



THE RESULT IS...



Unique new HPLC columns & automated column selectors which, if used together, empower you to develop virtually any HPLC method.



Synergi™ Method Development Concept

non-polar

Sample polarity range

polar



SYNERGI™ MAX-RP

A C12 BONDED PHASE WITH TMS ENDCAPPING

for method development of virtually all compound types:
polar or non-polar, acids and bases, at any pH

benefits

- one universal, all-purpose reversed phase method development column
- can function like your best high-performance C8 and C18 column
- improves basic compound peak shape even at pH 7.0
- unique 4 μ , 80Å silica gel gives higher efficiencies than 5 μ columns and lower backpressure compared to 3 μ high-performance C8 and C18 columns



SYNERGI™ POLAR-RP

AN ETHER-LINKED PHENYL PHASE WITH POLAR ENDCAPPING

for method development of highly polar analytes or mixtures
not retained or separated on Synergi Max-RP
or conventional alkyl-bonded phases

benefits

- an all-purpose polar-embedded reversed phase column
- gives longer retention for highly polar compounds
- provides unmatched selectivity for aromatic pharmaceuticals
- unique ether-linkage improves acid and base peak shape unlike competing amide-linked C18 and conventional polar-embedded phases

SYNERGI™ COLUMN SELECTOR

for use with Synergi Max-RP and Polar-RP to:

- develop and validate HPLC methods
- screen and select the best HPLC column dimension and bonded-phase
- optimize older HPLC methods

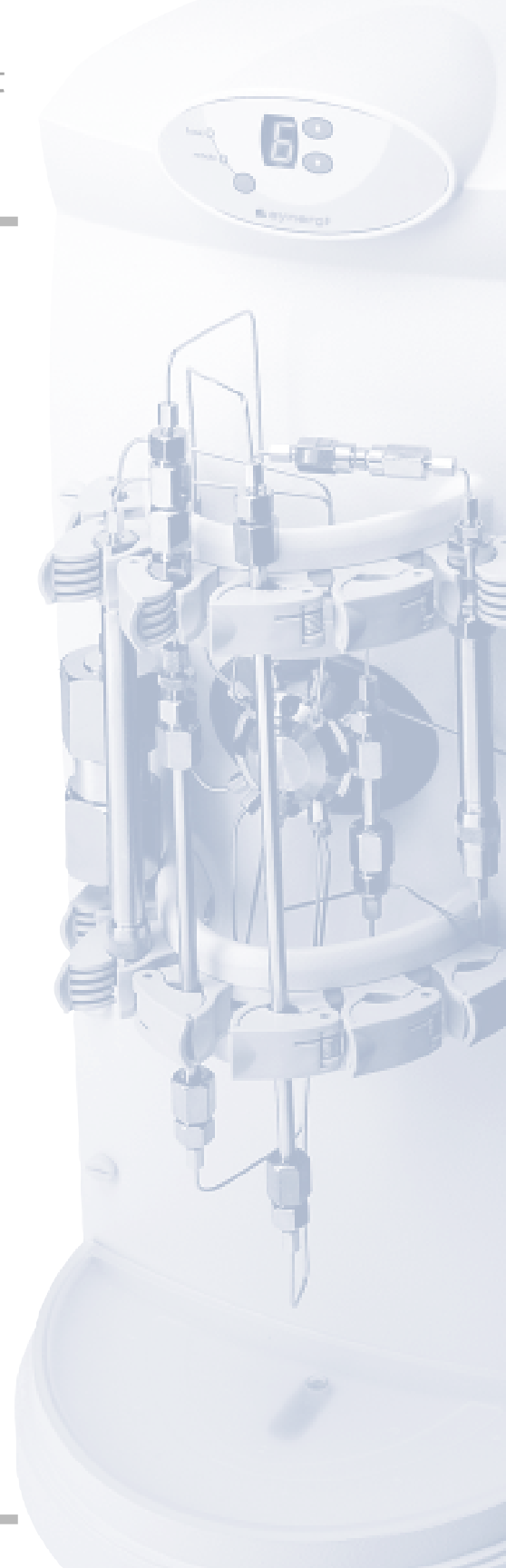




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A new silica

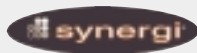
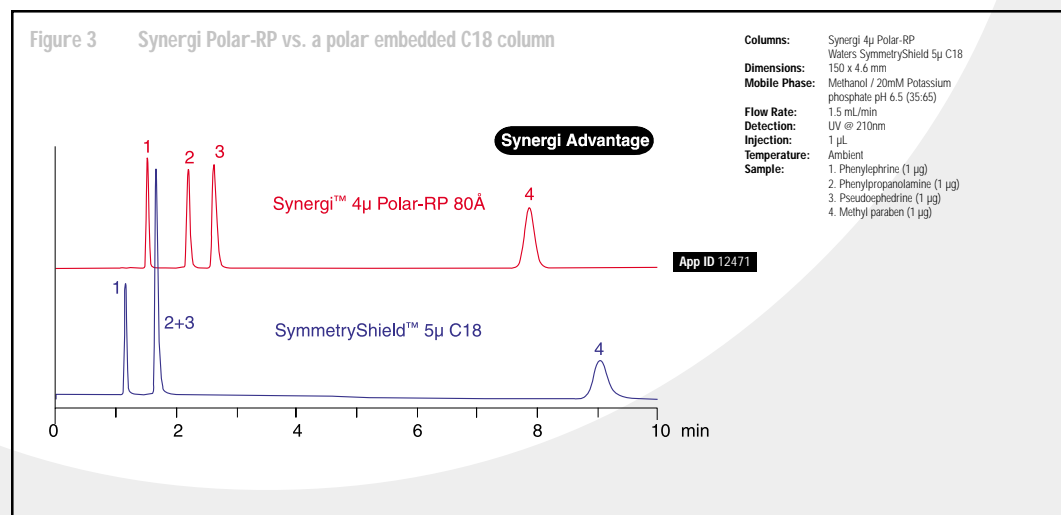
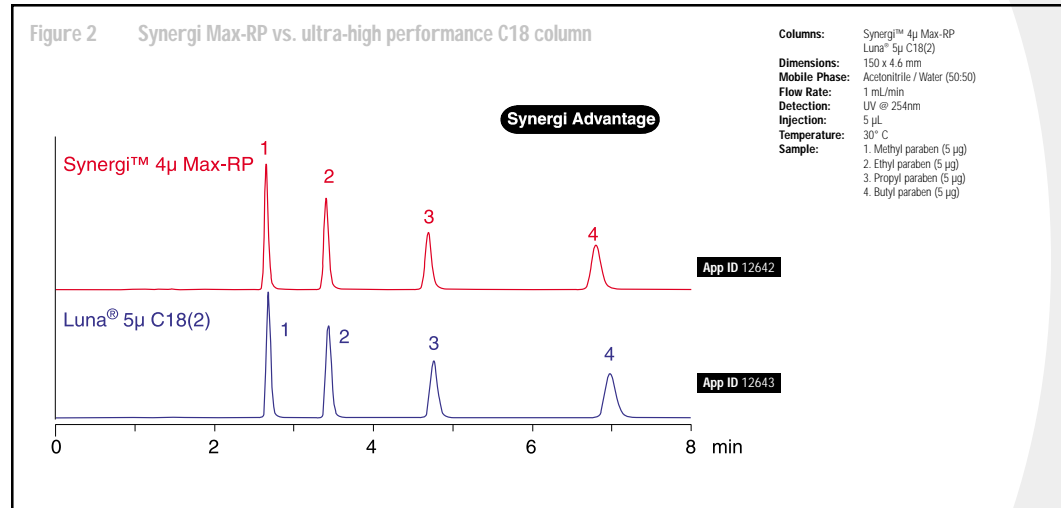
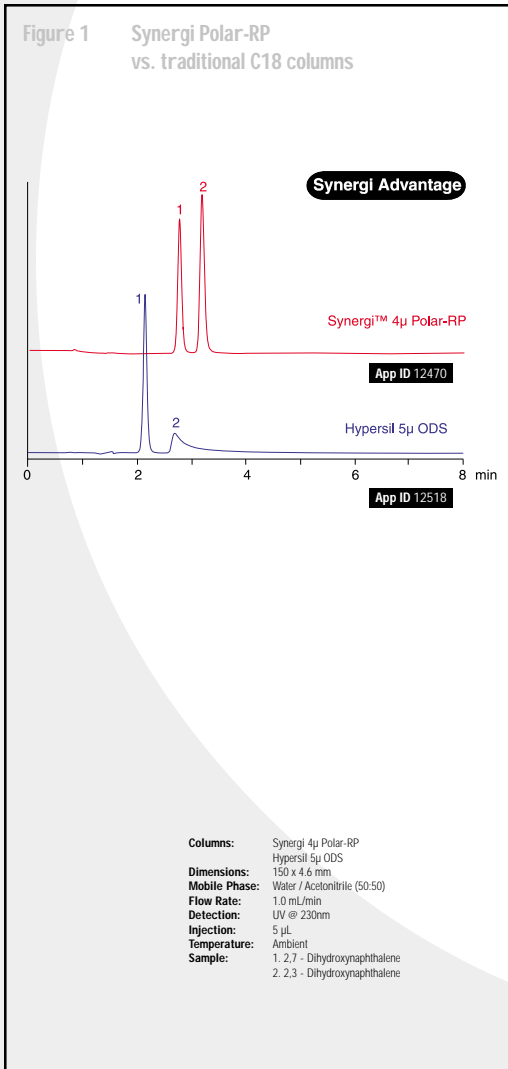
1 ULTRA-HIGH PURITY, TYPE-B BASE-DEACTIVATED SILICA

