Millipore®
Filtration, Separation
& Preparation

Data Sheet

PharmPrep™ P Sorbent

High-Performance Spherical Chromatography Sorbent

PharmPrep™ P Sorbent is the latest development in our silica sorbent range. The particles have a spherical shape and are available in two particle sizes: 10 and 20 µm. Together with a pore diameter of 100 Å (10 nm), these new sorbents fit perfectly into the polishing step of peptides, like insulin as well as other biopharmaceuticals and pharmaceutical APIs, like antibiotics and hormones.

This highly porous silica is produced by spray drying. Because we perform the entire manufacturing process, you benefit from consistent batch-to-batch purification, while ensuring superior quality standards and regulatory compliance.

MilliporeSigma

Preparative Liquid Chromatography

PharmPrep™ P sorbent for preparative liquid chromatography (LC) is a spherical, porous silica sorbent characterized by:

- Uniform and homogenous silica gel matrix with excellent batch-to-batch reproducibility
- Narrow particle size distribution for high performance and high packing stability
- Reproducible specific surface area and pore size distribution
- Enhanced mechanical stability
- General high-manufacturing quality and reproducibility
- Low back pressure

Benefits

- High productivity in peptide purification processes
- Superior loading capacity and selectivity
- High specific surface area
- Outstanding reproducible purification processes over many column packings
- Long lifetime due to high mechanical stability
- Excellent chemical stability

Polishing of Insulin

As seen in Figure 1, PharmPrep™ P sorbents demonstrate a perfect separation of insulin and the main impurities, e.g. des-amido insulin.

With this polishing step using PharmPrep™ P sorbent, a final outstanding insulin purity of 99.8% can be achieved. Typical load is 8 g crude Insulin per L Column volume which is equivalent to 15 g per kg stationary phase.

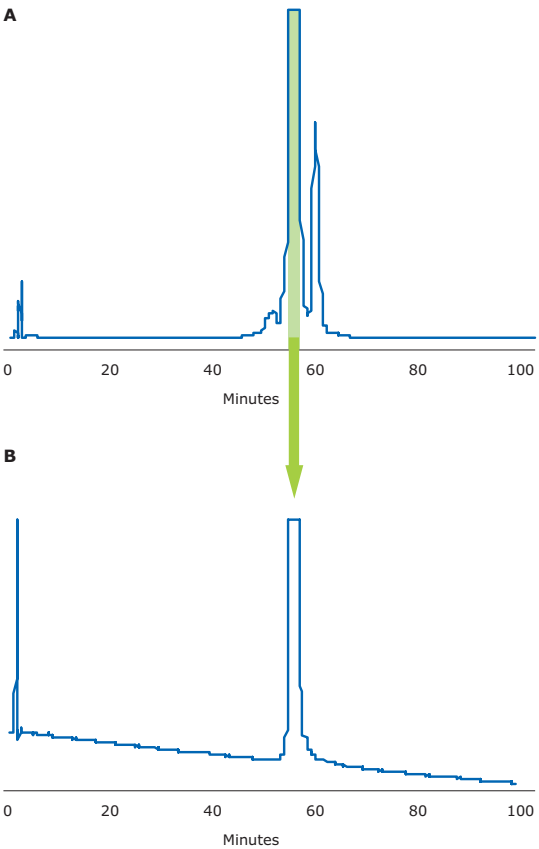


Figure 1.

(A) Process separation on PharmPrep™ P sorbent
(B) Inprocess control of insulin fraction

PharmPrep™ P 100 RP-18e, 10 µm sorbent chromatographic conditions for polishing of crude human insulin (90% pure)

Specifications	
Column size	250 x 4.6 mm
Mobile phase	A: 0.1 M $(NH_4)H_2PO_4$ pH 7.3
	B: 0.1 M $(NH_4)H_2PO_4$ pH 7.3 /ACN 50/50 (v/v) (Gradient mode 65% A to 30% A in 100 min)
Flow rate	1.325 mL/min
Temp.	25°C
Detection	UV 214 nm
Injection volume	100 µL
Sample	18 mg/mL crude human insulin rec. dissolved in water + 0.1% TFA

