



Preparative & Process LC

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Introduction

YMC is one of the very few global players in the market that meet the challenging demands in preparative scale chromatography. Our ambition is to provide chromatographic solutions for any compound from its discovery through scale-up to production and its quality control in the lab, as well as positive, active support, chromatographic tools and technical assistance at every stage.

Preparative & Process LC

In order to optimise preparative processes the employed bulk needs to provide:

- optimised selectivity → maximum output per run
- mechanical stability -> cost efficiency
- reproducibility -> reliability



Preparative & Process LC

YMC of today maintains three technology platforms:

• chemically re-enforced pH-stable YMC-Triart Prep with C18, C8 and customised (e.g. quarternary ammonium) surface chemistries

> high grade silica phases for preparative HPLC with improved mechanical stability, including polysaccharide phases for chiral applications (see page 252-279)

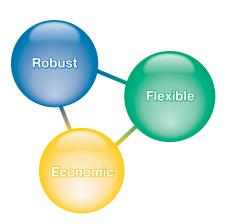
> > • high resolution IEX prep media in 10, 20, 30 or 75 µm particle sizes with an annual capacity beyond 40,000 litres





In addition to product supply, YMC is proud to be recognised for outstanding technical support by dedicated people with a mission to exceed expectations. YMC will happily share expertise and proactively contribute to make customers successful in their daily work. YMC support teams are located in Japan, China, Korea, Taiwan, Singapore, India and the USA in addition to Germany which provides support for the EMEA countries together with a network of authorised distributors who supply additional local support.

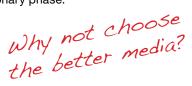
- extended pH range
- mechanical stability
- high loadability
- CIP with NaOH solutions applicable
- up to 4-fold longer lifetimes
- multi-ton capacity



Specifications	YMC-Triart Prep C18-S	YMC-Triart Prep C8-S
Base material	inorganic/or	rganic hybrid silica
Particle size / µm	10, 15, 20	10, 15, 20
Pore size / nm	12	20
Surface area / m ² g ⁻¹	360	220
Bonding	trifunctional	trifunctional
End-capping	yes	yes
Flexible pH range	2.0 ~ 10.0	2.0 ~ 10.0

General

YMC-Triart Prep is chemically stable up to pH 10.0. This provides more flexibility for method development and allows for more efficient cleaning-in-place (CIP) procedures. From real life process development work YMC-Triart Prep has been shown to outperform traditional silica-based materials 2- to 4-fold in terms of stability. Longer column lifetimes lead to more kilogram of product produced per kilogram of stationary phase.



Particle technology

YMC-Triart Prep materials provide improved particle and pore size distributions which result in reduction of backpressures and increased sample loadabilities are achieved during preparative operation.

With YMC-Triart Prep previously challenging pH and high temperature conditions can be used for demanding applications even in the day-to-day work in laboratories or production. Most importantly, due to its unique particle composition, a balanced hydrophobicity and silanol activity is achieved which makes YMC-Triart Prep a "First Choice" material in method development!

Homogeneous and uniform particles



YMC-Triart (12 nm, 5 µm)



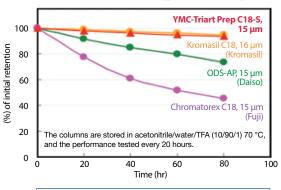
YMC-Triart Prep (20 nm, 15 µm)



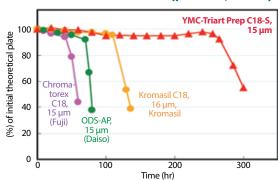
X-Bridge HILIC (13.5 nm, 5 µm) by courtesy of YMC Co., Ltd.