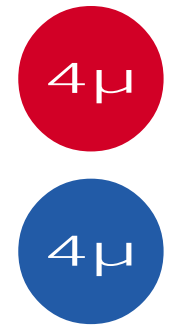
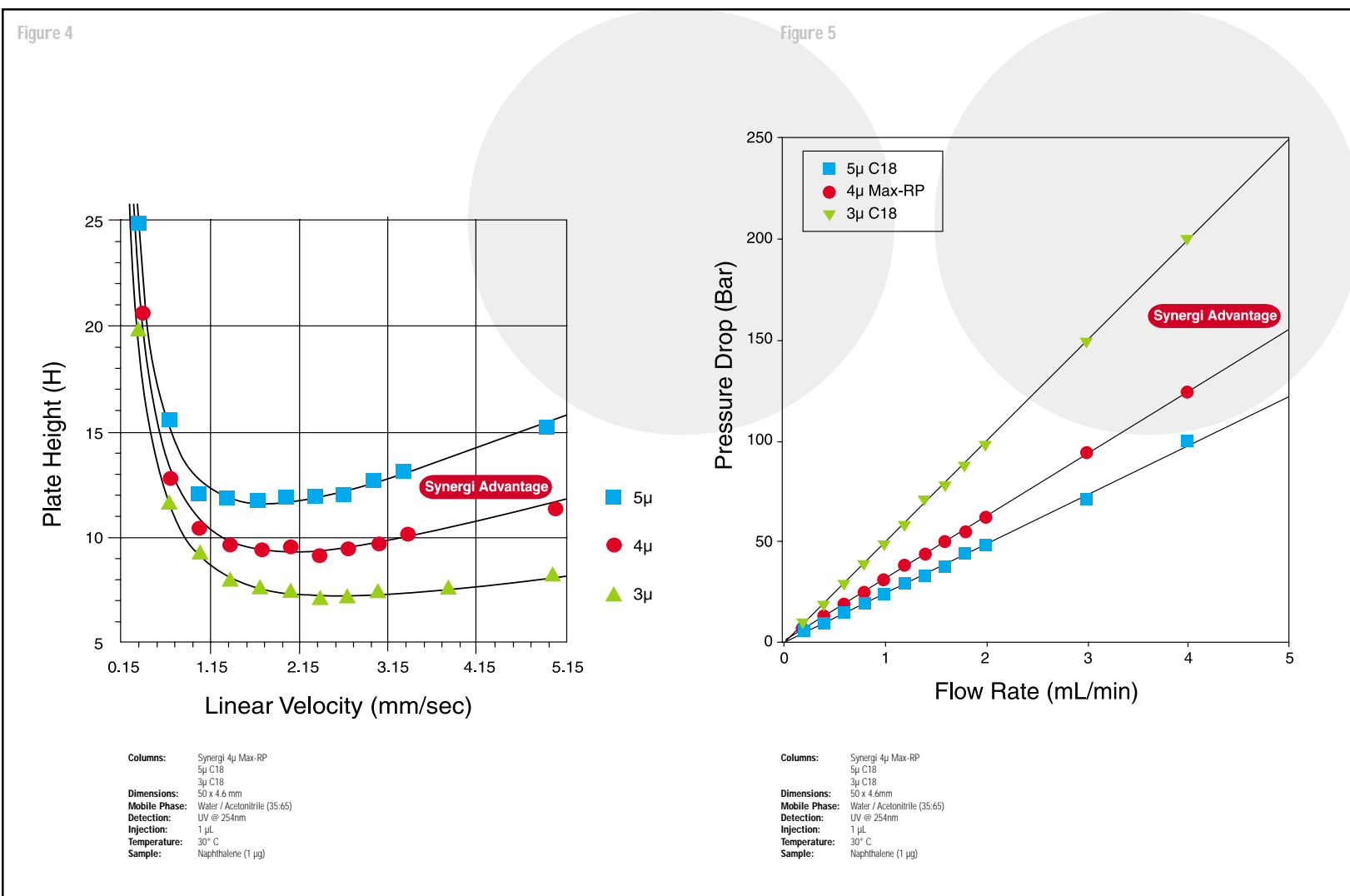
Synergi is based on a new 80Å ultra-high purity (>99.99% metal-free), base-deactivated, type-B silica which ensures minimal surface metal sites available for chelation and reduced silanol acidity even at neutral pH. The high metal content of older-generation, type-A silicas can result in poor recovery or adsorption of certain analytes due to chelation (Figure 1), and can contribute to peak tailing of basic compounds.

2 80 Å PORE SIZE FOR HIGH SURFACE AREA

The extreme [~500m²/g] surface area of Synergi 4µ silica results from a unique 80Å pore geometry. This high surface area compensates for the short C12-alkyl chains of Synergi 4µ Max-RP, resulting in a phase with hydrophobic retention and methylene selectivity of conventional C18 columns (Figure 2).

The high surface area also compensates for the reduced hydrophobicity of Synergi 4µ Polar-RP, allowing it to retain both hydrophobic and hydrophilic analytes through non-polar and polar interactions, respectively (Figure 3).



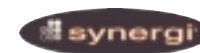
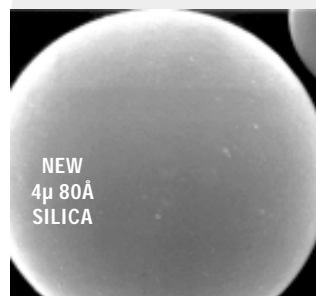


3 HIGH-EFFICIENCY 4µ SILICA PARTICLES

Synergi 4µ Max-RP and Synergi 4µ Polar-RP columns are bonded to a unique, 4µ silica. As can be expected, the particle size used generates columns with efficiencies intermediate to typical 3 or 5µ packed columns (Figure 4). However, pressure drops with Synergi 4µ Max-RP and Synergi 4µ Polar-RP are similar to those obtained with columns packed with 5µ particles (Figure 5).

4 SYNERGI SILICA CHARACTERISTICS

Particle Size (µ)	Particle Size Distribution	Surface Area (m ² /g)	Pore Size (Å)	Pore Volume (mL/g)	Metal Content (ppm)
4.00 ± 0.10	1.80	475 ± 25	80 ± 10	1.00 ± 0.05	< 55





A unique new C12 bonded phase

WHY A C12 PHASE?

PROBLEM

Our goal was to develop a column that had the retention characteristics and methylene selectivity of a C18, but with better protection of residual silanols. Conventional C18 columns have the hydrophobic selectivity chromatographers depend on for reversed-phase separations. However, the bulky nature of the C18-silanes used in bonding results in relatively low coverage of surface silanols, a factor that can contribute to peak tailing for basic analytes (Figure 6).

SOLUTION

The use of less sterically-hindered C8 silanes does result in better surface coverage as compared to C18 silanes, but often does not provide the necessary retention and methylene selectivity to separate analytes based upon subtle differences in hydrophobicity. Thus, we engineered a C12 ligand which is sterically less hindered than C18 silanes (25% higher surface coverage for C12) and, when combined with our extreme surface area silica, gives the retention and selectivity that you would expect from a C18 column (Figure 7).

RESULTS

The end result is Synergi 4µ Max-RP, a column with the selectivity of conventional C18 columns, but with improved peak shape for basic analytes due to better coverage of surface silanols (Figure 8).

