Small particle synthetic adsorbents for Insulin, peptide production

Polishing media Lineup : C8 Silica Alternative

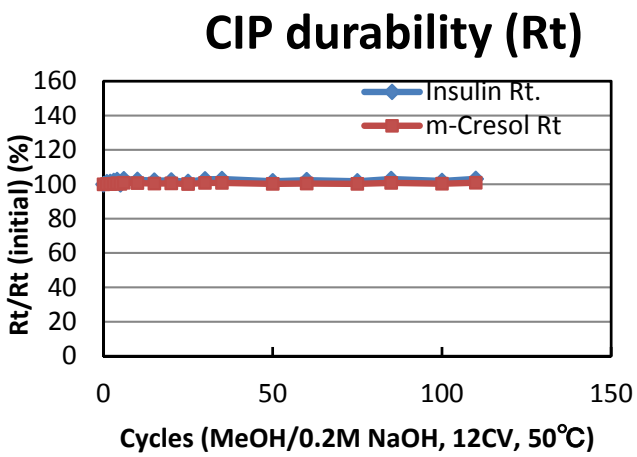
	CHP20/P10	CSP50/P10	CMG20/P10
Base polymer	Styrene	Styrene	Methacrylate
Average particle size	10 µm	10µm	10 µm
Reference			
Pore radius*	200 Å	150Å	200 Å
Surface Area*	760 m^2/g	690m^2/g	570 m^2/g

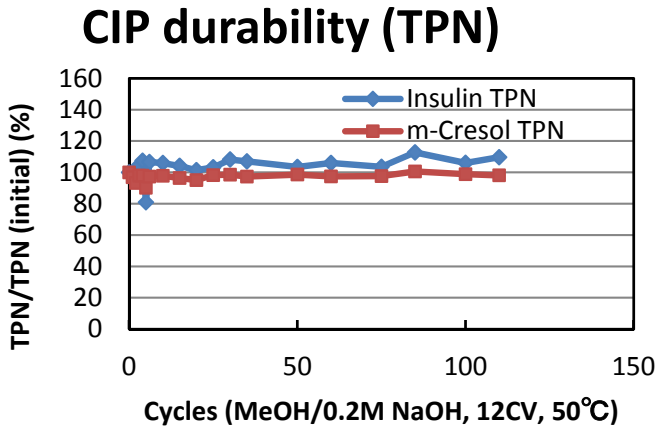
* Indicates referential, not specification, numbers

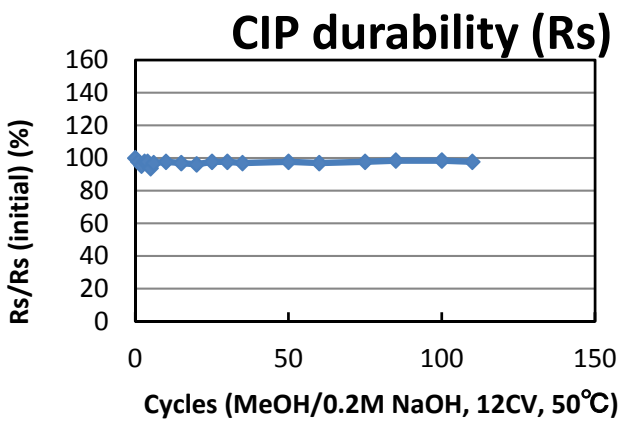
Advantage #1: Superior Alkaline Resistance

Mitsubishi resin = LONGER LIFE

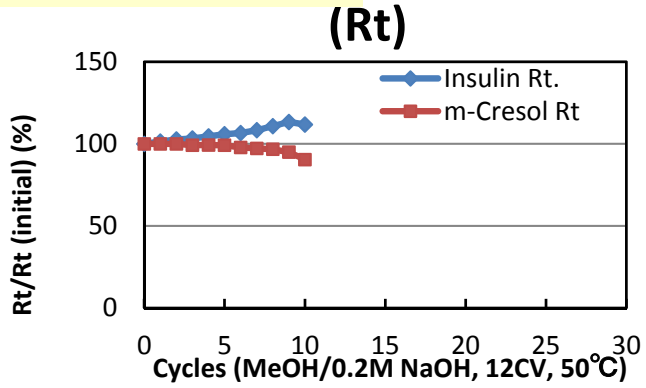
Mitsubishi (CHP20)

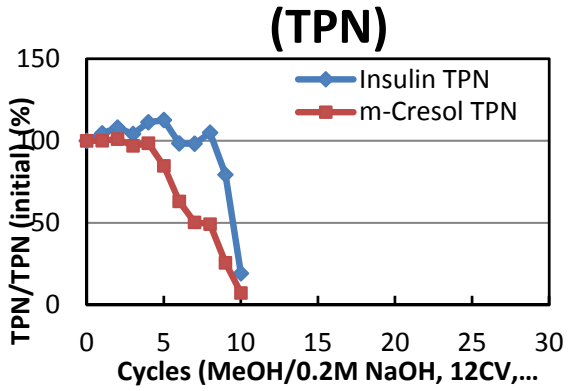


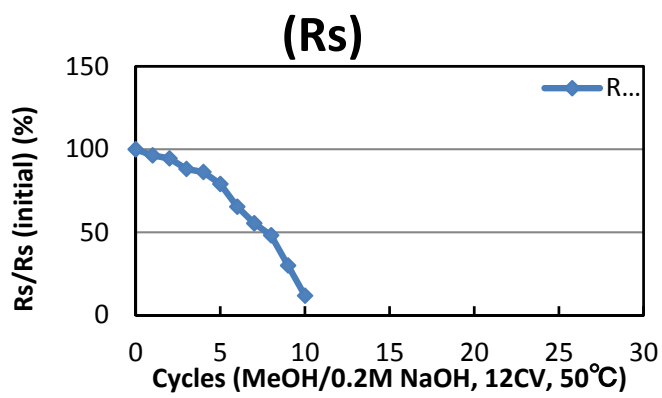




C8 Silica (Kromasil)