Excellent pH stability

Acidic condition (pH 1, 70 °C)*



Alkaline condition (pH 11.5, 50 °C)*



Column: Eluent: 150 x 4.6 mm ID 50 mM TEA in methanol /

50 mM TEA in water (pH 11.5) (20/80, v/v)

Flow rate: Detection: UV at 254 nm Sample: caffeine

Column: 250 x 6.0 mm ID acetonitrile / water (60/40) Eluent: Flow rate: 1.7 mL/min

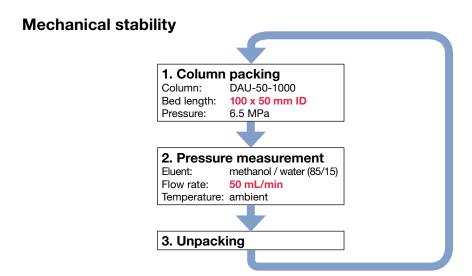
Temperature: 37 °C UV at 254 nm Detection: Sample: butyl benzoate

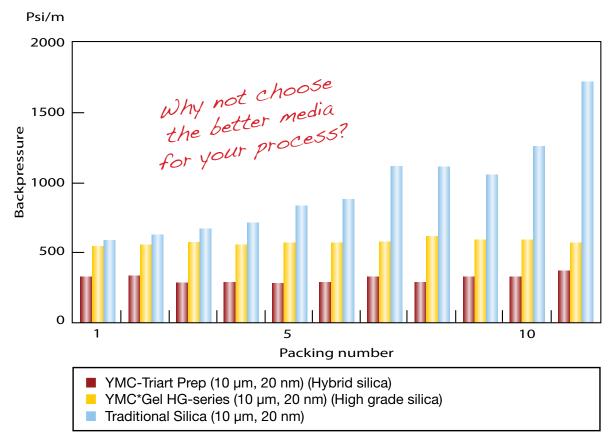
At high pH YMC-Triart Prep C18-S shows lifetimes of up to 4 times longer compared to conventional silica materials. This enables new separations to be carried out at high pH which are not possible with silica materials. Furthermore, the material can endure more CIP-cycles than conventional phases used in industrial processes.

Advantages of YMC-Triart Prep

Improvement	Your benefit
pH-stability 2.0 ~ 10.0	More stable to CIP-conditions Method development
Chemical and mechanical stability	Cost savings High production throughput Increased lifetimes
Uniform particle size	Improved packing = improved chromatographic performance = reduced backpressure
Narrow pore size distribution	High loadability
100% aqueous conditions	Separation of polar substances Method development

This makes YMC-Triart Prep "first choice" material for method development and process optimisation!

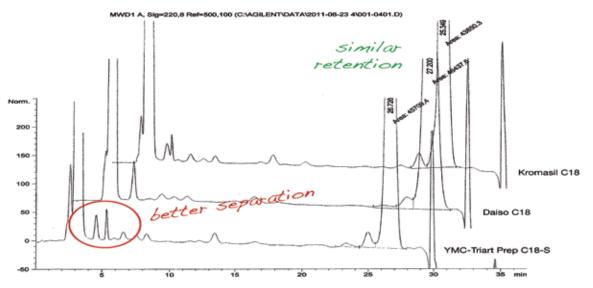




Shearing and crushing of silica particles lead to the formation of fines, which result in an increased backpressure. By using mechanically stable, spherical particles the formation of fines can be re-

Here, high mechanical stability of YMC-Triart Prep is demonstrated by means of repeated packing of a DAC column. Even after more than 10 repacking cycles using the same material the pressure does not increase. The absence of fines is demonstrated by a constant backpressure.

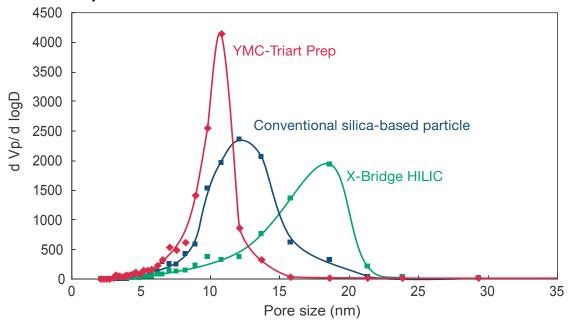
YMC Triart Prep C18-S vs. competitor material (client data)



Client data confirms that YMC-Triart Prep C18-S shows retention for hydrophobic compounds comparable to conventional silica materials. At the same time polar molecules are exceptionally well separated.