Figure 6
compound interacts with silanols
result=peak tailing

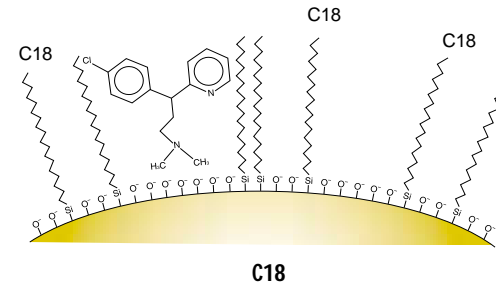
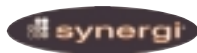
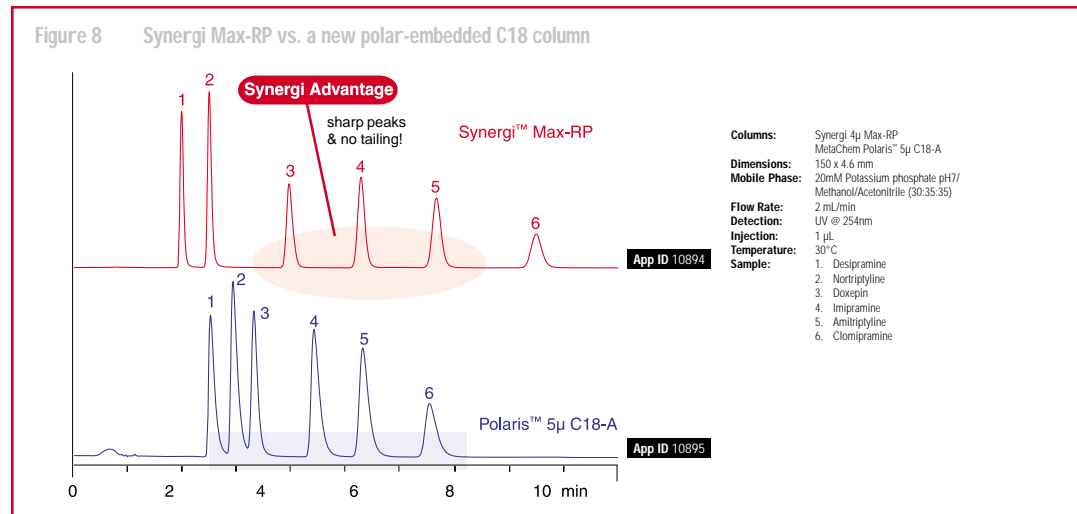
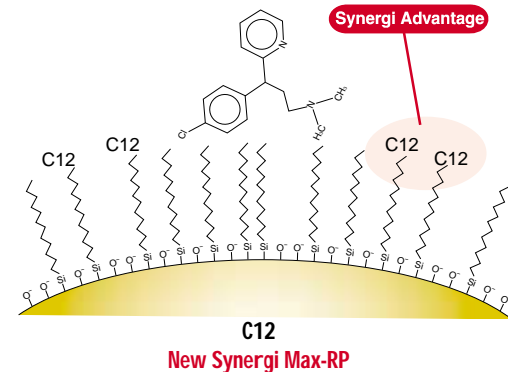


Figure 7
less silanol interaction
result=better peak shape



A better column for basic drugs

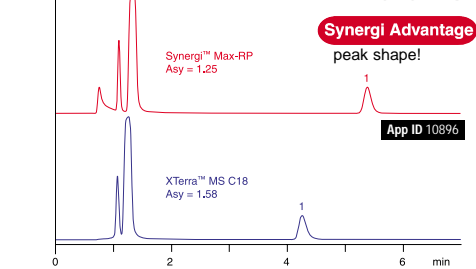


IMPROVED PEAK SHAPE

Analysis of basic drugs continues to pose a problem for many chromatographers. HPLC column manufacturers often suggest using low pH buffered-mobile phases for analyzing basic compounds. The reason for this is three-fold: first, to insure that the pH of the mobile phase is at least 1 pH unit from the pKa of the analyte; second, to protect their silica from dissolution at alkaline pH and third, to improve peak shape by reducing silanol ionization and therefore, silanol interaction with basic moieties on sample molecules. However, because the residual silanols of Synergi 4 μ Max-RP are so well-protected from interaction, analysis of basic analytes at neutral

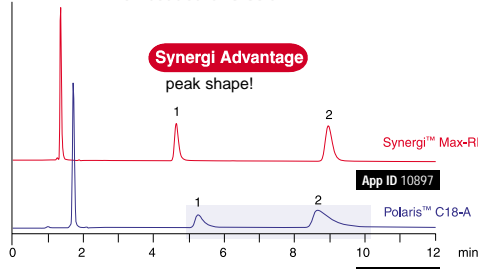
pH can be both robust and reproducible. The advantage of performing analyses under neutral pH conditions (as opposed to low pH conditions) is that basic compounds will be less ionized and therefore, more retained on reversed-phase stationary phases. This can be crucial in isocratic analyses of mixtures that contain weakly-retained basic analytes as well as more strongly retained molecules. As shown in Figures 9-12, basic pharmaceutical products can be routinely and easily chromatographed using simple buffered mobile phases at neutral pH on Synergi 4 μ Max-RP.

Figure 10 Synergi Max-RP vs. new 'hybrid' WATERS XTerra™ MS



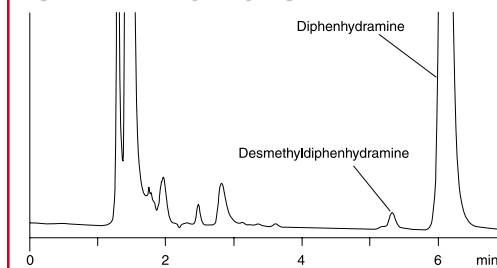
Columns: Synergi 4 μ Max-RP
Waters XTerra 5 μ MS C18
Dimensions: 150 x 4.6 mm
Mobile Phase: 20mM Potassium phosphate pH 7 / Acetonitrile / Methanol (50:25:25)
Flow Rate: 1.5 mL/min
Detection: UV @ 210nm
Injection: 1 μ L
Temperature: 30° C
Sample: Methanol extract from Chlortrimeton Allergy
1. Chlorpheniramine

Figure 11 Synergi Max-RP vs. a new polar-embedded C18 column



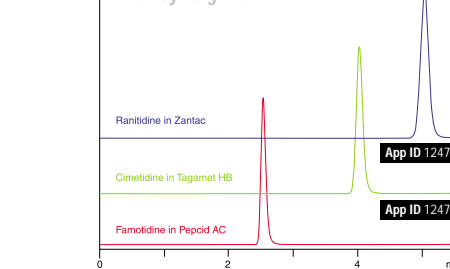
Columns: Synergi 4 μ Max-RP
MetaChem Polaris™ 5 μ C18-A
Dimensions: 150 x 4.6 mm
Mobile Phase: 20mM Potassium phosphate pH 7 / Acetonitrile / Methanol (65:10:25)
Flow Rate: 1.0 mL/min
Detection: UV @ 210nm
Injection: 1 μ L
Temperature: 30° C
Sample: 10-fold dilution of Opcon-A
1. Naphazoline
2. Pheniramine (Bausch and Lomb)

Figure 9 Benadryl on Synergi Max-RP



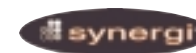
Column: Synergi 4 μ Max-RP
Dimensions: 150 x 4.6 mm
Order No.: 00F-4337-ED
Mobile Phase: 20mM Potassium phosphate pH 7 / Acetonitrile / Methanol (30:40:30)
Flow Rate: 1.0 mL/min
Detection: UV @ 210nm
Injection: 10 μ L
Temperature: Ambient
Sample: Methanol extract of Benadryl Allergy Chewables (Parke-Davis)
1. Desmethyldiphenhydramine
2. Diphenhydramine (Peak A_s = 1.4)

Figure 12 Ranitidine, Cimetidine, Famotidine on Synergi Max-RP



Columns: Synergi 4 μ Max-RP
Dimensions: 150 x 4.6 mm
Order No.: 00F-4337-ED
Mobile Phase: 20mM Potassium phosphate, pH 7 / Methanol (60:40)
Flow Rate: 1.0 mL/min
Detection: UV @ 220 nm
Injection: 1 μ L
Temperature: 30° C
Sample: Sample prepared according to USP #24
1. Famotidine in Pepcid AC
2. Cimetidine in Tagamet HB