PharmPrep™ P 100 RP-18e and RP-8e, 10 µm Sorbent

- High selectivity
- High loadability
- High flow rate
- High throughput

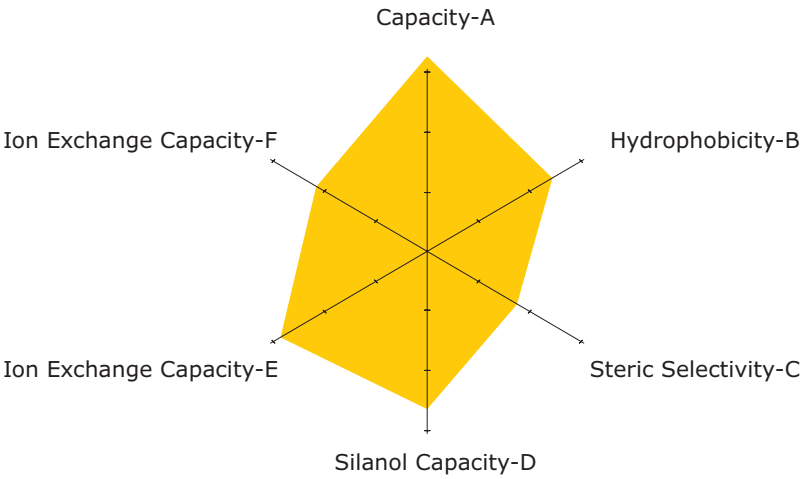
…and an insulin purity of 99.8%

High Selectivity

Controlling the physical and chemical properties of stationary phases is important, but only a comprehensive chromatographic characterization ensures a consistently high level of reproducibility. To characterize selectivity, different approaches have been applied by leading high performance liquid chromatography (HPLC) scientists.

The “Tanaka Test” is established worldwide as an industrial standard test that assesses selectivity and performance differences between HPLC columns. These column parameters are known for effectively choosing the appropriate HPLC column for a specific separation, and enables easy comparison of columns.

A set of seven selected substances is used to describe capacity, hydrophobicity, steric selectivity and silanophilic properties. To recognize the quality of a sorbent easily, the values of these parameters are outlined on the six axes of a hexagon. The more symmetrical the hexagon is and the larger its area, the more balanced the stationary phase is in the sum of its chromatographic properties.



Description			
A	Capacity	k’ (Pentylbenzene)	9.52
B	Hydrophobicity	α (Pentylbenzene/Butylbenzene)	1.54
C	Steric selectivity	α (Triphenylen/o-Terphenylen)	1.63
D	Silanol capacity	α (Caffeine/Phenol)	0.36
E	Ion exchange capacity	α (Benzylamine/Phenol) pH 7.6	0.08
F	Ion exchange capacity	α (Benzylamine/Phenol) pH 2.7	0.26

Figure 2.

Tanaka Hexagon[1] for PharmPrep™ P 100 RP-18e, 10 µm sorbent.

1. Prof. Tanaka, Kyoto Institute of Technology, *J. Chromatogr. Sci.* Vol. 27 (1989) 725.

Mechanical Stability

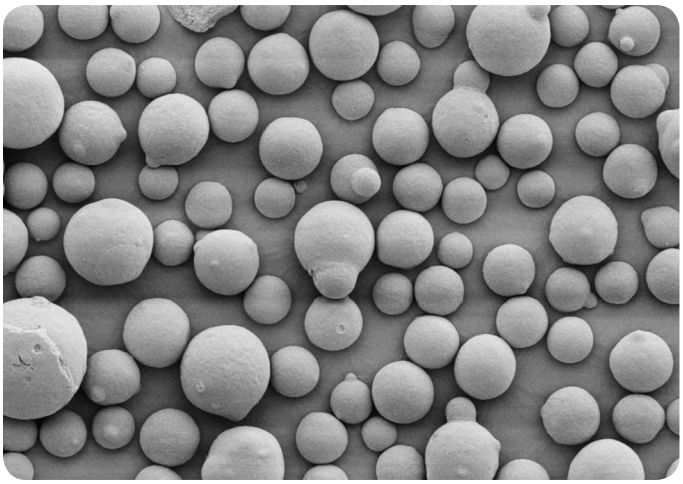
PharmPrep™ P 100 RP silicas are characterized by good mechanical stability. As a result, there are no restrictions on the type of packing method (vacuum or DAC) that may be used for packing columns.