Client data shows non-optimized scouting runs performed on the respective C18 material packed into 250 x 4.6 mm ID columns.

Narrow pore distribution*

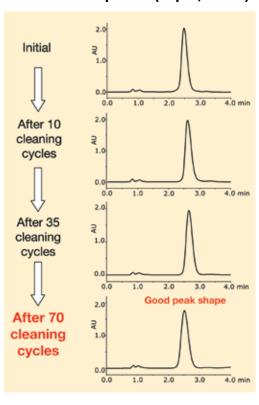


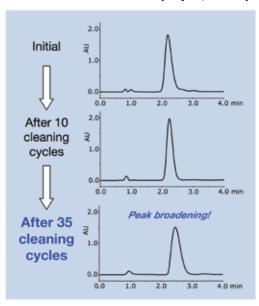
A narrow pore size distribution of a stationary phase beneficially affects peak width and sample loading in liquid chromatography. YMC-Triart Prep C18-S exhibits a narrower pore size distribution. This results in improved peak shapes and higher sample loading in your preparative processes.

CIP performance of YMC-Triart Prep C8-S

YMC-Triart Prep C8-S (10 µm, 20 nm)*

Silica based C8 material (10 µm, 20 nm)*





Column: 50 x 4.6 mm ID Eluent: A) water / TFA (100/0.1) B) acetonitrile / TFA (100/0.1) 29-36% B (0-2 min), 36% B (2-3 min), 29% B (3-6 min) Flow rate: 1.0 mL/min Temperature: 25 °C UV at 220 nm Detection: Injection: 10 mg/mL insulin bovine + human serum (2:1) Sample:

Column lifetime extended by factor > 2

In insulin production repeated injections of a solution of insulin in human plasma/serum are carried out. Consequently, absorption of impurities on the surface of the packing material reduces the retention capacity of the column.

Methodology: At this point a wash step with an alkaline solution (e.g. 0.1 M NaOH) removes the impurities and restores the full capacity of the column.

Problem: Silica materials are unsuitable for alkaline wash conditions, because of their limited stability at high pH.

Solution: Hybrid silica-based YMC-Triart Prep has an excellent stability at high pH. It is amenable to alkaline wash conditions and longer column lifetime.

This in turn reduces production costs: Lower consumption of packing material and less downtimes due to column repacking. An extension of column lifetime by a factor of more than two has been achieved!

Ordering Information

	YMC-Triart Prep C18-S		YMC-Triart Prep C8-S		
Pore size (nm) Particle size Product (µm) Code		Pore size (nm)			
	10	TAS12S11		10	T0S20S11
12	15	TAS12S16	20	15	T0S20S16
	20	TAS12S21		20	T0S20S21

Typical pack sizes:

Laboratory scale: 100 g - 5 kg PE bottle Industrial scale: 5 kg - 50 kg in double lined PE bags inside metal drum

Larger pack sizes on request

Regulatory support file available under non-disclosure agreement. Used in validated cGMP-manufacturing processes.

Other particle and pore size combinations on request. Examples of existing customised material: TAS08S11, TOS12S11, TOS12S16, TQP12S21

> Customised material available on request. DMF registered with FDA.

- Higher sample load
- Lower backpressure
- Longer column usage
- More repackings possible
- More efficient column packing



General

YMC has more than 35 years experience in the manufacture of silica-based stationary phases for high pressure liquid chromatography (HPLC).

The substantial investment into facilities and staff represent YMC's ongoing commitment towards high quality products and technical support. The company's state-of-the-art silica production facilities allow for large batches of more than 500 kg/lot. Our large-scale bonding site has allowed lots of over 200 kg of bonded silica to become routine operations.

