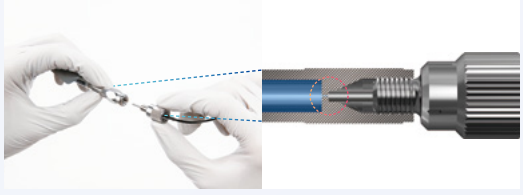
Improved Linearity in High Concentration Area

High-End Autosampler Reduces Peak Broadening and Carryover



The SIL-40C X4 is a high-end autosampler featuring a newly designed low-internal-volume high-pressure valve, low-dispersion injection mode, and high-speed needle internal/external rinsing. These capabilities make the SIL-40C X4 suitable for a wide range of samples, from those with extremely low concentrations that require high sensitivity to samples with high concentrations that require rinsing functionality.

Fitting Achieves Both Ease of Use and Low-Dispersion Performance



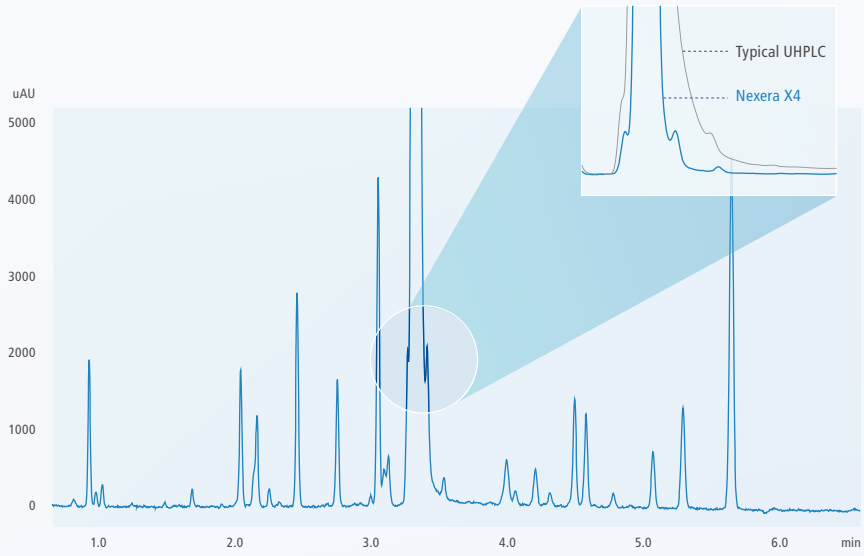
The newly developed “Nexlock™ II” employs an end-surface sealing structure that eliminates ferrules and minimizes dead volume in tubing connections. Its proprietary fitting design also allows tool-free column connections while maintaining high-pressure tolerance.

Ultra-Sharp Peaks

Reduces peak dispersion to achieve excellent chromatographic separation

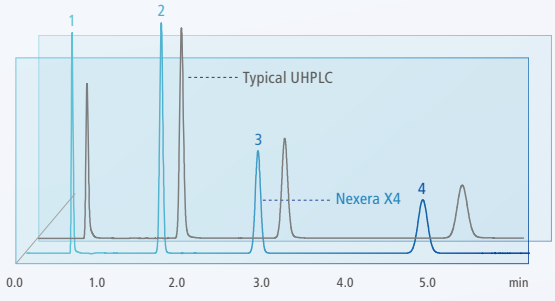
Improves Separation by Minimizing Peak Broadening

The Nexera X4 is equipped with Nexflow technology, which achieves low dispersion without changing the internal diameter of the flow lines, thereby minimizing system-derived peak broadening. This allows the performance of UHPLC columns to be fully utilized, resulting in high separation performance.



Chromatogram of Impurities in a Pharmaceutical Sample

Maximizes Column Performance



Peak	Ratio of theoretical plate numbers (%) Nexera X4 / Typical UHPLC
1	181
2	121
3	108
4	104

