

# Stability of TOYOPEARL® Ion Exchange and Hydrophobic Interaction Chromatography Resins Stored in 2% Benzyl Alcohol

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PERFORMANCE DATA

## Introduction

Traditionally 20% ethanol has been the preservative of choice as a storage solution for chromatography media. However, more stringent safety requirements are driving the demand for an alternative since large quantities of ethanol may be viewed as potentially hazardous. This is becoming more common as process scale chromatography columns increase in size and volume.

Benzyl alcohol is a commonly used preservative in the pharmaceutical industry. It is soluble in water up to approximately 40,000 ppm (4%), though it is typically used at much lower concentrations as a preservative in parenteral therapeutics. Benzyl alcohol solutions are microbiocidal, but are not considered sanitizing agents. Benzyl alcohol is non-flammable, inexpensive, and has fewer regulatory issues concerning its disposal than solutions containing ethanol.

A 2% solution of benzyl alcohol in water has been identified as a suitable alternative to 20% ethanol as a preservative in resin storage solutions. This note evaluates the stability of TOYOPEARL Ion Exchange (IEC) and Hydrophobic Interaction Chromatography (HIC) resins stored in a 2% benzyl alcohol solution.

TOYOPEARL chromatography media are hydroxylated methacrylic polymer resins and are made commercially in many different pore sizes and particle diameters. The general properties of the TOYOPEARL IEC and HIC resins that were evaluated in this study are detailed in [Table 1](#). Together, these eight products serve as a representative sample of all TOYOPEARL resins that may be stored in 2% benzyl alcohol solution as an alternative to 20% ethanol.

**Table 1.** Properties of TOYOPEARL Resins Used in this Study

Resin	Mode	Ligand	Particle Size (µm)	Pore Size (nm)
TOYOPEARL Butyl-650M	HIC	Butyl	65	100
TOYOPEARL Phenyl-650M	HIC	Phenyl	65	100
TOYOPEARL SuperQ-650M	AEX	Quaternary Amine	65	100
TOYOPEARL SP-650M	CEX	Sulfopropyl	65	100
TOYOPEARL GigaCap® S-650M	CEX	Sulfonic Acid	75	100
TOYOPEARL GigaCap CM-650M	CEX	Carboxymethyl	75	100
TOYOPEARL GigaCap Q-650M	AEX	Quaternary Amine	75	100
TOYOPEARL Q-600C AR	AEX	Quaternary Amine	100	75

## Experimental Conditions/Results

This study was executed to demonstrate the long term stability of TOYOPEARL IEC and HIC resins after storage in a 2% benzyl alcohol solution.

Samples of the TOYOPEARL resins tested were prepared by adding aqueous 2% benzyl alcohol to 500 mL of suction filtered resin producing a 1,000 mL, 50% resin slurry.

The resin and benzyl alcohol mixture was transferred to a 1,000 mL polyethylene bottle and stored at ambient temperature. Samples were tested at the following intervals: 0 months (pre-storage), three and six months, one and two years.

At the appropriate intervals, the samples of the stored resins were washed with sufficient volumes of DI water to remove the 2% benzyl alcohol solution from the resin and evaluated as per the parameters on the Certificate of Analysis for each resin. The test results for each resin are shown in [Tables 2-9](#).

**Table 2.** Stability Test Results of TOYOPEARL Butyl-650M

Parameters	C of A Specifications	0 Months	3 Months	6 Months	1 Year	2 Year
Particle size distribution (%)	Min. 80 (40 - 90 µm)	90	91	91	92	92
Binding capacity (g/L)	30 - 50	35	34	34	33	34
Eluable matter (%)	Max. 0.2	0	0	0	0	0
Foreign substances (unobserved)	unobserved	unobserved	unobserved	unobserved	unobserved	unobserved
Bioburden (CFU/mL)	Max. 100	0	0	0	0	0
Endotoxin (EU/mL)	Max. 10.0	< 0.2	< 0.2	< 0.2	< 0.2	< 0.2
<b>Protein elution volume</b>						
ribonuclease A (mL)	30 - 34	34	34	33	33	33
lysozyme (mL)	49 - 57	50	50	50	50	50