Besides innovations in the field of hybrid silica (YMC-Triart) and polymeric ion-exchange resins (BioPro) YMC dedicated considerable effort into improving chromatographic properties of silica based materials.

Availability

YMC provides an extensive selection of more than 20 fully scalable stationary phases from 1.9 to 50 µm in various pore sizes and specifications to address virtually any separation need. In addition, YMC can also custom manufacture products with specific properties, e.g. defined pore size and/or carbon content, to provide optimal suitability to individual separations. This unique choice of selectivities meets the highest demand in conventional column separations and also dynamic axial or dynamic radial compression columns and simulated moving bed (SMB) techniques.

Bulk Packing Material

Preparative and process scale YMC bulk packing materials (10 to 50 µm) can be obtained in gram to multi-ton scale quantities. YMC's advanced production facilities are able to manufacture multiton quantities of silica per annum, with large batches in excess of 500 kg/lot. YMC's large-scale bonding plants have a capacity of more than 200 kg/lot.

Long Term Supply

In order to meet increasing demands in analytical and preparative chromatography, chromatographers highly depend on a reliable source of supply throughout a validated method. Therefore, YMC will never knowingly change or modify an existing product which has any such customer base. Any product improvements will result in an entirely new YMC product.

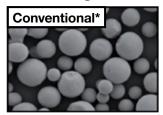
World Wide Availability

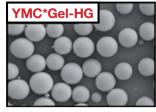
Pre-packed columns and bulk materials are available worldwide through a dedicated support network headed by YMC operations in Japan, the US and in Europe to ensure facile method transfer between research and production sites across the world.

Improved silica base for better performance

Improvements in the production process of the base silica yield particles with higher mechanical stability and more uniform particle and pore size distribution.

SEM image

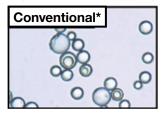


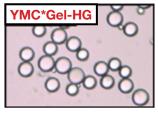




Reduced backpressure and improved chromatographic efficiency due to more uniform particle size distribution.

Optical microscope image







Better column packing efficiency and less fines due to reduction of "balloon particles".

^{*} for illustration purposes a section highlighting chipped particles and balloon particles was chosen.

Improvement	Your benefit
Improved morphology and mechanical stability	Higher productivity due to longer usage of bulk material Less fines Reduced backpressure More repackings possible
Narrower particle size distribution	Reduced backpressure Increased productivity due to higher flowrates at constant pressure More efficient columns due to faster column packing
Narrower pore size distribution	Higher (over-) loading capacity Increased productivity

YMC*Gel HighGrade (HG)-series

Go for the better!

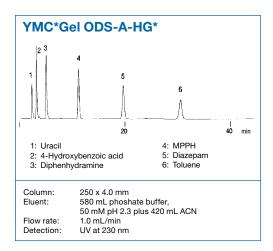
Discover optimum selectivity with YMC*Gel HG-series silica products

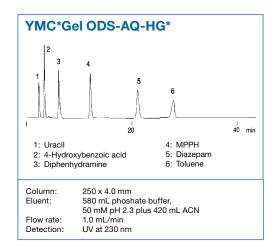
The basis for every successful separation is the selection of the appropriate stationary phase. YMC offers one of the world's largest portfolios of selectivities, designed to handle even the most demanding separations.

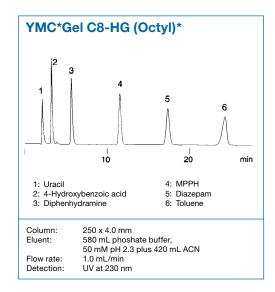
Your benefits:

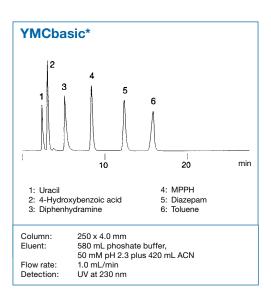
- 10 preparative phase chemistries -> solving virtually any separation need
- · full scalability
- pore sizes from 8 to 30 nm
- particle sizes from 10 to 50 µm
- customised bulk properties (pore size, carbon content, endcapping)

The retention characteristics of a selection of YMC's preparative selectivities are shown in the chromatograms below. Conditions were selected to simulate a broad application range on both basic and acidic compounds.