PharmPrep™ P sorbent has the best mechanical stability and allows repeated packing/unpacking procedures at up to 300 bar. The eluent pressure shows only a 4-bar pressure difference after the repeated packings, which indicates no blocking of the column frit by fines of broken particles.

The results of 10 repeated packings with a compression from 50 up to 350 bar mechanical pressure are shown in Figure 3.

Figure 4 shows the trend of the solvent pressure after 10 repeated column packings with the same silica gel.

A



B

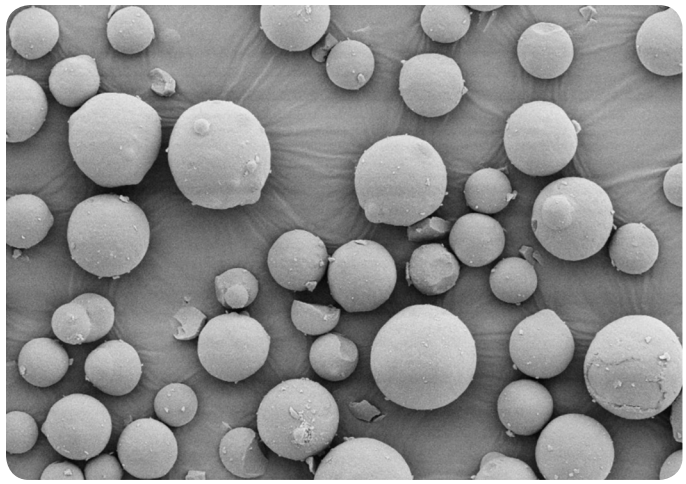


Figure 3.

(A) Before packing, (B) After 10 repeated packings.