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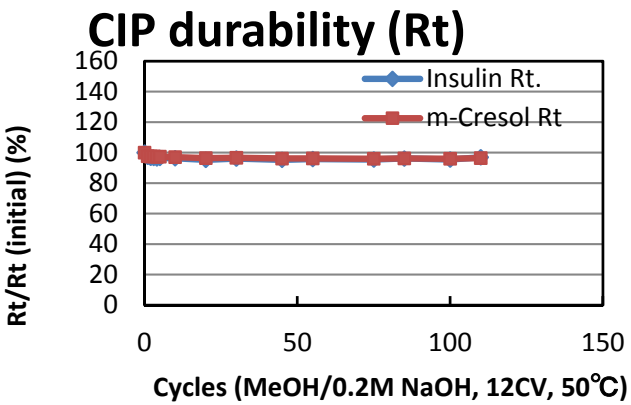
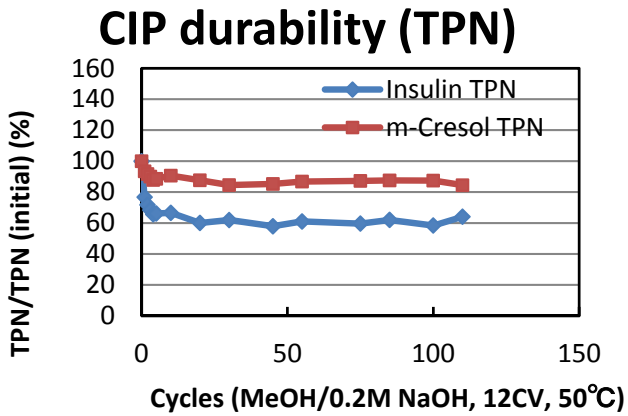
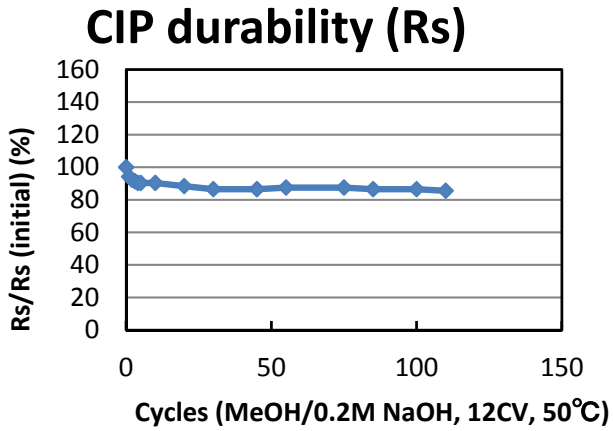
> Superior alkaline resistance

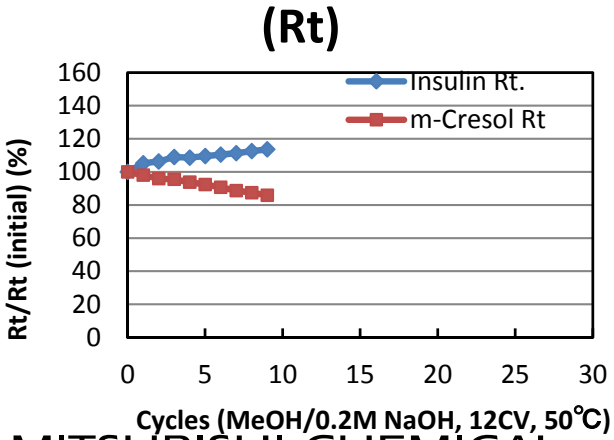
MCC resin (CMG20)

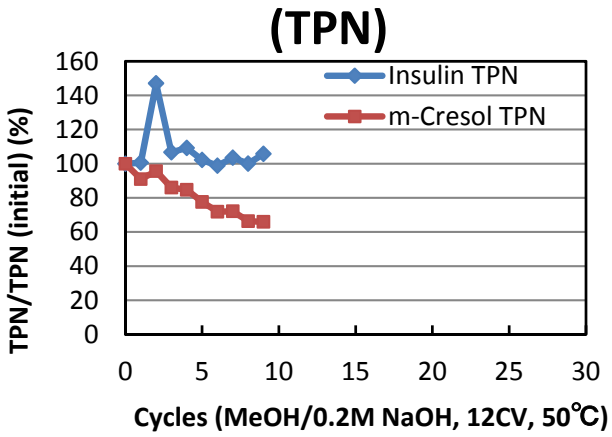


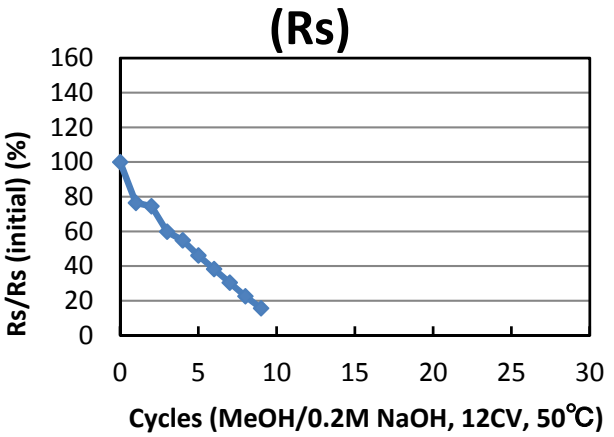




Silica (YMC Triart Prep C8-S)







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Advantage #2: Higher Surface Area

	CHP20/P10	CSP50/P10	CMG20/P10	AkzoNobel Kromasil C8
Base Matrix	**Styrene**	**Styrene**	**Methacrylate**	**Silica**
Pore size	400 Å	300 Å	400 Å	80 Å
Surface area	**760 m^2/g**	**690m^2/g**	**570 m^2/g**	**200 m^2/g**