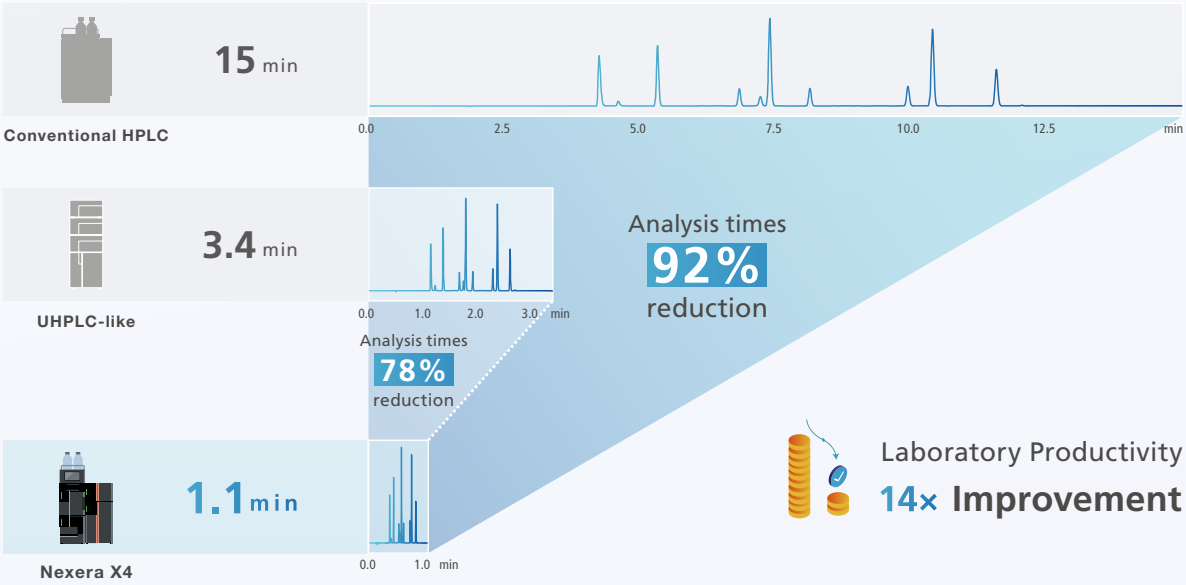
Columns play a critical role in achieving high-speed, high-resolution analysis by minimizing band broadening within the column and delivering superior chromatographic separation. The Nexera X4 enhances column performance by minimizing broadening of sample peaks outside the column. In particular, it improves theoretical plate numbers for weakly retained components in isocratic analysis, where extra-column band broadening tends to be the dominant factor.

Ultra-Fast Analysis

Higher productivity with consistent ultra-fast gradients

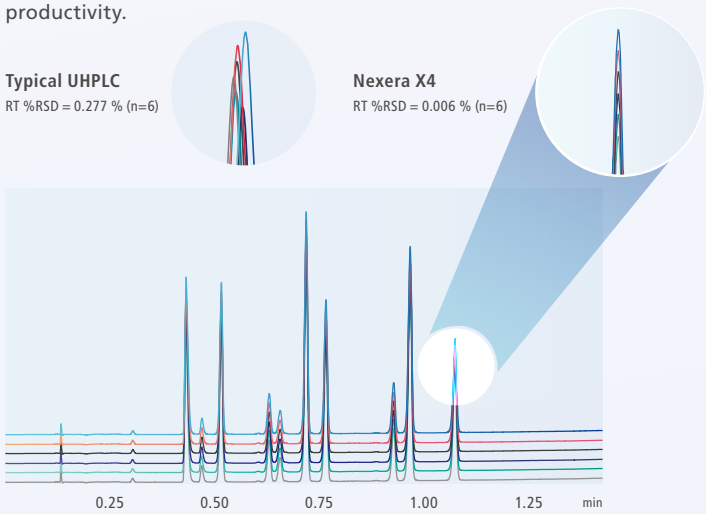
Dramatically Improves Productivity

Four independently actuated plungers and a pressure feedback mechanism significantly improve solvent delivery responsiveness and enable ultra-fast analysis. Analysis times are 92 % and 78 % shorter compared to those achieved with typical HPLC and existing UHPLC-like systems, respectively, resulting in up to 14 times higher laboratory productivity.



Achieves Consistent Analytical Results Even for Ultra-Fast Gradients

The Nexera X4 enables gradient analysis with highly consistent solvent delivery, resulting in excellent retention time reproducibility, even for ultra-fast analysis. The combination of significantly faster speeds and analysis quality equivalent to conventional HPLC dramatically improves productivity.