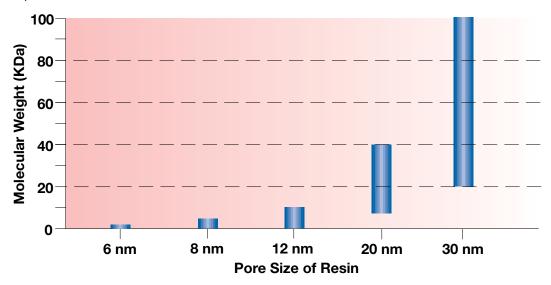






Impact of Pore Size Differences*

YMC*Gel is available in a variety of different pore sizes. Pore sizes are usually matched to sample molecule sizes. Pore sizes can also be used to adjust ligand density and hence retention characteristics of a bonded phase, since the size of the pores also affects the total media surface area in a packed column.



Please note extended molecular weight range when applying SEC.

Pore Size [nm]	Surface Area [m²/g]	Recommendation
12	330	Suitable for the majority of separations For most organic compounds For peptides less than 20 kDa Higher surface area and sample loading than 20 nm and 30 nm media
20	175	For peptides and smaller proteins from 10 kDa to 50 kDa For bulky organic compounds Higher surface area and higher sample loading than 30 nm media
30	100	For large proteins and biomolecules larger than 40 kDa For organic compounds with excessive retention on smaller pore materials

Further pore sizes available on request.

Available YMC*Gel HG-Series Products

		• · · · · · · · · · · · · · · · · · · ·	
PRODUCT	PHASE CODE	BONDING	PHASE DESCRIPTION
ODS-A-HG	AAG	C18	high performance C18 silica
ODS-AQ-HG	AQG	C18	"hydrophilic" endcapping, for 100% aqueous eluent systems, substantially increased retention of polar compounds
C8-HG (Octyl)	OCG	C8	C8 phase, high coverage monomeric bonding chemistry
C4-HG (Butyl)	BUG	C4	C4 phase, less hydrophobic surface structure than C8 packing material
TMS-HG (C1)	TMG	C1	trimethylsilane bonding, excellent hydrolytic stability
Ph-HG (Phenyl)	PHG	Phenyl	monomeric bonded phenyl, the π electron interaction gives a separation selectivity different from ODS
NH ₂ -HG (Amino)	NHG	Aminopropyl	primary amino derivative, high coverage monomeric bonding chemistry, suitable for HILIC
CN-HG (Cyano)	CNG	Cyanopropyl	for RP and NP applications, useful also for SFC and HILIC
Diol-HG	DLG	Diol	for normal phase applications, high recovery for biological material, suitable for HILIC and SFC
SIL-HG (Silica)	SLG	_	ultra high purity, high mechanical stability, suitable for HILIC and SFC

Available Products for Specific Applications

PRODUCT	PHASE CODE	BONDING	PHASE DESCRIPTION
YMCbasic	ВА	C8	specifically designed for the separation of basic compounds and peptides
YMC Omega	OMG	proprietary	specifically designed for the separation of polyunsaturated fatty acids

Analytical grades (3 and 5 μ m) are routinely available in pre-packed columns. Particle sizes as indicated. If not listed, please ask for quotation. Multi-ton capacity. Customised packing materials available on request. Pore sizes in parenthesis on request.

^{*}Not all combinations available.

^{**}With respect to pore size.