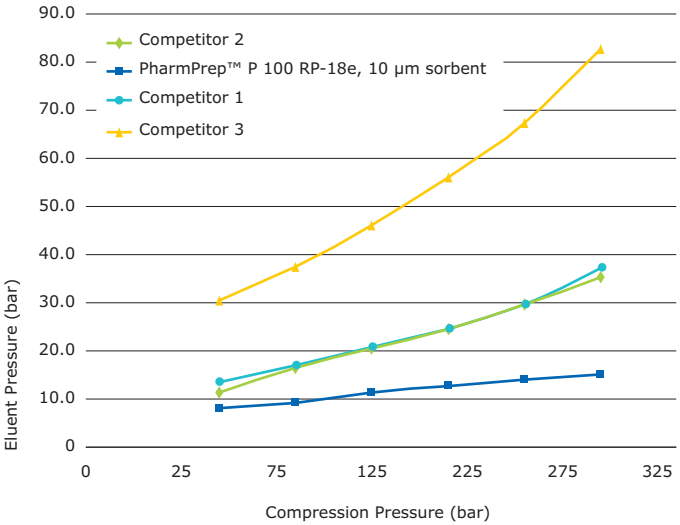


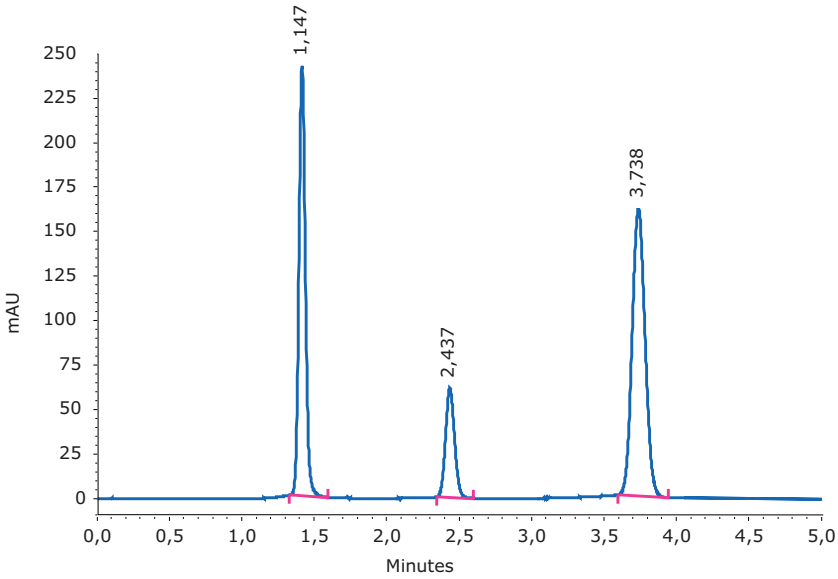
Figure 4.

Solvent pressure after 10 repeated column packings with the same silica gel.

Packing

PharmPrep™ P sorbent can be packed with high efficiency into different types of columns. Using the standard dynamic axial compression (DAC) technology with acetone as the slurry liquid, results in a column efficiency of above 45,000 N/m in a 5 cm I.D. column. Vacuum suction packing methods can also be used. In the same stainless steel column with 5 cm I.D., vacuum removal of the slurry liquid following compression of the packed bed resulted in comparable column efficiency.

DAC packing of PharmPrep™ P 100 RP-8e, 10 µm sorbent



Test Compounds	N/m	Asym
Uracil	25.427	1.11
Acetophenone	39.208	1.06
Toluene	46.421	1.08

Column dimensions	50 mm I.D. x 225 mm
Slurry	800 mL in acetone
Compression	40 bar
Eluent pressure drop	30 bar
Eluent	ACN/H20 75/25

Figure 5.

Packing of PharmPrep™ P 100 RP-8e, 10 µm sorbent into a 5 cm I.D. dynamic axial compression (DAC) column

High Throughput

The very moderate pressure increase running an eluent mix of acetonitrile/water 75/25 (v/v) with increasing flow rates enables a manufacturer to speed up the process.

Higher flow rate > higher throughput > higher productivity

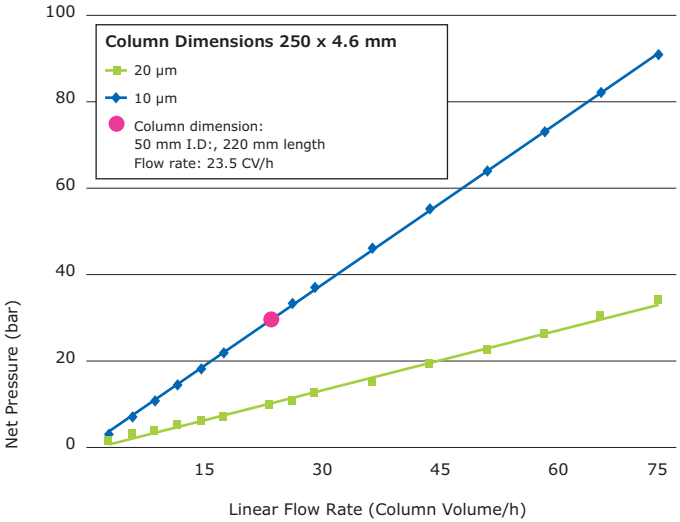


Figure 6.