3. Ranitidine in Zantac

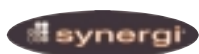
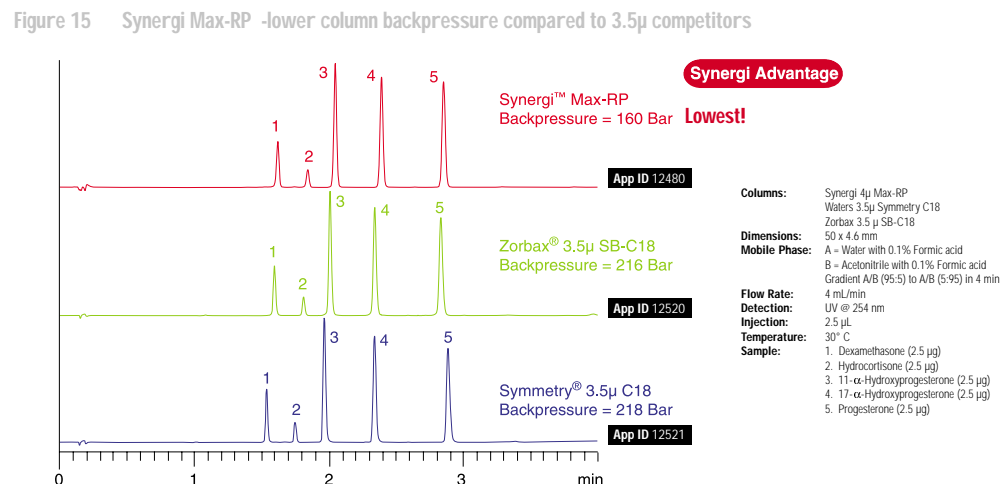
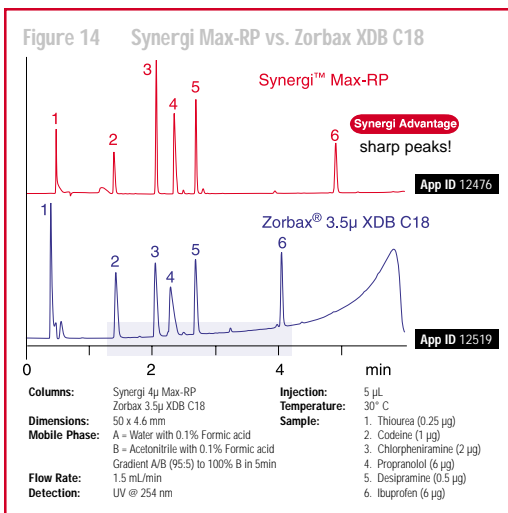
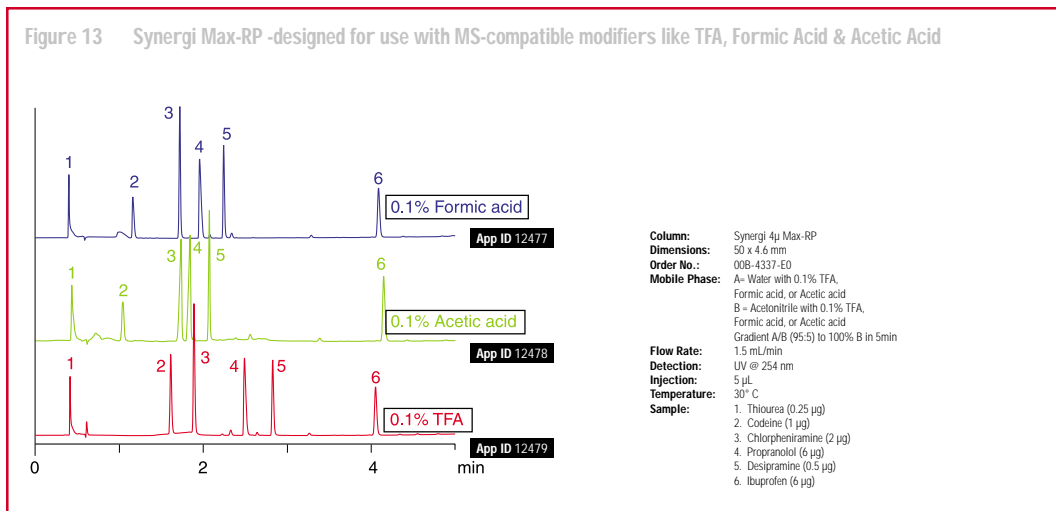




The ideal column for LC/MS

LC/MS COMPATIBLE

Synergi 4µ Max-RP may be the ideal column for LC/MS applications. Synergi 4µ, ultra-high purity silica gives excellent efficiency and peak shape for basic analytes and is intended to be used with a wide variety of MS-compatible mobile phase modifiers such as TFA, formic acid, or acetic acid (Figure 13). Despite the fact that Synergi Max-RP is based on a 4µ silica, it often gives efficiencies and peak shapes equivalent or superior to that of 3.5µ-particle size competitor HPLC columns (Figure 14) at significantly lower backpressures (Figure 15). As shown in the stability data (Figures 17-18), Synergi Max-RP is extremely stable using either low or high pH running conditions, including 0.1% TFA. The highly reproducible retention times (over 18,000 column volumes at pH 1.5!) indicates that little or no phase is hydrolyzed at low pH and that Synergi 4µ Max-RP will suffer little, if any, bleed when used under typical LC-MS running conditions.



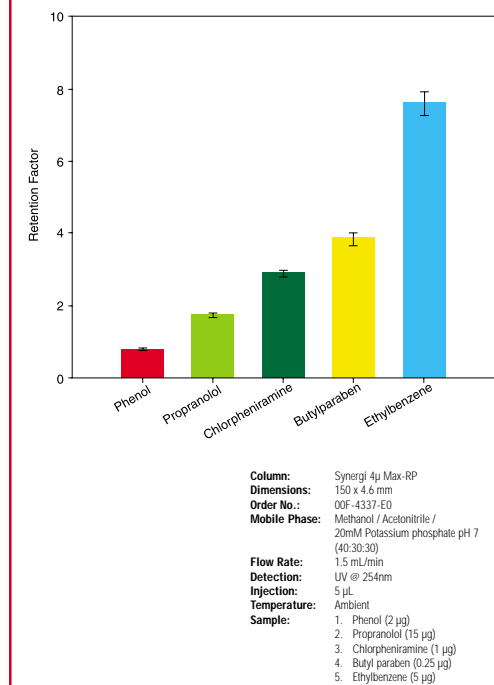
Reproducible performance from pH 1.5-10



REPRODUCIBLE

The high batch-to-batch reproducibility of Synergi 4 μ Max-RP begins with strict control of silica physico-chemical qualities. In addition, our new, proprietary bonding and endcapping procedure results in a surface chemistry that is both robust and reproducible. As shown in Figure 16, Synergi Max-RP can be expected to deliver reproducible, excellent performance batch after batch.

Figure 16 Batch reproducibility of Synergi™ Max-RP



pH STABLE

Our bonding and endcapping procedures give Synergi 4 μ Max-RP pH stability from pH1.5 (0.1% TFA) to as high as pH10 when using organic buffers such as TEA or Ammonium hydroxide (Figures 17-18). This robust pH range ensures that there will be little bleed at low pH due to silane cleavage and that a broad range of mobile phases can be used without damaging the column. It also allows analysts to use high pH to overcome basic ionization and to overcome sample solubility issues.

Figure 17 stability @ pH1.5

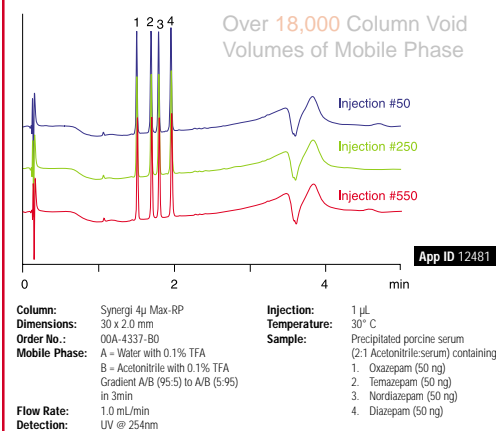
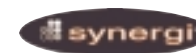
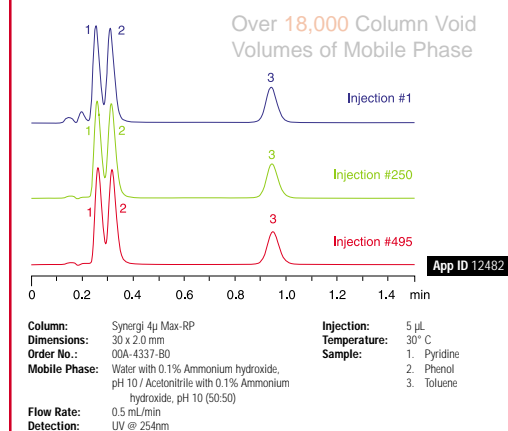
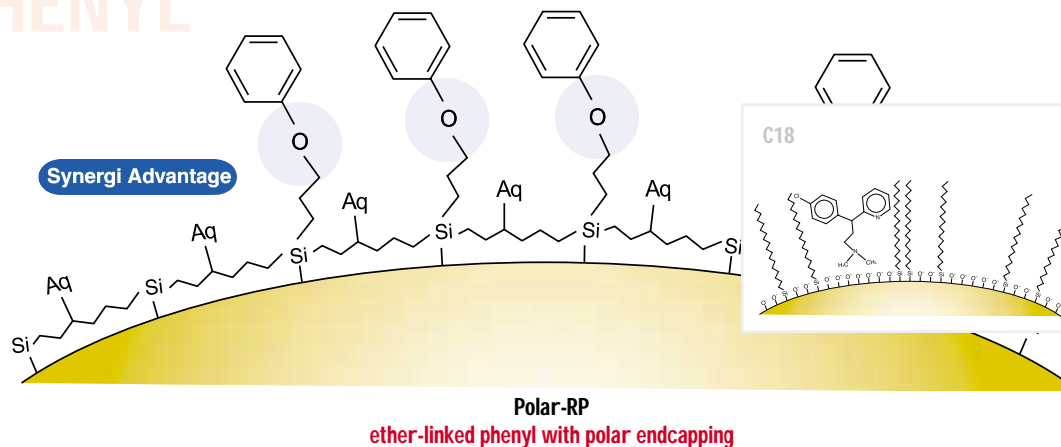