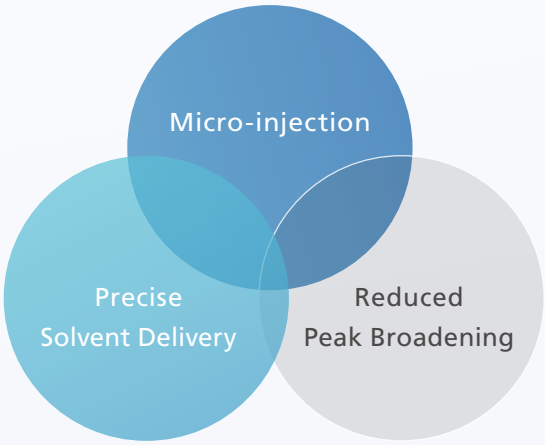
Overlaid Chromatograms from Repeated Analyses (n = 6) of Pharmaceutical Mixed Samples

Ultra-Low Solvent Consumption

In combination with narrow-bore columns, it significantly reduces the quantity of solvent consumed

Provides the Instrument Performance Required for Analytical Miniaturization

Analytical Miniaturization requires precise injection of micro quantities compatible with narrow-bore columns, accurate delivery of mobile phases, and prevention of band broadening within flow channels. The Nexera X4 offers exceptional instrument performance that satisfies all of those requirements, even when using narrow-bore columns.



Micro-injection

Achieve micro-injection for analytical miniaturization with a high-precision measuring pump. Good repeatability is obtained with injection amounts of 1 µL or less.

Precise Solvent Delivery

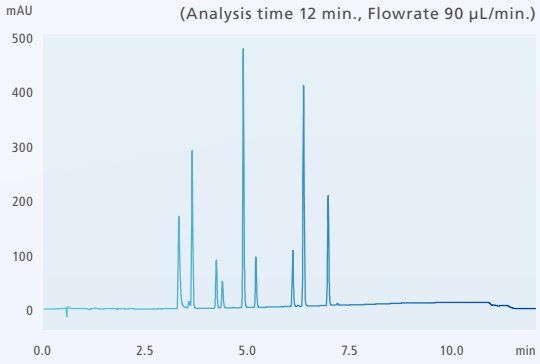
Precise solvent delivery is possible at minute flow rates. The small internal volume makes the system suitable for gradient analysis with narrow-bore columns.

Reduced Peak Broadening

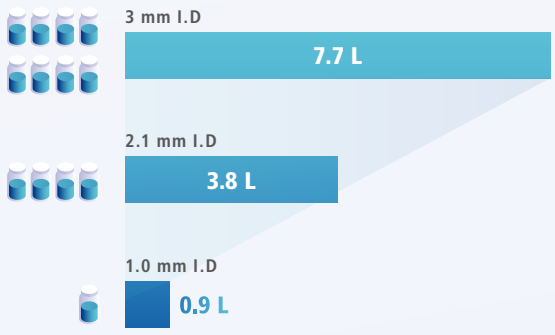
Nexflow technology reduces peak broadening. Separation performance remains excellent even after analytical miniaturization.

Reducing Solvent Consumption with Narrow-Bore Columns

Shimadzu provides narrow-bore columns with a 1-mm internal diameter as part of the Shim-pack Scepter™ series of columns, packed with a fully porous hybrid organosilica base material, and the Shim-pack™ NovaCore series of core-shell columns, also packed with a hybrid organosilica base material. Used in combination with the Nexera X4, these columns enable analytical miniaturization and significantly reduce solvent consumption.



Analysis Results of Pharmaceutical Mixed Samples
using Shim-pack Scepter C18 1.0 mm ID Columns



Comparison of Solvent Consumption
at 800 Analyses Per Month

Best Partner for Mass Spectrometry

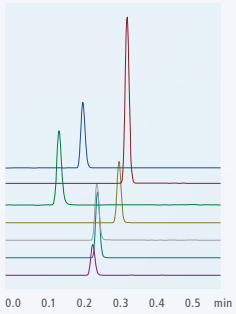
Combinations that Maximize Mass Spectrometer Performance

Nexflow Tubing for MS

The Nexflow Tubing for MS is a dedicated tubing kit for Nexera X4 systems that reduces peak broadening between the column outlet and MS interface. By fully leveraging the ultra-fast and high-separation performance of the Nexera X4, the kit maximizes mass spectrometer performance.