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**Table 3.** Stability Test Results of TOYOPEARL Phenyl-650M

Parameters	C of A Specifications	0 Months	3 Months	6 Months	1 Year	2 Year
Particle size distribution (%)	Min. 80 (40 - 90 $\mu$ m)	91	91	92	91	90
Binding capacity (g/L)	30 - 50	32	32	32	32	32
Eluable matter (%)	Max. 0.2	0	0	0	0	0
Foreign substances (unobserved)	unobserved	unobserved	unobserved	unobserved	unobserved	unobserved
Bioburden (CFU/mL)	Max. 100	0	0	0	0	0
Endotoxin (EU/mL)	Max. 10.0	< 0.2	< 0.2	< 0.2	< 0.2	< 0.2
<b>Protein elution volume</b>						
ribonuclease A (mL)	18.5 - 26.5	21.7	21.7	21.7	21.9	21.2
lysozyme (mL)	31.0 - 39.0	36.9	36.8	36	36.7	36.2
$\alpha$ -chymotrypsinogen A (mL)	46.0 - 54.0	50.8	51	50.4	50.6	49.7

**Table 4.** Stability Test Results of TOYOPEARL SuperQ-650M

Parameters	C of A Specifications	0 Months	3 Months	6 Months	1 Year	2 Year
Exclusion limit	(1.05 - 1.95) $\times 10^4$	1.86 $\times 10^4$	1.84 $\times 10^4$	1.86 $\times 10^4$	1.83 $\times 10^4$	1.79 $\times 10^4$
Pressure drop (kPa)	Max. 20	5	3	4	6	
Particle size distribution (%)	Min. 80 (40 - 90 $\mu$ m)	94	95	95	95	94
Ion exchange capacity (eq/L)	0.20 - 0.30	0.26	0.26	0.25	0.26	0.27
Binding capacity (g/L)	105 - 155	120	119	116	118	119
Eluable matter (%)	Max. 0.2	0	0	0	0.1	0
Foreign substance	unobserved					
Bioburden (CFU/mL)	Max. 100	0	0	0	0	0
Endotoxin (EU/mL)	Max. 10.0	< 0.2	< 0.2	< 0.2	< 0.3	< 0.2

**Table 5.** Stability Test Results of TOYOPEARL SP-650M

Parameters	C of A Specifications	0 Months	3 Months	6 Months	1 Year	2 Year
Exclusion limit	(0.70 - 1.30) $\times 10^5$	0.92 $\times 10^6$	0.92 $\times 10^6$	0.92 $\times 10^6$	0.92 $\times 10^6$	0.92 $\times 10^6$
Particle size distribution (%)	Min. 80 (40 - 90 $\mu$ m)	94	94	94	94	93
Ion exchange capacity (eq/L)	0.13 - 0.17	0.17	0.17	0.18	0.18	0.18
Binding capacity (g/L)	40 - 60	43	43	42	39	43
Eluable matter (%)	Max. 0.2	0	0	0	0	0
Foreign substances	unobserved	unobserved	unobserved	unobserved	unobserved	unobserved
Bioburden (CFU/mL)	Max. 100	0	0	0	0	0
Endotoxin (EU/mL)	Max. 10.0	< 0.2	< 0.2	< 0.2	< 0.2	< 0.2
<b>Protein elution volume</b>						
trypsinogen A (mL)	7.5 - 12.5	9.4	9.5	9.1	9.1	9.7
ribonuclease A (mL)	9.5 - 14.5	11.8	11.9	11.3	11.1	12.2
$\alpha$ -chymotrypsinogen A (mL)	13.5 - 18.5	15.9	15.9	15.4	14.9	16.2
cytochrome C (mL)	17.0 - 23.0	20.7	20.8	20.4	19.4	20.8