Figure 18 stability @ pH10



A polar phase for polar compounds

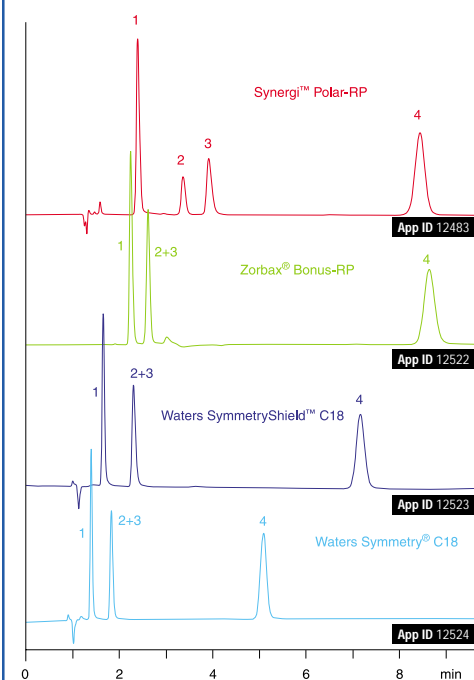
ETHER-LINKED PHENYL WITH POLAR ENDCAPPING



WHAT IS SYNERGI™ 4μ POLAR-RP?

Synergi 4μ Polar-RP is an ether-linked phenyl phase with proprietary hydrophilic endcapping designed specifically to maximize retention and selectivity for polar, aromatic analytes that are so often encountered in the pharmaceutical industry. Due to its unique bonding chemistry, Synergi 4μ Polar-RP column displays a polar selectivity that complements the more conventional selectivity of our Synergi 4μ Max-RP column. (Figures 19-24)

Figure 19 Extreme polar selectivity of Synergi Polar-RP



Columns: Synergi 4μ Polar-RP
Waters 5μ Symmetry C18
Waters 5μ SymmetryShield C18
Zorbax 5μ Bonus-RP

Dimensions: 150 x 4.6 mm

Mobile Phase: 20mM Ammonium formate pH 3.5 / Methanol (70:30)

Flow Rate: 1.5 mL/min

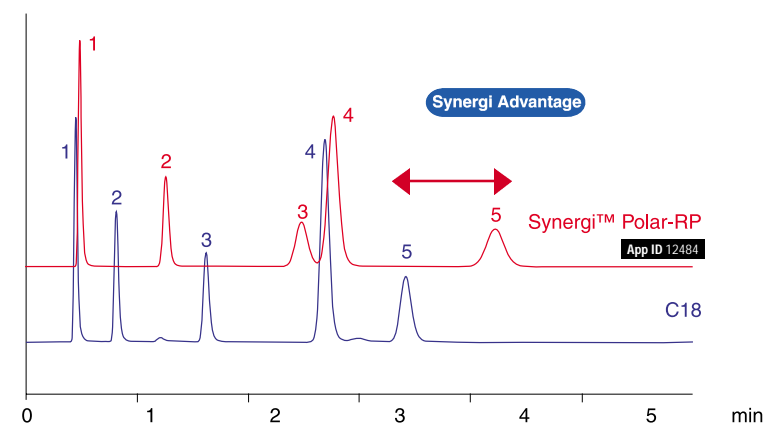
Detection: UV @ 210 nm

Injection: 1 μL

Temperature: Ambient

Sample: 1. Phenylpropanolamine (0.5 μg)
2. (D) Amphetamine (0.16 μg)
3. Methamphetamine (0.16 μg)
4. Guafenesin (0.8 μg)

Figure 20 Longer polar compound retention on Synergi Polar-RP



Columns: Synergi 4μ Polar-RP
Typical C18 3μ

Dimensions: 50 x 4.6mm

Mobile Phase: Water with 0.1% Formic acid / Methanol with 0.1% Formic acid (60:40)

Flow Rate: 1.5 mL/min

Detection: UV @ 254 nm

Injection: 1 μL

Temperature: 30 °C

Sample: 1. Thiourea
2. Caffeine
3. Phenol
4. Acetophenone
5. Dimethylphthalate

Enhanced selectivity for polar analytes

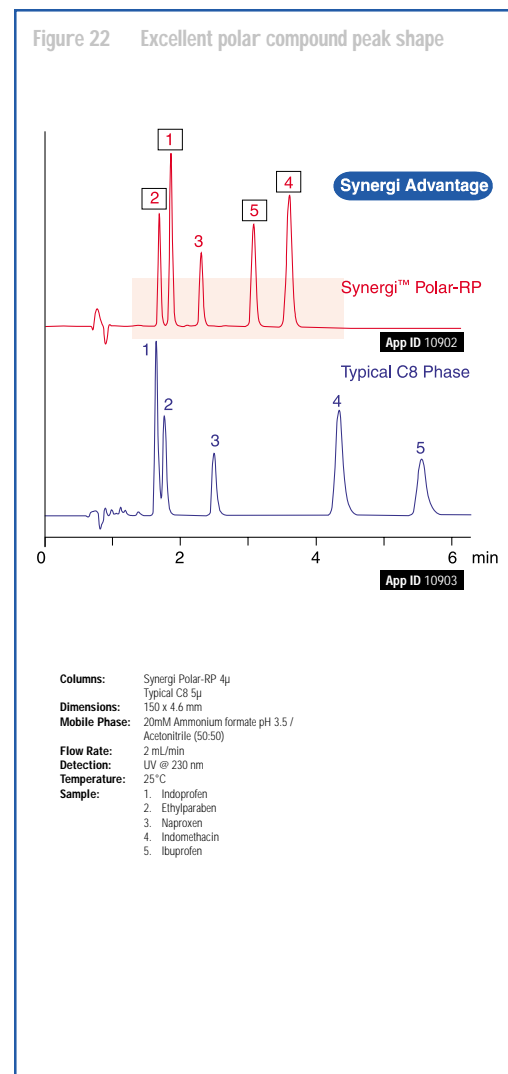
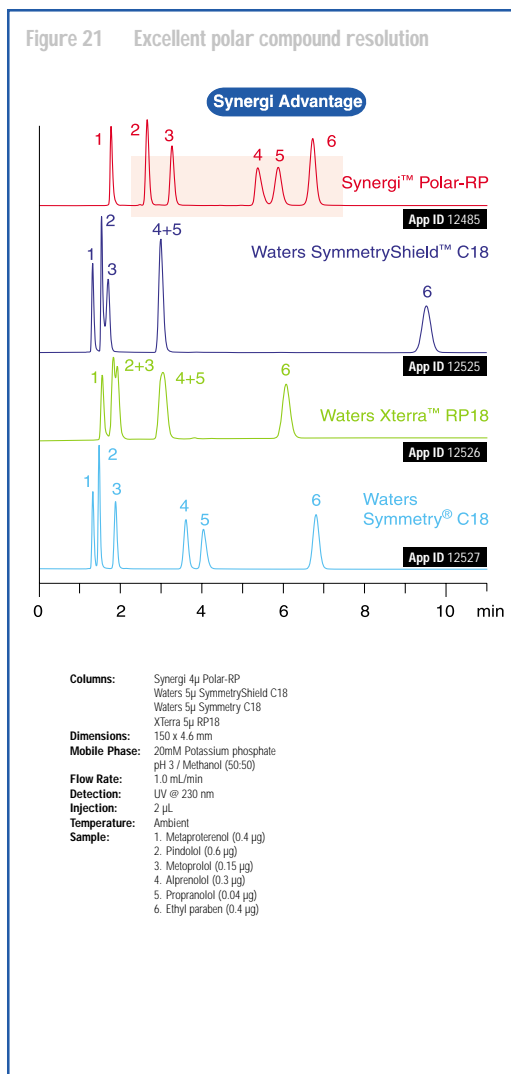
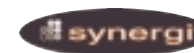
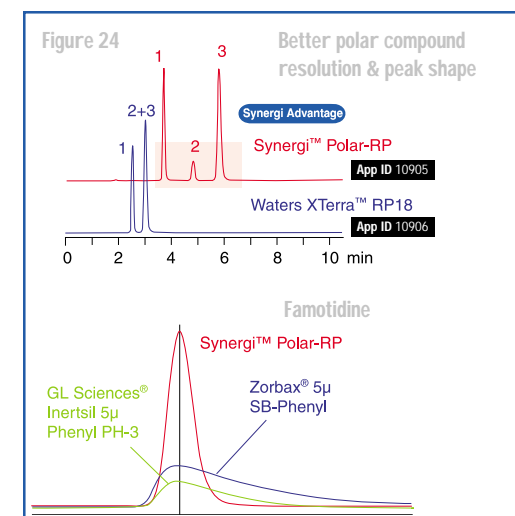
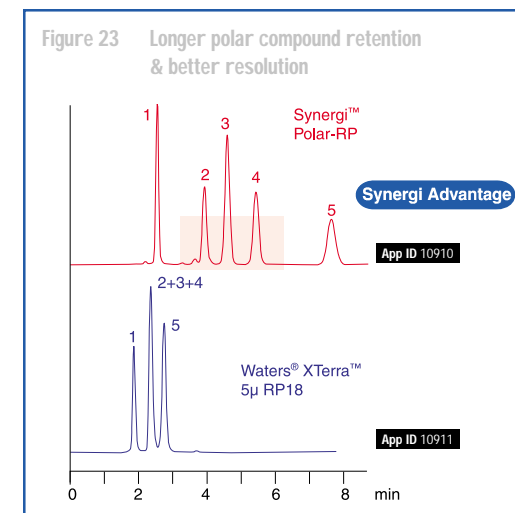