Mitsubishi resins with higher surface area
= "higher" adsorption capacity

Advantage #3: Superior Performance
--- C8 Silica Alternative, CMG20 ---

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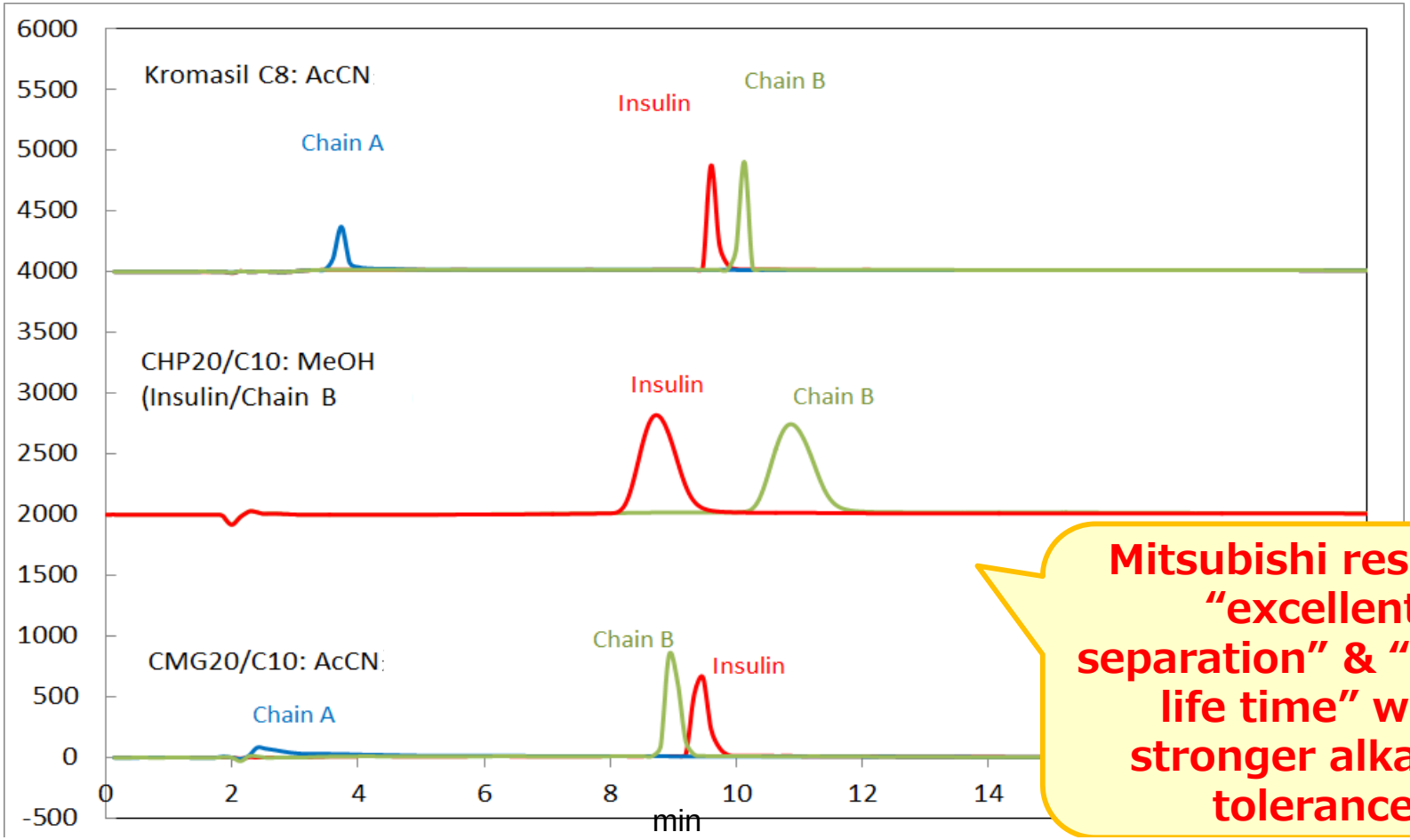
C8 Silica

MCC CHP20

MCC CMG20



Mitsubishi resins = "excellent separation" & "longer life time" with stronger alkaline tolerance

Conditions
Column : Kromasil C8 CMG20/C10
Column size : 150 x 4.6mmI.D. Flow rate : 1.0ml/min Eluent A): water/TFA = 100/0.1 B): acetonitrile/TFA = 100/0.1
Gradient : 20-60%B over 20min Injection : 10µL (1mg/mL) Temperature : 40℃ Detection : UV 214nm
Sample : 1, Insulin bovine 2, Insulin Chain A Oxidized ammonium salt from bovine pancreas
3, Insulin Chain B Oxidized from bovine pancreas
Column : CHP20/C10, 150 x 4.6mmI.D.
Flow rate : 1.0ml/min Eluent A): : water/TFA = 100/0.1 B): MeOH/TFA = 100/0.1
Gradient : 60-90%B over 20min Injection : 10µL (0.5mg/mL) Temperature : 40℃ Detection : UV 220nm