Available YMC*Gel HG-Series Products

PORE SIZE* (nm)	PARTICLE SIZE* (µm)	CARBON LOAD** (%C)	рН	TYPICAL APPLICATIONS
12; 20; 30	10; 15; 20; 50	17; 12; 7	2.0-7.5	pharmaceuticals, vitamins, peptides, PTC-amino acids, general purpose phase
8; 12; 20	10; 15; 20; 50	15; 14; 10	2.0-7.5	strong polar compounds, pharmaceuticals, antibiotics, peptides and proteins, nucleic acids, amino acids and nucleotides
12; 20; 30	10; 15; 20; 50	10; 7; 4	2.0-7.5	proteins and peptides, estrogens, general purpose phase
12; 20; 30	10; 15; 20; 50	7; 5; 3	2.0-7.5	biological separations, polar compounds, proteins
12; (20; 30)	10; 15; 20; 50	4	2.0-7.5	water-soluble vitamins
12; (20; 30)	10; 15; 20; 50	9	2.0-7.5	phenols, fullerenes, sweeteners, aromatics
12; (20; 30)	10; 15; 20; 50	3	2.0-7.5	saccharides, nucleotides, water-soluble vitamins
12; (20; 30)	10; 15; 20; 50	7	2.0-7.5	proteins, steroids, catechols, for SFC applications
12; 20; 30	10; 15; 20; 50	-	2.0-7.5	polar natural products, pharmaceuticals, for HILIC and SFC applications
12; 20; 30	10; 15; 20; 50	-	_	small organic molecules, fat-soluble vitamins, tocopherols, steroids

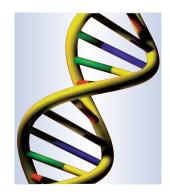
Available Products for Specific Applications

PORE SIZE* (nm)	PARTICLE SIZE* (µm)	CARBON LOAD** (%C)	рН	TYPICAL APPLICATIONS	
20	10; 15; 20	7	2.0-7.5	basic molecules w/o modifiers, peptides	
proprietary	10; 20; 50	15	2.0-7.5	polyunsaturated fatty acids, EPA, DHA	

Regulatory support file available under non-disclosure agreement. Used in validated cGMP-manufacturing processes.

Customised material available on request. DMF registered with FDA.

- high dynamic binding capacity
- low non-specific adsorption
- excellent recovery
- easy removal
- cleaning-in-place with NaOH solutions applicable



BioPro

Ion exchange chromatography (IEX) is widely used in the analysis and purification of bio-molecules. Using reversible charge-charge interactions offers several advantages in comparison to other chromatographic methods, e.g. high capacity and fast throughput. Therefore, IEX is often used in the capture or intermediate purification of bio-molecules.

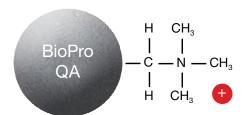
BioPro is a series of ion exchange resins specifically designed for use in bio-chromatography. This media is based on a hydrophilic polymer matrix, with a particle size of 10, 20, 30 or 75 µm. It is available as a strong anion exchanger (BioPro QA) or a strong cation exchanger (BioPro SP). BioPro offers a high dynamic binding capacity (DBC), together with low non-specific adsorption and excellent recovery.

Currently, BioPro is manufactured in lot sizes up to 200 L. In future, lot sizes up to 1,200 L will be available.

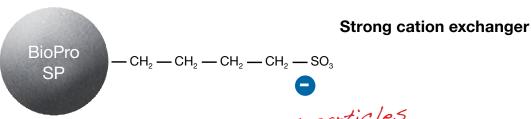
Examples of possible preparative applications of BioPro resins:

Antibody purification	Protein purification	Peptide purification
Trastuzumab Bevacizumab IgG, Antibody variants	Histones Interferon Factor VIII, Factor IX	Insulin