FIGURE 23

Columns: Synergi 4µ Polar-RP, Waters Xterra RP18 5µ
Dimensions: 150 x 4.6 mm
Mobile Phase: 20mM Ammonium formate pH3.5/Methanol (65:35)
Flow Rate: 1mL/min
Detection: UV @ 254 nm
Temperature: 25°C
Sample: 1. Cafadovol, 2. Cafachlor, 3. Cephalixin, 4. Cephradine, 5. Cefazolin

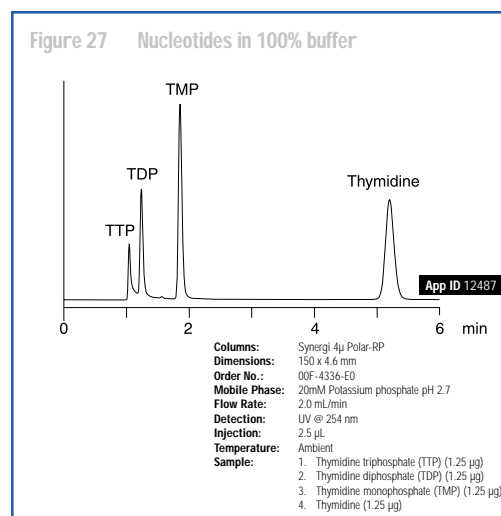
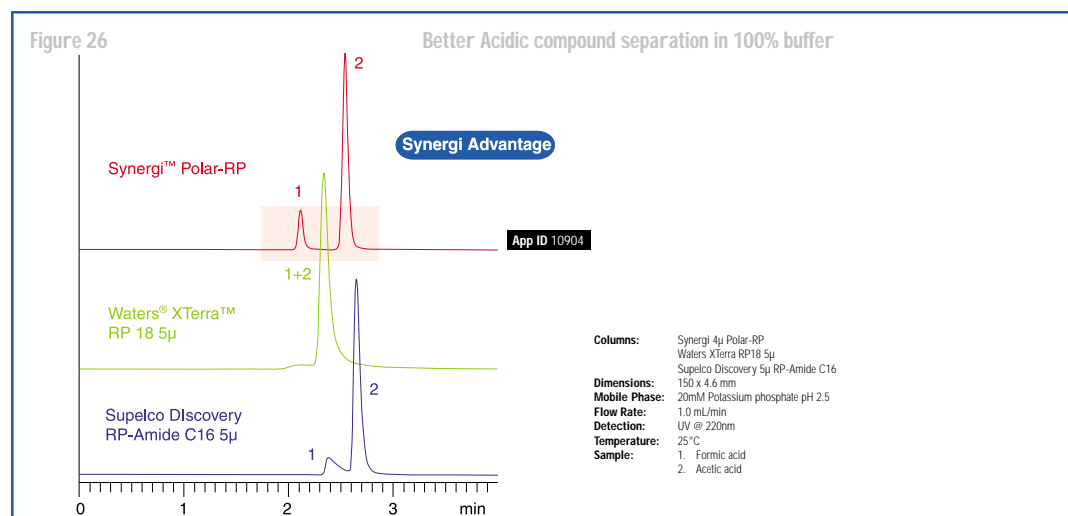
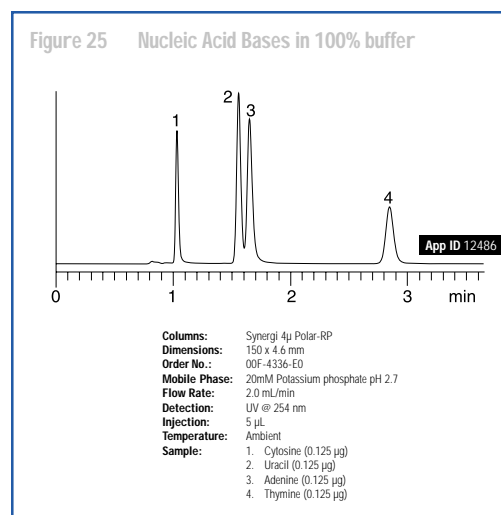
FIGURE 24

Columns: Synergi 4µ Polar-RP, Zorbax 5µ SB-Phenyl, Inertsil 5µ Phenyl PH-3, Compeltor Polar-Embedded C18 5µ
Dimensions: 150 x 4.6 mm
Mobile Phase: 20mM Potassium phosphate pH7.0/Acetonitrile (80:20)
Flow Rate: 1mL/min
Detection: UV @ 254 nm
Temperature: 25°C
Sample: 1. Famotidine, 2. Cimetidine, 3. Ranitidine



STABLE IN 100% BUFFER

The ether-linkage on the Synergi 4 μ Polar-RP phase contributes not only to improved peak shapes for acidic and basic analytes, but also gives high aqueous mobile phase stability (Figures 25-27). Very polar analytes, such as organic acids like formic acid, are typically poorly retained on alkyl-bonded phases. However, using highly aqueous mobile phases, in this case 100% buffer, an assay for identifying formic acid as an impurity in acetic acid was developed (Figure 26). Other polar-embedded phases typically use a nitrogen-containing amide linkage or carbamate group. This embedded basic group can interfere with the resolution of highly acidic, polar compounds. However, since Synergi 4 μ Polar-RP uses an ether-linkage as the polar-embedded group, the result is improved peak shape and separation of highly acidic, polar analytes, such as formic acid.