Advantage #3: Superior Performance
--- C8 Silica Alternative, CHP20 & CMG20 ---

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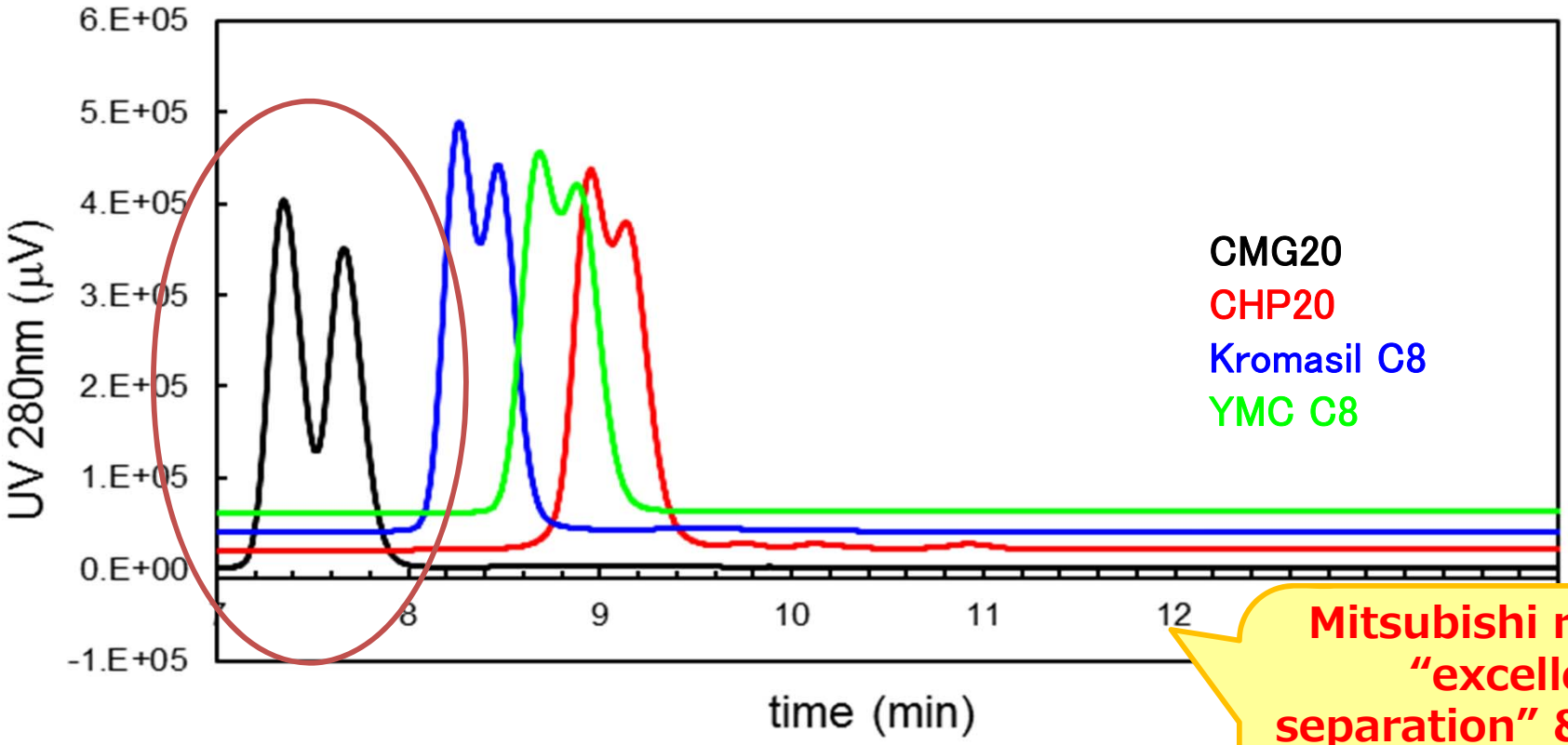

Mitsubishi resins = "excellent separation" & "longer life time" with stronger alkaline tolerance

Size: 150mm*4.6mm
Eluent A: H2O / AN =9/1 (0.2%-H3PO4)
Eluent B: H2O / AN =1/1 (0.2%-H3PO4)
Flow rate: 1.0ml/min
Gradient: Bconc 30%----100% /20min,2min hold
Column temp: 40C UV: 280nm
Sample: A21 desamido 40% in Insulin / 1mg/mL Injection: 10ul

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Advantage #4: Customize resin
--- CSP50, CHP20 & CMG20 ---

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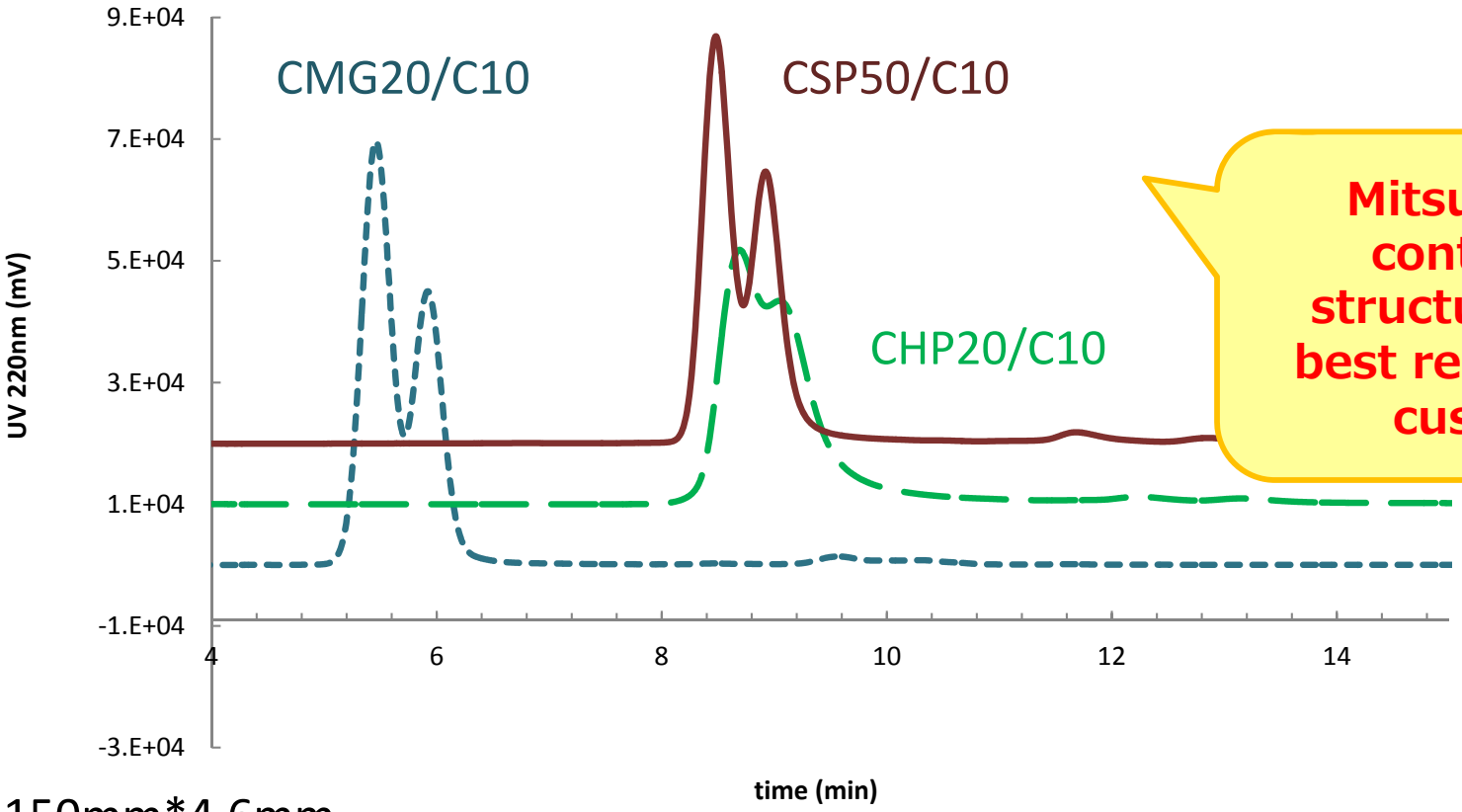