Combining Nexera X4 and LCMS-8060 Series Systems for High-Speed and High-Sensitivity Analysis

The triple quad LCMS-8060 series achieves positive and negative ionization switching in just 5 msec with UFswitching™ technology. Suppressing ion intensity loss, even during ultra-fast switching, enables users to consistently obtain stable, high-sensitivity data. The combination of an LCMS-8060 system with the Nexera X4, which achieves excellent gradient control performance, results in a next-generation LCMS platform that delivers unmatched throughput and reliability.



Compound	Polarity	Retention time		Area	
		Mean value (min)	%RSD	Mean value	%RSD
1'-Hydroxy Bufuralol	+	0.214	0.14	2485474	2.37
Oxidized Nifedipine	+	0.337	0.11	6510872	2.82
Acetaminophen	+	0.146	0.10	708714	2.87
4'-hydroxydiclofenac	+	0.315	0.11	399563	4.22
1-hydroxymidazolam	+	0.251	0.20	2066492	3.15
Hydroxy Tolbutamide	–	0.254	0.20	445907	4.14
7-Hydroxycoumarin	–	0.240	0.10	64490	4.90

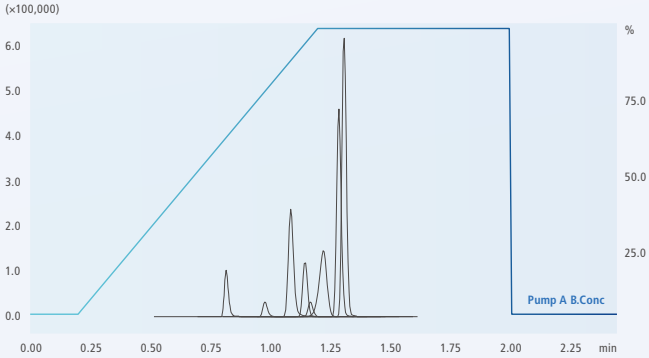
Improved Efficiency of Pharmacokinetic Analysis

Pharmacokinetic research demands fast, reliable analysis to keep pace with large sample volumes. Using the Nexera X4 in combination with the LCMS-8060RX, eight anticoagulants were analyzed with outstanding accuracy and precision, even with straightforward protein precipitation sample preparation. With a total analysis time of just 2.45 minutes, including column equilibration, this solution enables true high-throughput pharmacokinetic workflows.

High-Speed Analysis of Anticoagulants in Plasma

	Accuracy (%)	Precision (%CV)
	LLOQ (10 µg/L)	LLOQ (10 µg/L)
8 targets	96-109	3-14
Criteria	80-120	20
Result	Pass	Pass

n=6



Enhanced Workflow Efficiency

Unique Solutions that Improve Workflow Efficiency and Drive Productivity

Maintaining Analysis Robustness

Analytical Intelligence

The Nexera X4 offer three key functionalities to maintain analytical robustness. During startup, the system checks the status of the check valve and autosampler, preventing analysis if any issues are detected. It also safeguards data quality by stabilizing flow and protecting against column degradation. Additionally, the system continuously monitors operations during analyses, automatically restoring functionality and minimizing downtime in case of problems.

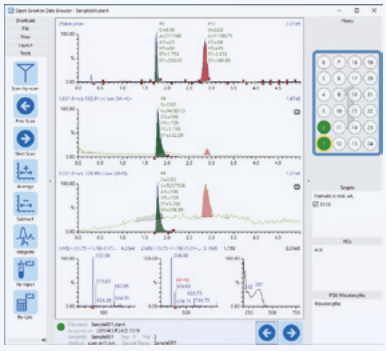
ANALYTICAL INTELLIGENCE

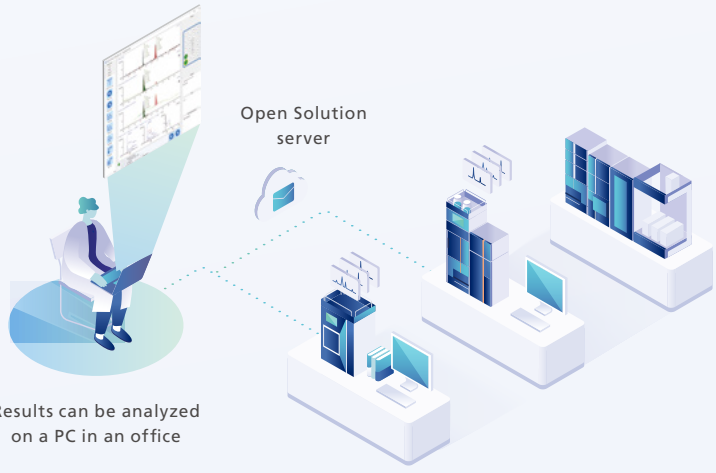
- Automated support functions utilizing digital technologies, such as M2M, IoT, and Artificial Intelligence (AI), that enable higher productivity and maximum reliability.
- Allows a system to monitor and diagnose itself, handle any issues during data acquisition without user input, and automatically behave as if it were operated by an expert.
- Supports the acquisition of high quality, reproducible data regardless of an operator's skill level for both routine and demanding applications.