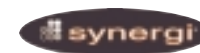
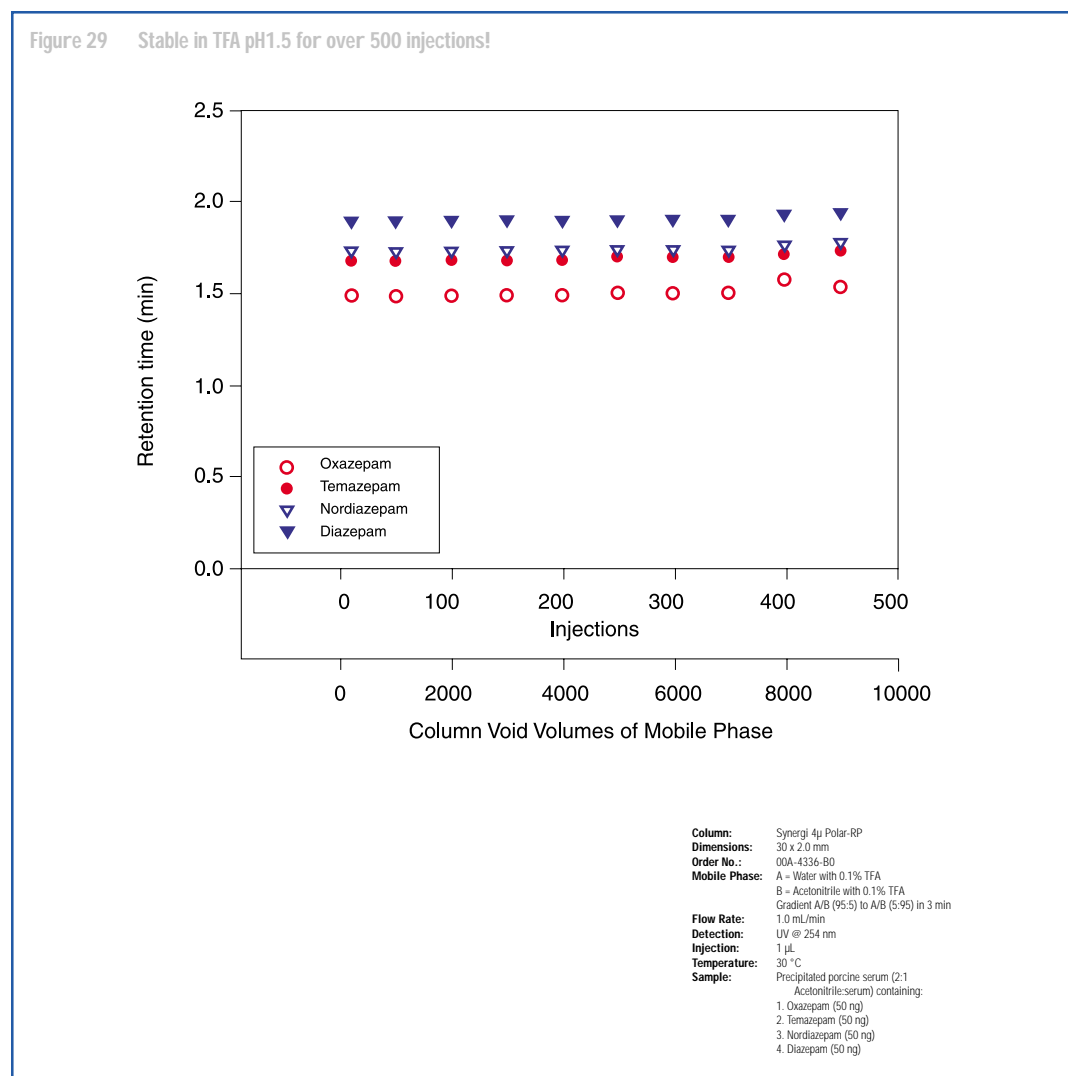
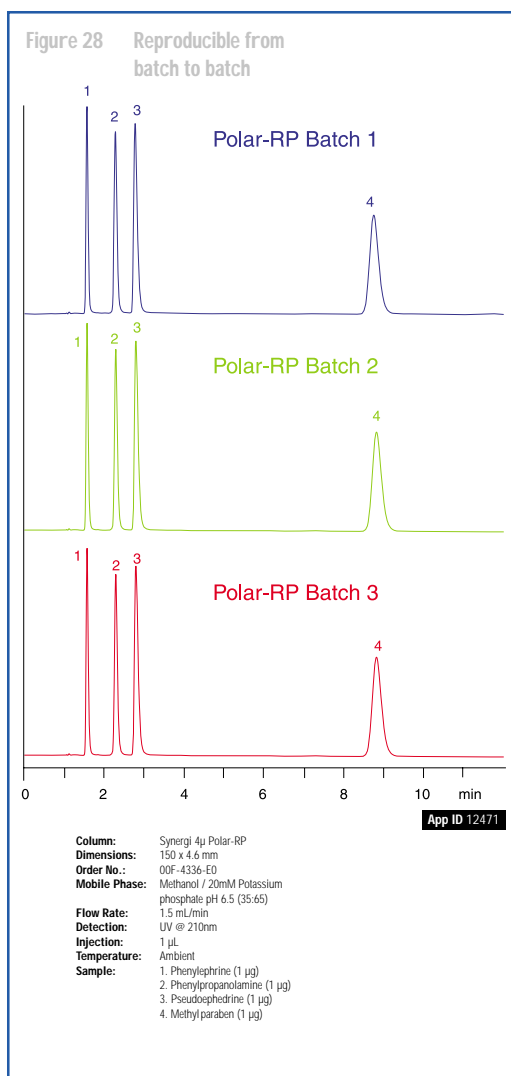


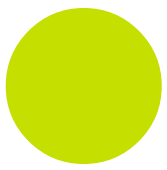
Reproducible performance from pH 1.5-7.0



FINALLY A REPRODUCIBLE & STABLE POLAR COLUMN

Although some people may be wary of the reproducibility and stability of polar-embedded phases, the reproducibility of Synergi 4 μ Polar-RP is indicated by the overlay of chromatograms from three separate batches of bonded stationary phase (**Figure 28**). In addition, Synergi 4 μ Polar-RP's ether-linkage is extremely resistant to hydrolysis, even at pH 1.5, thus enabling separations even under relatively harsh 0.1% TFA running conditions for thousands of column volumes (**Figure 29**). At the other end of the pH spectrum, Synergi 4 μ Polar-RP is stable to a pH of 7.0



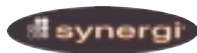
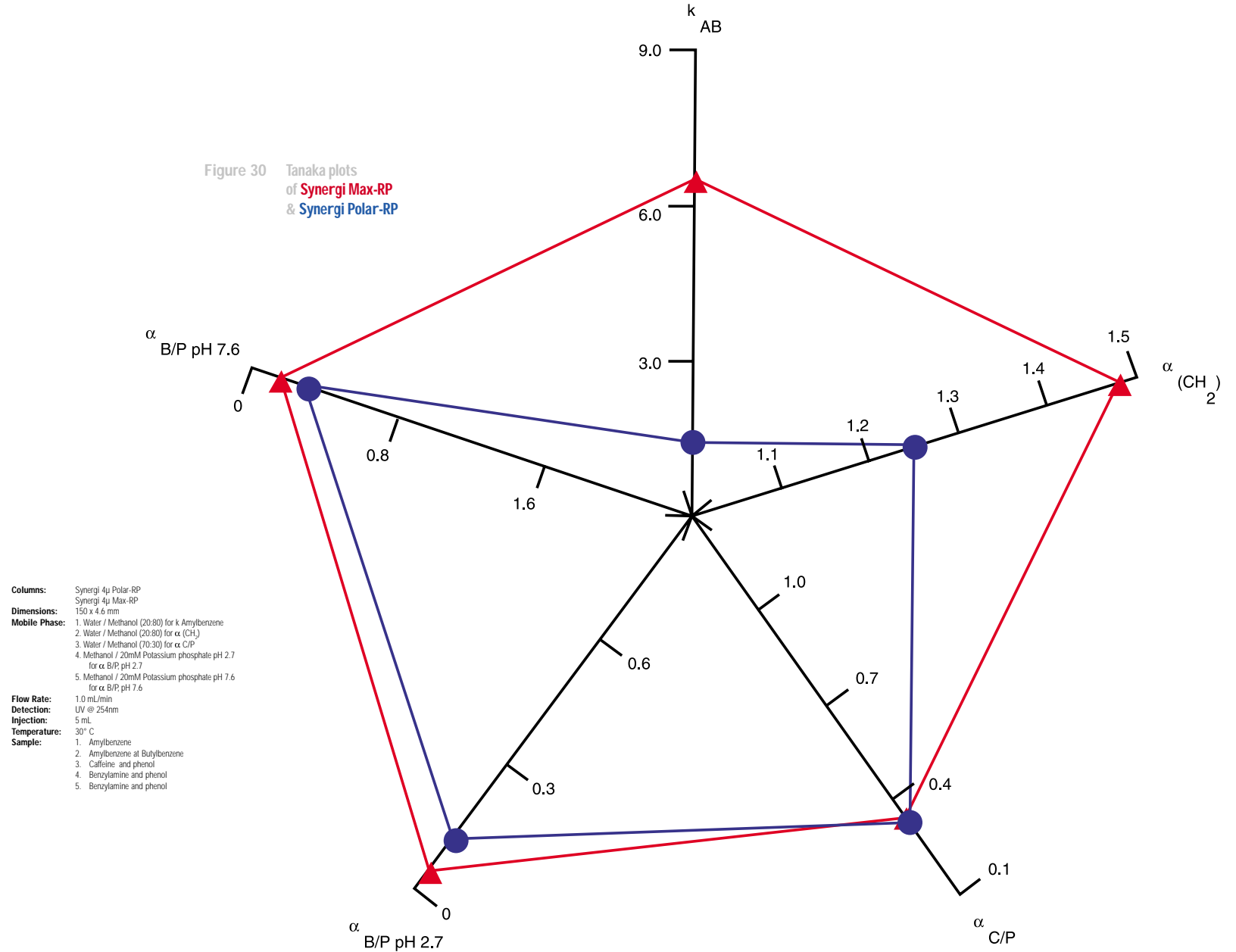


Technical specifications

Material Characteristics

Packing Material	Particle Shape/Size (μ)	Pore Size (Å)	Pore Volume (mL/g)	Surface Area (m ² /g)	Carbon Load %	Calculated Bonded Phase Coverage (μmole/m ²)	End Capping
Synergi™ Max-RP	Spher. 4	80	1.05	475	15	N/A	TMS
Synergi™ Polar-RP	Spher. 4	80	1.15	475	11	N/A	Hydrophilic