Mitsubishi can control pore structure → offer best resin for each customers

Size: 150mm*4.6mm
Eluent A: 0.2M CH3COONH4+0.5M CH3COOH / AN =9/1
Eluent B: 0.2M CH3COONH4+0.5M CH3COOH / AN =1/1
Flow rate: 1.0ml/min
Gradient: Bconc 40%----80% /20min,2min hold
Column temp: 40C UV: 280nm
Sample: A21 desamido 40% in Insulin / 5mg/mL Injection: 10ul

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Comparison of Insulin separation

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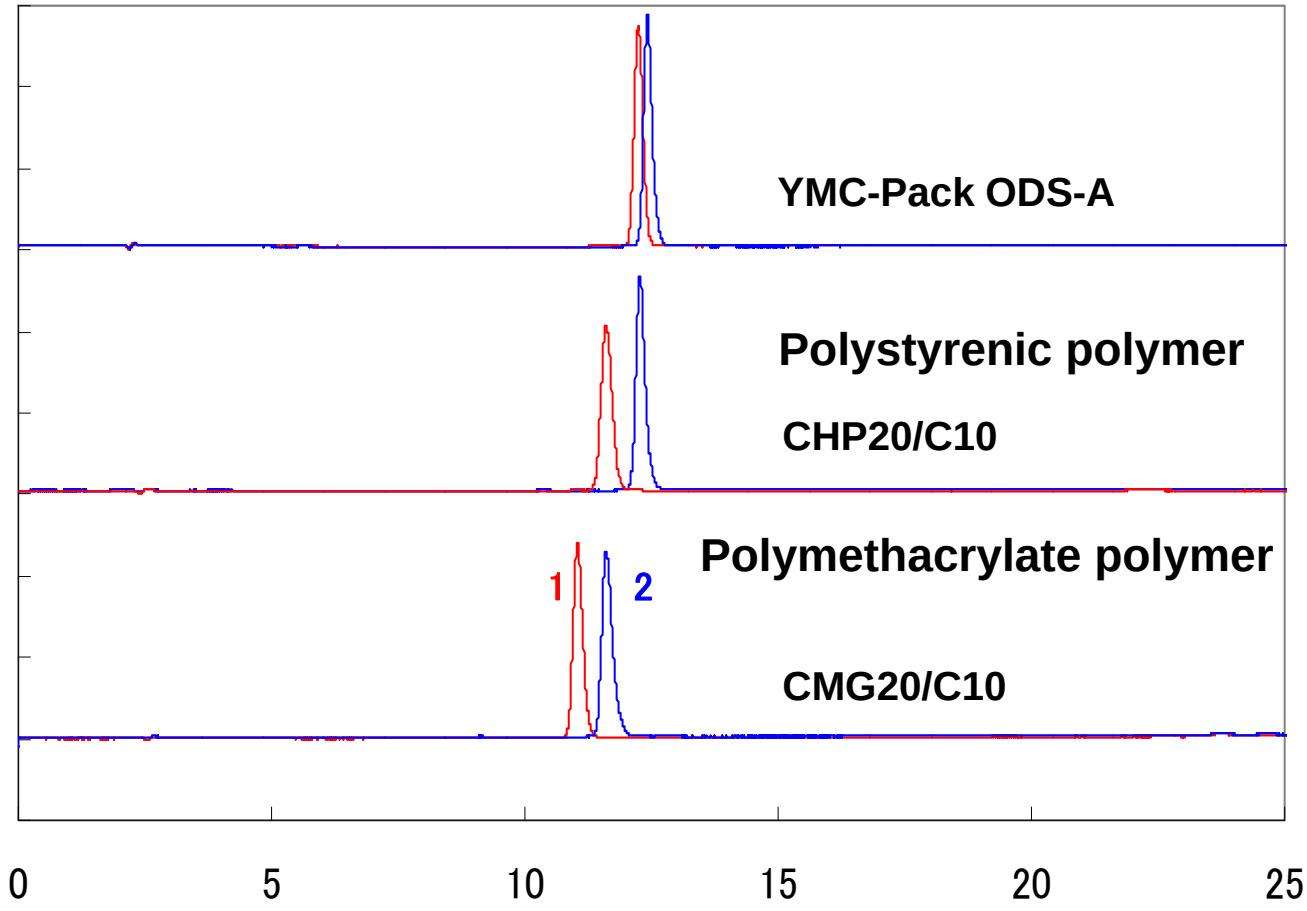