Maximizing Laboratory Productivity

Open Solution

Open Solution





Open Solution software provides a platform for efficiently sharing an instrument among multiple operators. By combining this software with the powerful analysis capabilities of the Nexera X4, it is possible to reduce the number of analytical instruments needed in a laboratory, and to handle the analyses of multiple operators with a single high-throughput instrument, maximizing productivity while reducing costs.

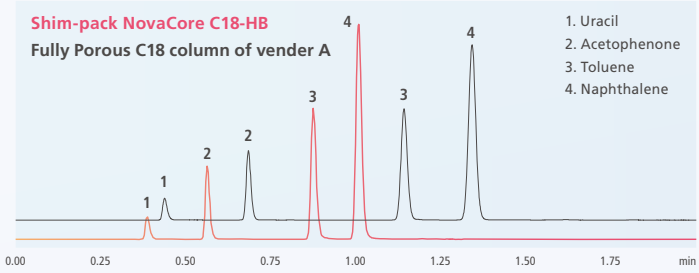
Superficially Porous Organic Silica Hybrid Column

Shim-pack NovaCore C18 Series (Particle Size < 3 µm)

A core-shell column featuring an organic silica hybrid base material. Combining the sharp peaks unique to core-shell technology with broad pH tolerance for compatibility under basic conditions, it delivers exceptional performance for fast analysis of pharmaceuticals containing basic compounds.

	C18-HB
Chemistry	
Bonded Phase	Octadecyl groups
Pore Size	10 nm
Surface Area	200 m^2/g
Carbon Loading	11%
Endcapping	○
Column Hardware	Stainless (SUS)
Usable pH Range	1–12
Common Temperature	20 – 40 °C
Maximum Temperature	60 °C*

* The upper temperature limit is 60 °C, but using it at conditions where the pH of the mobile phase exceeds 8 at 60 °C will accelerate the degradation rate of the column.



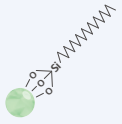
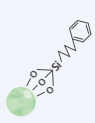
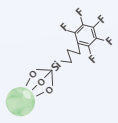
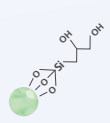
Comparison of Shim-pack NovaCore C18-HB (Core-Shell Column) and Other Companies' Fully Porous C18 Column

Column: Shim-pack NovaCore C18-HB (100 mm ×2.1 mm I.D., 1.7 µm)
Fully Porous C18 Column (100 mm ×2.1 mm I.D., 1.7 µm)
Mobile phase: Acetonitrile/Water=70/30 (v/v)

Fully Porous Hybrid Particle Based Column Series

Shim-pack Scepter Series

Fully porous columns featuring an organic silica hybrid material. With different chemistry characteristics, Shim-pack Scepter columns are effective for method development/scouting with suitability for use in a wide variety of applications. In addition to 1.9 µm particles optimized for UHPLC analysis, the lineup includes 1 mm I.D. columns that are effective for solvent-saving analysis.

	Reversed Phase							HILIC
	C18-120	C18-300	HD-C18	C8-120	C4-300	Phenyl	PFPP	Diol-HILIC
Chemistry								
Bonded Phase	Octadecyl groups		Octadecyl groups (High Density type)	Octyl groups	Butyl groups	Phenylbutyl groups	Pentaflorophenyl propyl groups	Dihydroxypropyl groups
Particle	Organic Silica Hybrid							
Particle Size (µm)	1.9, 3, 5							
Pore Size (nm)	12	30	8	12	30	12		
End Capping	Proprietary						None	
pH Range	1 – 12				1 – 10		1 – 8	2 – 10
100 % Aqueous Condition	Yes	Yes	No	No	Yes	Yes	Yes	N/A
USP Code	L1		L1	L7	L26	L11	L43	L20

Shimadzu Corporation

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