Particle technology



Strong anion exchanger



N.B.: Fully porous particles

BioPro SmartSep for intermediate purifications and polishing

BioPro Series	BioPro SmartSep Q10	BioPro SmartSep Q20	BioPro SmartSep Q30	BioPro SmartSep S10	BioPro SmartSep S20	BioPro SmartSep S30
Ion exchange type	stro	ng anion exchar	nger	stro	ng cation exchar	nger
Charged group		-R-N⁺(CH ₃) ₃			-R-SO₃⁻	
Matrix			Hydrophilic p	olymer beads		
Pore size			Por	ous		
Compression factor			1.1 -	- 1.4		
Particle size	10 µm	20 µm	30 µm	10 µm	20 µm	30 µm
Pressure resistance	Regular use: 3 MPa Max.: 4 MPa	Regular use: 2 MPa Max.: 3 MPa		Regular use: 3 MPa Max.: 4 MPa	Ž N	ar use: 1Pa 3 MPa
Ion-exchange capacitiy	min	. 0.08 meq/ml-re	08 meq/ml-resin min. 0.08 meq/ml-resin		esin	
Dynamic binding capacity	mi	n. 100 mg/ml-re: (BSA)	sin	mi	n. 100 mg/ml-re: (lysozyme)	sin

BioPro for capture

BioPro Series	BioPro Q75	BioPro S75				
Ion exchange type	strong anion exchanger	strong cation exchanger				
Charged group	-R-N ⁺ (CH ₃) ₃	-R-SO ₃ -				
Matrix	Hydrophilic polymer beads					
Pore size	Porous					
Compression factor	1.1 - 1.4					
Particle size	75 μm					
Pressure resistance	0.3 MPa					
lon-exchange capacitiy	min. 0.10 meq/ml-resin					
Dynamic binding capacity	min. 160 mg/ml-resin (BSA)					

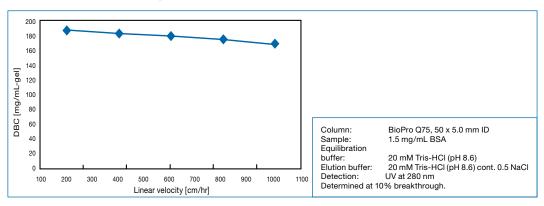
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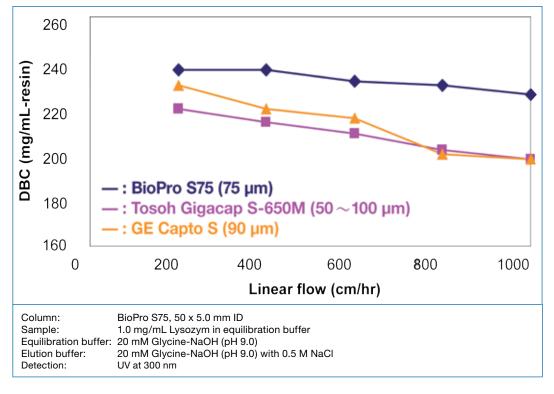
Customized material available on request. DMF registered with FDA.

Advantages of BioPro

Improvement	Your benefit
Excellent flow properties	Low backpressure High production throughput
Highly uniform particle and pore size distribution	Easy and efficient column packing Improved chromatographic performance
pH stability	Stable towards CIP-conditions Flexibility in method development
High dynamic binding capacity at high flow rates	High loadability Process more raw material
Flexible production capacities	Column filling from a single lot
Economic resin	Cost effective

Excellent DBC at high linear flow rates*



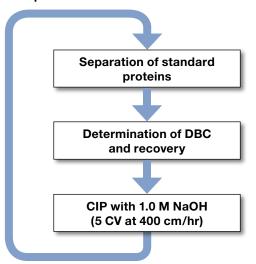


High sample loading at high flow rates is determined by the dynamic binding capacity of an ion exchange resin.

The dynamic binding capacity of BioPro is excellent even at high flow rates. When compared to similar competitor products it consistently exhibits a higher dynamic binding capacity. This results in higher sample loading in your preparative processes.