Conditions

Column : ① **YMC-Pack ODS-A**
② **CHP20/C10**
③ **CMG20/C10**
Column size : 150 x 4.6mmI.D.
Flow rate : 1.0ml/min
Eluent A) : water/TFA = 100/0.1
B) : acetonitrile/TFA = 100/0.1
Gradient : 10-60%B over 25min
Sample : **1** Insulin glargine
2 Insulin human recombinant
Injection : 10µL (1mg/mL)
Temperature : 40℃
Detection : UV 280nm

Polymer media showed superior performance for Insulin separation

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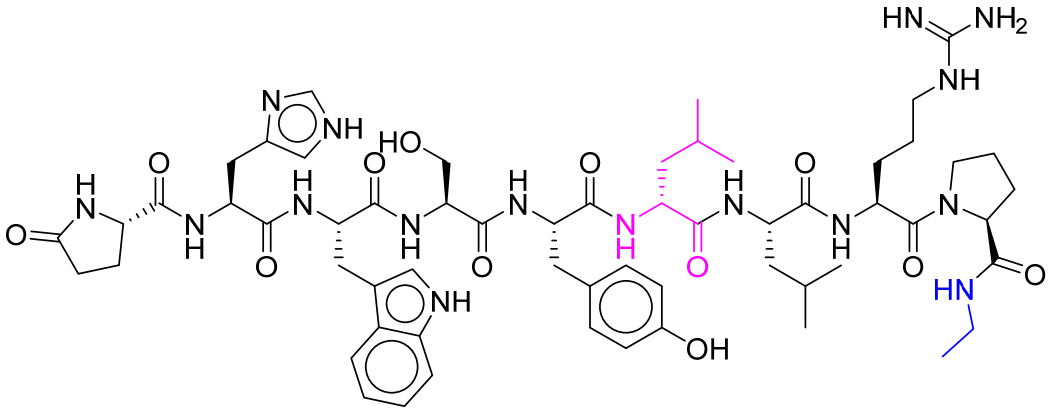
Chemical structure of Leuprorelin and related peptides

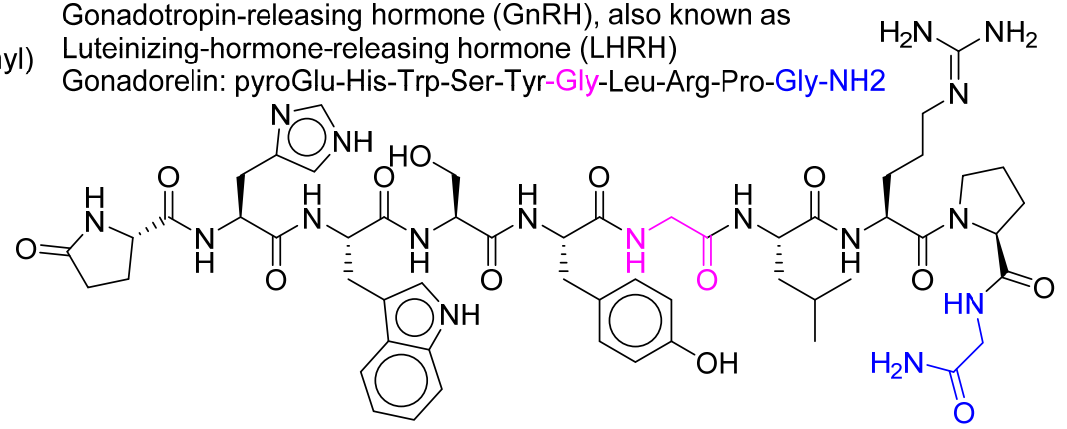
LH-RH(Luteinizing hormone and similar)

- Leuplin is medicine for prostate and breast cancer.

Leuprorelin (INN) or leuprolide acetate (USAN) is a GnRH analog.
Proper Sequence: Pyr-His-Trp-Ser-Tyr-D-Leu-Leu-Arg-Pro-NHEt (Pyr = L-Pyroglutamyl)

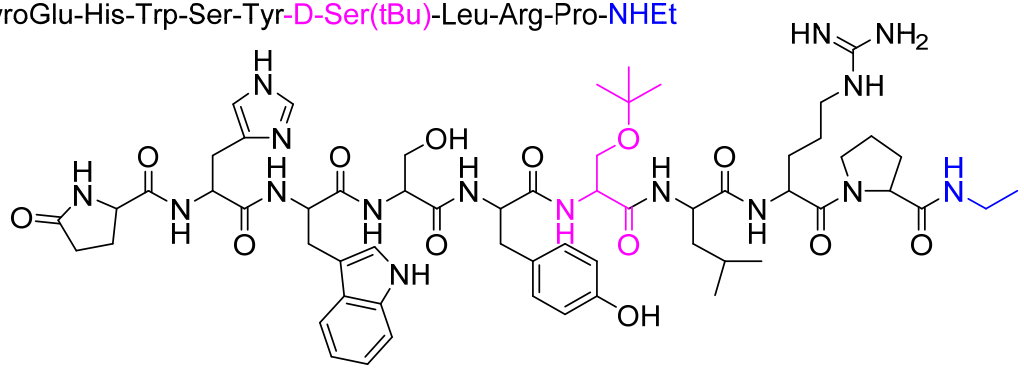


Gonadotropin-releasing hormone (GnRH), also known as
Luteinizing-hormone-releasing hormone (LHRH)
Gonadorelin: pyroGlu-His-Trp-Ser-Tyr-Gly-Leu-Arg-Pro-Gly-NH2