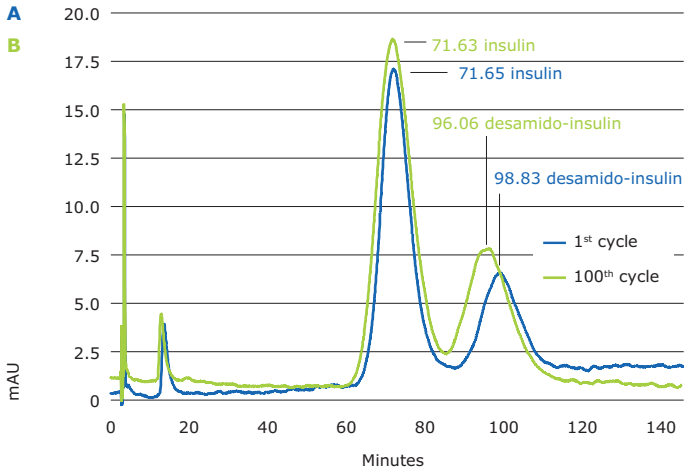
Pressure flow curves for PharmPrep™ P 100 RP-18e (10 µm and 20 µm) sorbents.

PharmPrep™ P 100 sorbent has a very low back pressure at high flow rates.

Chemical Stability

Long-term stability under harsh conditions ensure the long lifetime of PharmPrep™ P sorbent. Long sorbent lifetime resulting in good productivity.

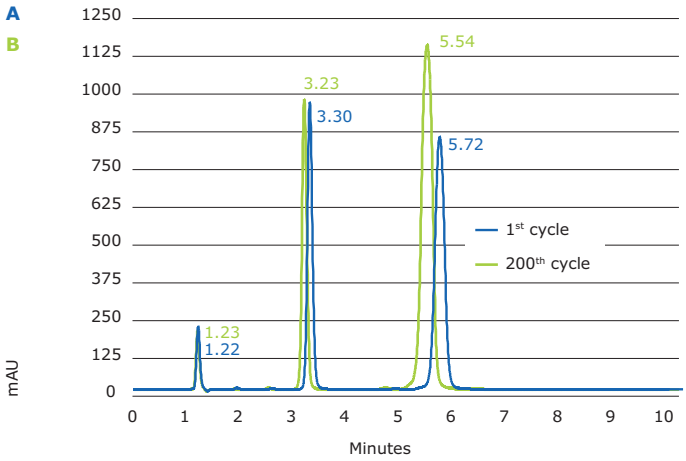
Performing more production cycles without replacing the sorbent saves money. Not only for the production of small biomolecules, customers do not want to interrupt a stable process by introducing a new filled column to the process. PharmPrep™ P 100 sorbent perfectly resists alkaline CIP conditions (see Figure 7), demonstrated by real CIP situations met during the separation of insulin from desamido-insulin. PharmPrep™ P silica is also robust enough to withstand strong acidic conditions, as shown in Figure 8.



	RT Insulin	RT Desamido-insulin
(A) Start CIP test	71.6 min	98.8 min
(B) After 100 column volumes 0.1 N NaOH/EtOH 50/50 (v/v)	71.6 min	96.1 min

Figure 7.

Alkaline CIP with 0.1M NaOH.



(A) 1st cycle α of anthracene/toluene	2.17
(B) 200th cycle α of anthracene/toluene	2.16

Figure 8.

Stability at pH 2.

Production

The Gernsheim plant, based in Germany, where PharmPrep™ P silica is produced, complies with DIN ISO 9001 and DIN ISO 14001, and several GMP-related measures have been implemented.

- Reliable, well-controlled production processes
- More than 100 years of chromatography know-how
- We are the largest dedicated producer of chromatographic silica gels in the world
- Large batch sizes
- Custom packaging sizes to meet your requirements — from a single source, ranging from grams to tons
- MilliporeSigma silica packing materials are designed to meet the highest demands in HPLC, SFC and SMB, from analytical to process scale.