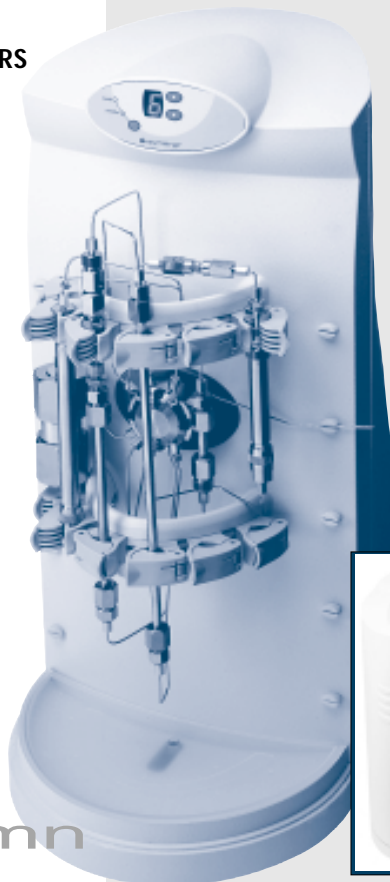
Figure 30 Tanaka plots of Synergi Max-RP & Synergi Polar-RP



Synergi™ HPLC Column Selector

3- OR 6-COLUMN AUTOMATED SELECTORS FOR HPLC METHOD SCREENING, DEVELOPMENT AND VALIDATION

- Safe and convenient solvent containment is provided by the built-in drip tray.
- Environmental isolation and ambient temperature stabilization is maintained by the magnetically secured cover.
- Tubing connections are organized with side tubing fasteners.



Column selector ordering information

Order No.	Description	Price
AV0-6080	Synergi 6-Column Selector, Stainless Steel, 4 Line BDS Control and RS-232 communication, Universal power supply 100-240 VAC, 50-60 Hz	
AV0-6081	Synergi 3-Column Selector, Stainless Steel, 4 Line BDS Control and RS-232 communication, Universal power supply 100-240 VAC, 50-60 Hz	

1. Synergi systems are warranted for one year parts and labor.
2. Call your technical representative for more information on individual systems and your specific requirements. For your ordering convenience the two most popular systems are listed above.
3. All units supplied with 10-32 threaded PEEK nuts and ferrules for all ports, 3.5m (12 ft) of 1/16" OD PEEK tubing, universal power supply, power line cord (please specify) and interface cable.

Power Line Cords (Specify Order No., Included at no charge.)

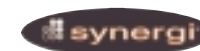
Australia and New Zealand	AV0-6088
Italy	AV0-6089
Japan	AV0-6090
North America	AV0-6091
Schuko (most of Europe)	AV0-6092
Switzerland	AV0-6093
United Kingdom	AV0-6094

HPLC Column ordering information

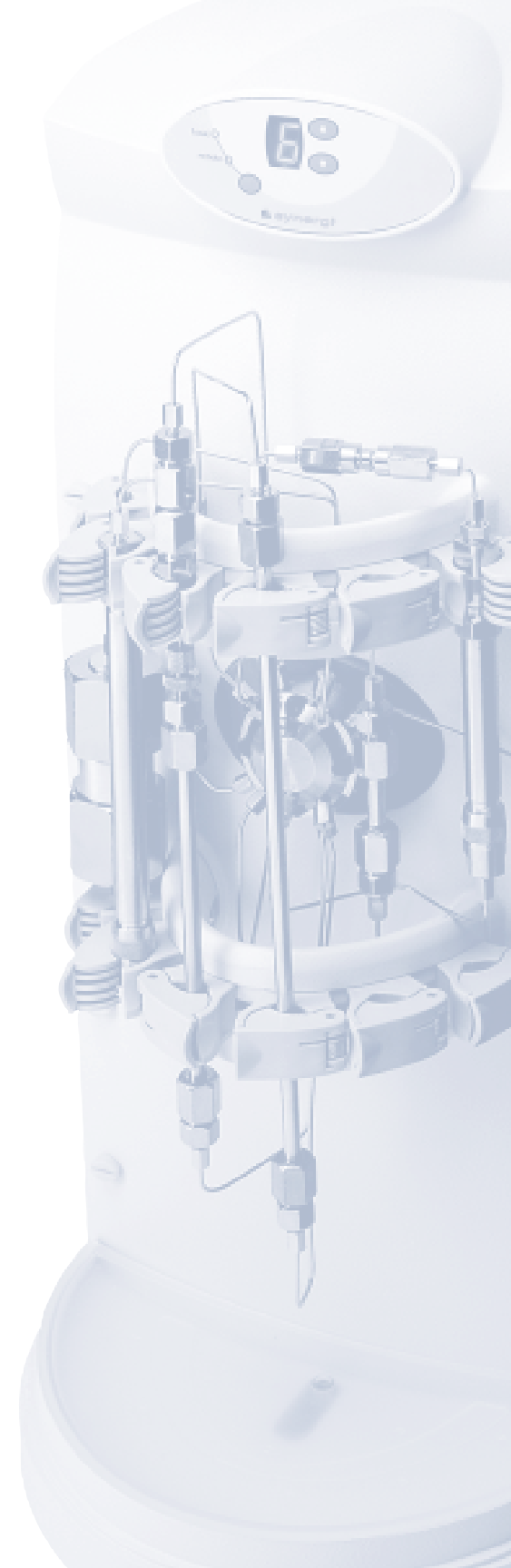
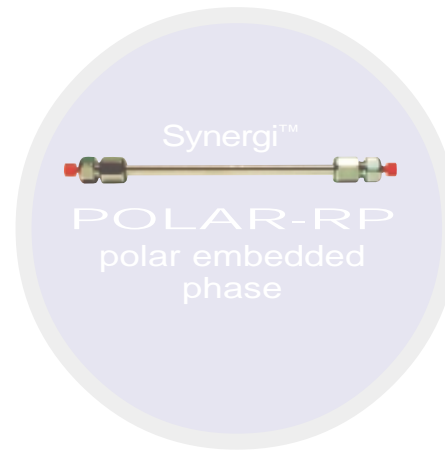
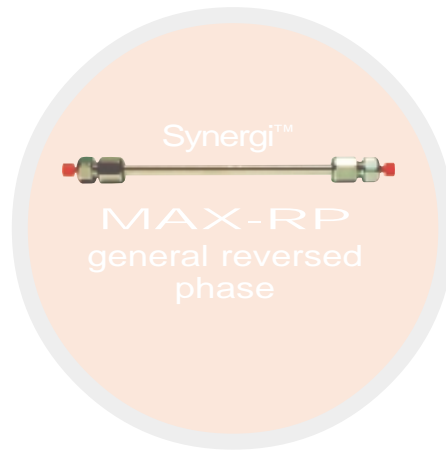
SecurityGuard™ Cartridges require universal holder. Order No.: KJO-4282

Narrow Bore		Columns (mm)				SecurityGuard™ Cartridges 10/pk	
	30 x 2.0	50 x 2.0	75 x 2.0	150 x 2.0	250 x 2.0	4 x 2.0mm for column ID 2.0-3.0	4 x 3.0mm for column ID 3.2-8.0
Synergi Max-RP 80Å	00A-4337-B0	00B-4337-B0	00C-4337-B0	00F-4337-B0	00G-4337-B0	AJO-6073	AJO-6074
Synergi Polar-RP 80Å	00A-4336-B0	00B-4336-B0	00C-4336-B0	00F-4336-B0	00G-4336-B0	AJO-6075	AJO-6076
Analytical		Columns (mm)				SecurityGuard™ Cartridges 10/pk	
	30 x 4.6	50 x 4.6	75 x 4.6	150 x 4.6	250 x 4.6	4 x 2.0mm for column ID 2.0-3.0	4 x 3.0mm for column ID 3.2-8.0
Synergi Max-RP 80Å	00A-4337-E0	00B-4337-E0	00C-4337-E0	00F-4337-E0	00G-4337-E0	AJO-6073	AJO-6074
Synergi Polar-RP 80Å	00A-4336-E0	00B-4336-E0	00C-4336-E0	00F-4336-E0	00G-4336-E0	AJO-6075	AJO-6076
Preparative		Columns (mm)					
	60 x 21.2	100 x 21.2	150 x 21.2	250 x 21.2			
Synergi Max-RP 80Å	00R-4337-P0	00D-4337-P0	00F-4337-P0	00G-4337-P0	Method Development & Method Validation Kits can be customized for your application. Please call your technical consultant at Phenomenex.		
Synergi Polar-RP 80Å	00R-4336-P0	00D-4336-P0	00F-4336-P0	00G-4336-P0			

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