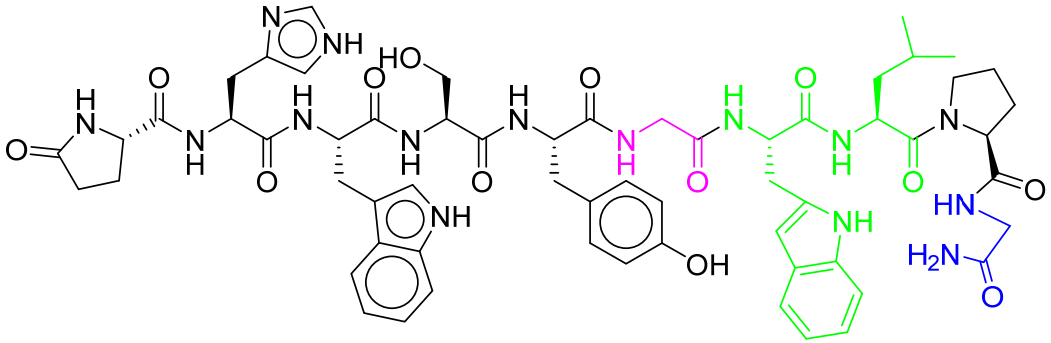


Arg (pI:10.8) - Try (pI: 5.9)

Buserelin: GnRH agonist
pyroGlu-His-Trp-Ser-Tyr-D-Ser(tBu)-Leu-Arg-Pro-NHEt



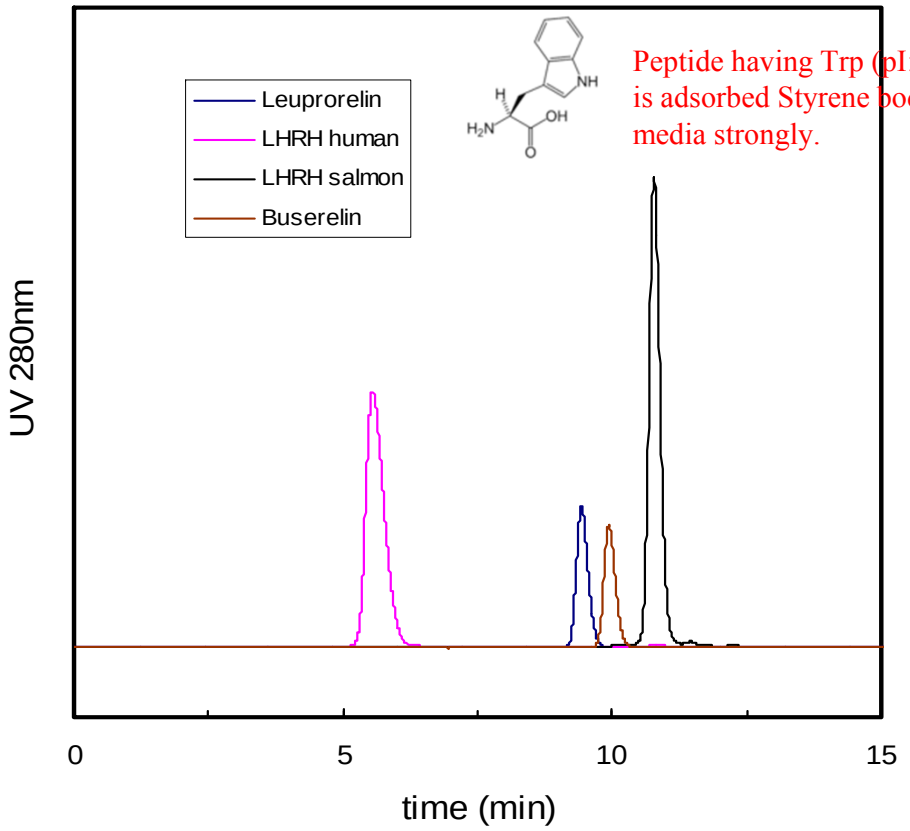
Salmon LHRH: pyroGlu-His-Trp-Ser-Tyr-Gly-Trp-Leu-Pro-Gly-NH2



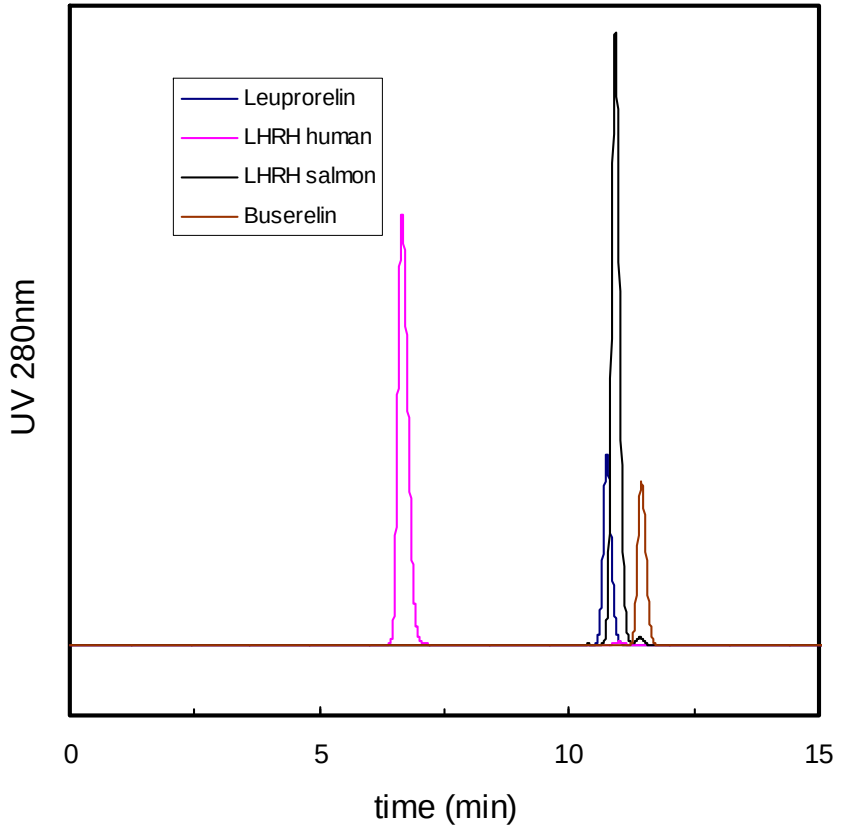
Comparison of Leuplin separation

- LH-RH(Luteinizing hormone) and similar
  - Methacrylate CMG20/C10 is superior peptide separation than ODS.