**Table 6.** Stability Test Results of TOYOPEARL GigaCap S-650M

Parameters	C of A Specifications	0 Months	3 Months	6 Months	1 Year	2 Year
Particle size distribution (%)	Min. 80 (50 - 100 $\mu$ m)	98	98	98	98	98
Ion exchange capacity (eq/L)	0.10 - 0.20	0.16	0.16	0.17	0.16	0.16
Binding capacity (g/L)	136 - 176	152	152	152	150	155
Eluable matter (%)	Max. 0.2	0.2	0.2	0.1	0.1	0.1
Foreign substances	Max. 6	unobserved	unobserved	unobserved	unobserved	4
Bioburden (CFU/mL)	Max. 100	0	0	0	0	0
Endotoxin (EU/mL)	Max. 10.0	< 0.2	< 0.2	< 0.2	< 0.2	< 0.2

**Table 7.** Stability Test Results of TOYOPEARL GigaCap CM-650M

Parameters	C of A Specifications	0 Months	3 Months	6 Months	1 Year	2 Year
Particle size distribution (%)	Min. 80 (50 - 100 µm)	91	92	92	89	90
Ion exchange capacity (eq/L)	0.17 - 0.28	0.23	0.23	0.23	0.23	0.22
Binding capacity (g/L)	Min. 110	129	128	129	129	132
Eluable matter (%)	Max. 0.2	0.2	0.3	0.3	0.2	0.2
Foreign substances	Max. 6	unobserved	unobserved	unobserved	1	2
Bioburden (CFU/mL)	Max. 100	0	0	0	0	0
Endotoxin (EU/mL)	Max. 10.0	< 0.2	< 0.2	< 0.2	< 0.2	< 0.2

**Table 8.** Stability Test Results of TOYOPEARL GigaCap Q-650M

Parameters	C of A Specifications	0 Months	3 Months	6 Months	1 Year	2 Year
Particle size distribution (%)	Min. 80 (50 - 100 µm)	97	97	97	97	97
Ion exchange capacity (eq/L)	0.10 - 0.20	0.12	0.12	0.12	0.12	0.11
Binding capacity (g/L)	Min. 162	171	171	165	168	167
Eluable matter (%)	Max. 0.2	0	0	0.1	0.1	0.1
Foreign substances	Max. 6	unobserved	unobserved	unobserved	unobserved	unobserved
Bioburden (CFU/mL)	Max. 100	0	0	0	0	0
Endotoxin (EU/mL)	Max. 10.0	< 0.2	< 0.2	< 0.2	< 0.2	< 0.2

**Table 9.** Stability Test Results of TOYOPEARL Q-600C AR

Parameters	C of A Specifications	0 Months	3 Months	6 Months	1 Year	2 Year
Particle size distribution (%)	Min. 90 (50 - 150 µm)	100	100	100	100	100
Ion exchange capacity (eq/L)	0.14 - 0.23	0.17	0.17	0.17	0.17	0.18
Binding capacity (g/L)	Min. 120	145	148	137	139	152
Eluable matter (%)	Max. 0.2	0.1	0	0	0.1	0
Foreign substances	Max. 6	unobserved	unobserved	unobserved	4	unobserved
Bioburden (CFU/mL)	Max. 100	0	0	0	0	0
Endotoxin (EU/mL)	Max. 10.0	< 0.2	1.8	0.5	0.3	0.5

## Conclusions

TOYOPEARL IEC and HIC resins are stable for up to 2 years when stored in an aqueous 2% benzyl alcohol solution at ambient temperature.

The TOYOPEARL resins evaluated for this study showed no appreciable loss in capacity or performance as a result of being stored in 2% benzyl alcohol. As such, benzyl alcohol can be used as an alternative storage solution to 20% ethanol with TOYOPEARL IEC and HIC resins.

Although TOYOPEARL HIC resins are stable in 2% benzyl alcohol, its use as a storage solution is not recommended as the volume of buffer necessary to adequately remove 2% benzyl alcohol from TOYOPEARL HIC resins is not feasible for large scale chromatographic operations.

For additional information concerning the removal of 2% benzyl alcohol from TOYOPEARL resins, please request this instructional sheet: *Clearance of 2% Benzyl Alcohol from TOYOPEARL Resin*.

Please note: Customers wishing to store TOYOPEARL resins in 2% benzyl alcohol should evaluate resin performance post-storage to determine whether this method of resin storage is suitable for their intended use and particular application.

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