Physical and Chemical Data

Parameter	Range		Typical Value		Method
PharmPrep™ P Si100 sorbent					
Particle Size Distribution	10 µm d_{50}	10–13 µm	d_{50}	10 µm	Particle size distribution
	20 µm d_{50}	15–20 µm	d_{50}	18 µm	
	d_{90}/d_{10}	≤2.5	d_{90}/d_{10}	≤2.5	
Specific Surface Area	320 – 400 m^2/g		370 m^2/g		Nitrogen sorption of basic silica gel (BET)
Specific Pore Volume	0.8 – 0.9 mL/g		0.8 mL/g		
Mean Pore Size	10 nm		10 nm (100 Å)		
Metal Ion Content	Na ≤25 µg/g		Na ≤2 µg/g		ICP-MS
	Al ≤50 µg/g		Al ≤20 µg/g		
	Fe ≤25 µg/g		Fe ≤2 µg/g		
Efficiency	≥18000 (N/m) (10 µm)		25000 (N/m)		2-nitro toluene, n-heptane/1.4-dioxane 99/1 (v/v), flow rate: 1.3 mL/min, 250 x 4.6 mm columns
Pressure	≤25 bar (10 µm)		10 bar		n-heptane/1, 4-dioxane 99/1 (v/v), flow rate: 1.3 mL/min, 250 x 4.6 mm column
	≤10 bar (20 µm)		4 bar		
PharmPrep™ P 100 RP-18e sorbent					
Carbon	17% – 21%		20%		Elemental analysis
Efficiency	≥20000 (N/m) (10 µm)		30000 (N/m)		Toluene, acetonitrile/water 75/25 (v/v), flow rate: 1.3 mL/min, 250 x 4.6 mm columns
Pressure	≤40 bar (10 µm)		10 bar		Acetonitril/water 75/25 (v/v), flow rate: 1.3 mL/min, 250 x 4.6 mm columns
	≤25 bar (20 µm)				
Selectivity alpha (Phenol/Pyridine)	≥1.8 – ≤3.0		2.5		Acetonitrile/water 70/30 (v/v), flow rate: 1.3 mL/min
Capacity factor (3-Nitro Acetanilide)	2.9 – 3.9		3.4		Acetonitrile/water 70/30 (v/v), flow rate: 1.3 mL/min
PharmPrep™ P 100 RP-8e sorbent					
Carbon	11% – 14%		13%		Elemental analysis
Efficiency	≥20000 (N/m) (10 µm)		30000 (N/m)		Toluene, acetonitrile/water 75/25 (v/v), flow rate: 1.3 mL/min, 250 x 4.6 mm columns
Pressure	≤40 bar (10 µm)		25 bar		Acetonitril/water 75/25 (v/v), flow rate: 1.3 mL/min, 250 x 4.6 mm columns

Ordering Information

Description	Catalogue No.
PharmPrep™ P Si100, 10 µm silica sorbent	**119681**
PharmPrep™ P Si100, 20 µm silica sorbent	**119682**
PharmPrep™ P 100 RP-8e, 10 µm silica sorbent	**119132**
PharmPrep™ P 100 RP-18e, 10 µm silica sorbent	**119995**
PharmPrep™ P 100 RP-18e, 20 µm silica sorbent	**119996**
Ready-to-use HPLC columns	
Scout column 250 x 4.6 mm PharmPrep™ P 100 RP-8e, 10 µm silica sorbent	**120594**
Scout column 250 x 4.6 mm PharmPrep™ P 100 RP-18e, 10 µm silica sorbent	**120571**
Scout column 250 x 4.6 mm PharmPrep™ P 100 RP-18e, 20 µm silica sorbent	**120572**
HIBAR® pre-packed columns 250 x 25 mm PharmPrep™ P RP-8e, 10 µm silica sorbent	**120588**
HIBAR® pre-packed columns 250 x 25 mm PharmPrep™ P 100 RP-18e, 10 µm silica sorbent	**120573**
HIBAR® pre-packed columns 250 x 25 mm PharmPrep™ P 100 RP-18e, 20 µm silica sorbent	**120574**
HIBAR® pre-packed columns 250 x 50 mm	On request

HIBAR® and scout pre-packed columns are manufactured under strictly controlled conditions to ensure both excellent results and reproducibility. Each packed column is provided with a Certificate of Analysis.

Validation kits	
3 x 100 g packages of 3 different lots PharmPrep™ P 100 RP-8e, 10 µm silica sorbent	**1.19132.0003**
PharmPrep™ P 100 RP-8e, 10 µm silica sorbent	**1.19681.0003**
PharmPrep™ P 100 RP-18e, 20 µm silica sorbent	**1.19682.0003**

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