CMG20/C10 (Polymethacrylate 10μm)



ODS (10μm)



Conditions: Column size, 150 x 4.6mmI.D.; Flow rate, 1.0ml/min;
Eluent A, 0.1% TFA; Eluent B, 0.1% TFA in AcCN; Gradient, 20-60%B over 20min;
Sample concentration, 1mg/ml; Injection, 10μl;
Temperature, 40deg-C; Detection, UV 280nm.

Protein separation

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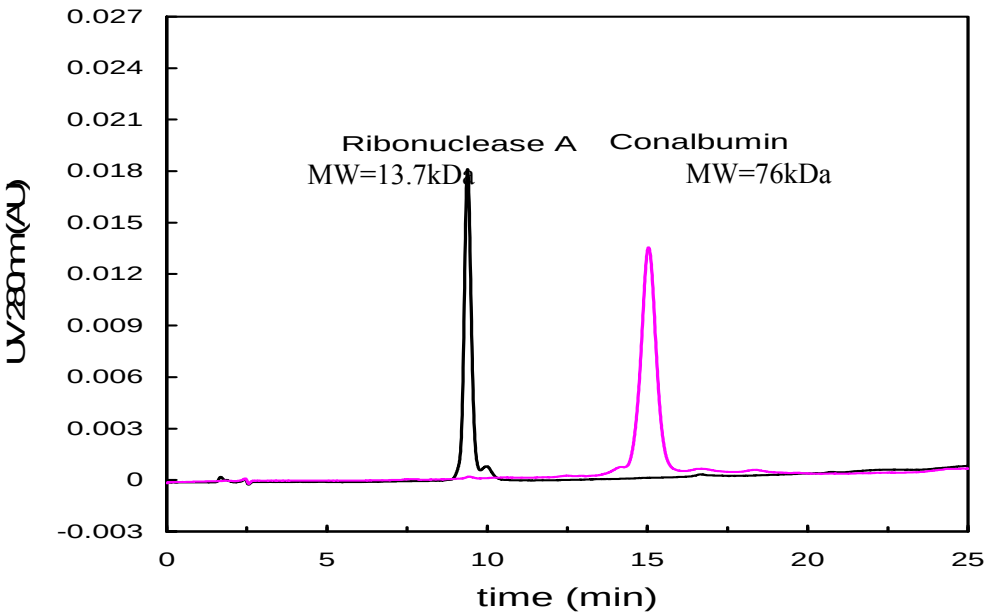
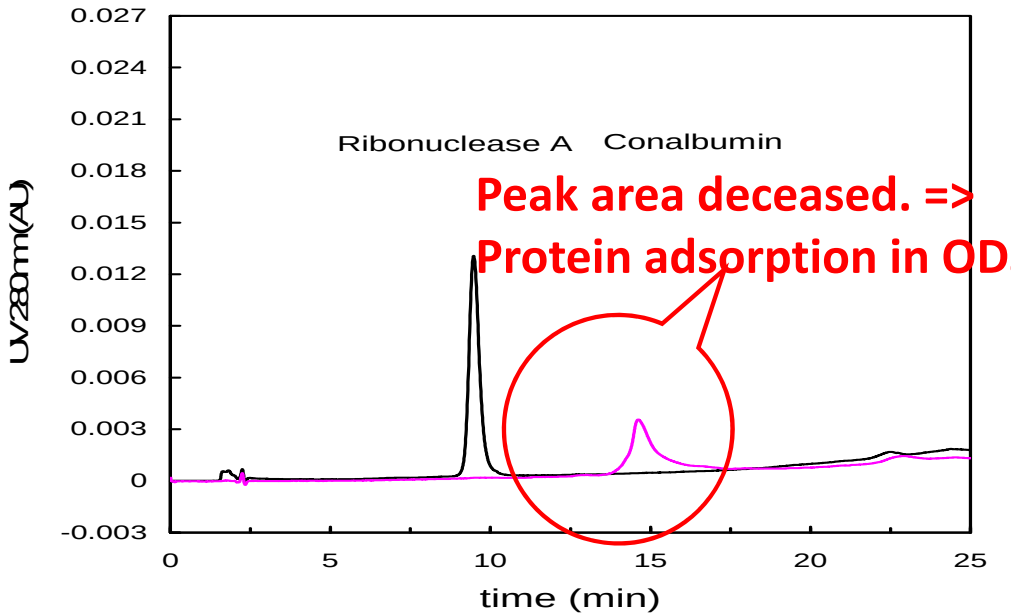
(A) CHP20/C10 10μm



(B) ODS 10μm



Separation of proteins on uniform sized 10μm polystyrenic adsorbent and conventional 10μm ODS.

Column size: 150 x 4.6mm I.D.; Flow rate: 1.00ml/min.
Eluent A, 0.1% TFA; Eluent B, 0.1% TFA in AcCN
Gradient, 20%B - 60%B over 20min; Detection, UV 280nm;
Samples, Ribonuclease A and Conalbumin 2mg/ml; Injection, 10μl

No reversible adsorption was seen in CHP20/C04

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