Cleaning-in-place (CIP) performance of BioPro

Test protocol



Column: BioPro S75, 50 x 5.0 mm ID

Conditions of standard protein separation
Eluent:
A) 20 mM NaH2PO4-Na2HPO4 (pH 6.8)
B) 20 mM NaH2PO4-Na2HPO4 (pH 6.8)

containing 0.5 M NaCl

Gradient: 0-100% B (0-60 min, Linear) Flow rate: 0.59 mL/min (180 cm/hr)

Temperature: UV at 220 nm Detection: Injection: 24 µL

Conditions of DBC determination

Equilibration

20 mM Glycine-NaOH(pH 9.0) buffer: Elution buffer: 0.5 M NaCl in equilibration buffer Flow rate: 2.62 mL/min (800 cm/hr) Sample: 1.0 mg/mL Lysozyme in equilibration buffer

ambient (25 °C) Temperature: UV at 300 nm Detection:

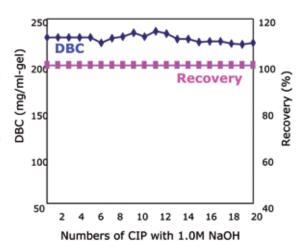
DBC is determined at 10% breakthrough.

CIP performance of BioPro

Separation of standard proteins*

20 cycles 10 cycles Initial 50 min

DBC and recovery*



BioPro is well suited for alkaline CIP procedures.

The dynamic binding capacity (DBC) and the selectivity are unaffected by 20 cycles of CIP with 1.0 M NaOH. The recovery of proteins is maintained at 100%, which demonstrates the absence of nonspecific adsorption of proteins of this hydrophilic resin.

Preparative Screening Kits

The BioPro Ion Exchange Screening Kits consist of columns that are packed with resins designed for the separation of proteins, nucleotides, and other biomolecules. The various types of kit offer significant advantages and efficiencies for resin screening and purification method development.

Laboratory scale column sizes





Specification

	Strong Anion Exchanger BioPro (SmartSep) Q	Strong Cation Exchanger BioPro (SmartSep) S	Weak Anion Exchanger BioPro DA	Weak Cation Exchanger BioPro CM	
Matrix	Porous hydro	ophilic polymer	Porous methacrylate polymer		
Particle size (μm)	30, 75	30, 75	60	60	
Ion exchanger	-CH ₂ N ⁺ (CH ₃) ₃	-CH ₂ CH ₂ CH ₂ CH ₂ SO ₃ -	-R-N(CH ₃) ₂	-R-COOH	
pH range	2 - 12	2 - 12	Regular use: 3 - 12 Short term: 1 - 13	Regular use: 3 - 12 Short term: 1 - 13	

Ordering Information

Strong anion exchanger BioPro Q

	Particle Size		Pack Sizes*					
Product		Code	50 ml	250 ml	1L	5 L	10 L	20 L
BioPro SmartSep Q10	10 µm	QSA0S10	~	✓	~	~	~	~
BioPro SmartSep Q20	20 µm	QSA0S20	~	~	~	~	~	~
BioPro SmartSep Q30	30 µm	QSA0S30	~	V	~	~	~	~
BioPro Q75	75 µm	QAA0S75	~	~	~	~	~	~

Strong cation exchanger BioPro S

	Particle Size	Code	Pack Sizes*					
Product			50 ml	250 ml	1L	5 L	10 L	20 L
BioPro SmartSep S10	10 µm	SSA0S10	~	/	~	~	~	~
BioPro SmartSep S20	20 µm	SSA0S20	~	/	~	~	~	~
BioPro SmartSep S30	30 µm	SSA0S30	~	~	~	~	•	~
BioPro S75	75 µm	SPA0S75	~	/	~	/	~	~

^{*} Larger or customised pack sizes are available on request.
** Conventional BioPro Q30/S30 (QAA0S30/SPA0S30) available on request.

