Bio-Works

APPLICATION NOTE

Platform for mAb purifications

Therapies based on monoclonal antibodies (mAbs) currently represent the largest and fastest developing biopharmaceutical market. The need for efficient mAb purification platforms is therefore fundamental. The three-step platform described in this application note is an effective strategy for mAb purifications, where most impurities are removed very early in the purification process and very pure final mAb products are obtained. This platform consists of three steps, all of which include pure agarose-based resins: a pre-treatment step with a multimodal high salt tolerant anion exchanger, a capture step with a protein A resin and a final polishing step with a cation exchanger.

Introduction

Monoclonal antibodies (mAbs) are important components in many different therapies due to their target specificities. This specificity also makes them important tools in biochemistry and molecular biology, especially in the diagnostics field. As of October 2020, 9 antibody therapeutics had been granted first approvals in the US and an additional 16 are in regulatory review[1]. The market size of the antibody market is expected to grow on a large scale during the forecast period (2019-2026)[2]. Therapeutic mAbs are subjected to very stringent purity requirements and there is high demand for efficient and economical purification processes.

Purification of mAbs or Fc-fusion proteins from mammalian host cells, such as Chinese Hamster Ovary (CHO), which today is the primary mAb expression system, is commonly performed with a three-step chromatographic purification process consisting of one capture step and two polishing steps. The main impurities that need to be removed are host cell nucleic acids, such as host cell DNA, RNA, host-cell proteins, viruses, and mAb aggregates. All these process-related impurities can be toxic in a pharmaceutical product and thus must be removed.

New three-step mAb purification platform; ECP

The chromatographic mAb purification platform described here is an alternative to the traditional CEP (capture-enhance-polish) setup and it is called ECP (enhance-capture-polish, or Enhanced Capture Process as it is often called).

WorkBeads™ affimAb is well suited as the protein A capture step (now as the second step) if high flow rates and pure mAb eluates are the primary focus. A multimodal high salt tolerant anionic exchange chromatography resin (AIEX), WorkBeads 40 TREN, is placed upstream of the capture step (the first step). It is used in flow through mode (FT) and here the majority of host cell DNA (HCD) and host cell proteins (HCP), as well as viruses will be removed. This upstream multimodal AIEX step is a combination of a pre-treatment step that is usually performed in bulk and an early polishing step that will remove many impurities early in the process. The final polishing step consists of a cation exchanger (CIEX) in binding-elution mode (BE) that will remove the remaining host cell proteins, potential protein A leakage and, importantly, the mAb aggregates.

Certain mAbs are more challenging to purify having a more complex impurity profile and then this proposed purification platform (see Figure 1) is especially beneficial due to the early removal of impurities. In this setup WorkBeads 40 TREN bridge the transition between the upstream and downstream processes. Using this platform for a mAb expressed in CHO cells generates a final mAb product with very high purity that will be described in detail below.

WorkBeads resins presented in this study are third-generation agarose resins with a very rigid structure based entirely on pure agarose. The resins are not grafted with dextran and hence more stable during effective CIP (cleaning-in-place) solutions, and there will be no leached dextran in the final target product.

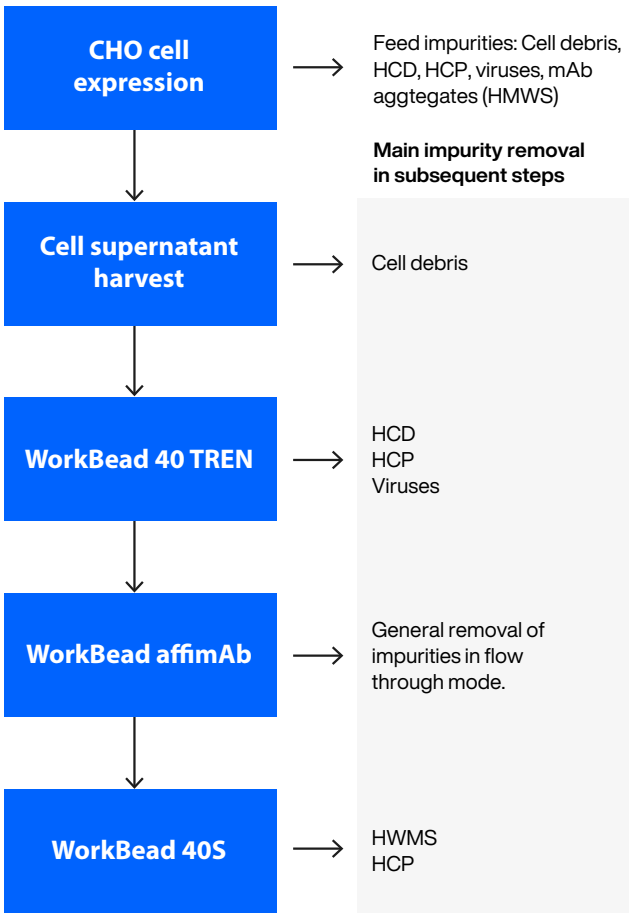

Figure 1. Three-step chromatographic purification platform consisting of WorkBeads 40 TREN, WorkBeads affimAb and WorkBeads 40S. The grey box to the right displays the major impurities removed in each subsequent step.

Step 1:
Pre-treatment of the feed on WorkBeads 40 TREN

One key advantage of employing WorkBeads 40 TREN as an upstream, feed cleaning step prior to the capture protein A step is the removal of nucleic acids (DNA and RNA) that create viscosity issues as well as interference with subsequent chromatographic steps[3,4]. The use of WorkBeads 40 TREN in flow through mode (for mAbs) will also not only facilitate removal of nucleic acids but also viruses, host cell proteins and other cell-derived impurities. Notice that the majority of mAbs are basic, and are thus mainly positively charged at neutral pH, and therefore do not bind to the resin.

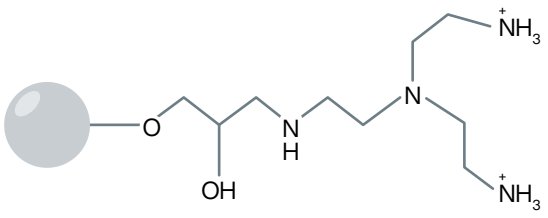

Figure 2. Structure of the ligand used in WorkBeads 40 TREN.

WorkBeads 40 TREN is a high salt tolerant multimodal AIEX resin that contains ligands based on Tris(2-aminoethyl)amine (TAEA). The ligands have two amine groups that are positively charged below approx. pH 9. WorkBeads 40 TREN has previously been shown to efficiently bind *e.g.* nucleic acids.

Virus removal

For biopharmaceutical processes that result in products for use in humans, virus clearance studies need to be conducted. Viruses in the final product can prove to be fatal, and therefore need to be removed in the purification process. In our proposed purification platform, this virus removal is performed in the first pre-treatment step using WorkBeads 40 TREN.

WorkBeads 40 TREN was packed in a 10×100 mm (7.9 mL) column and run using an ÄKTA™ system. The feed (clarified supernatant containing mAbs expressed from CHO cells) was spiked with two viruses, MVM and X-MuLV (which may be present in CHO cells), one at a time and in duplicates.

MVM, Minute Virus of Mice, is a small (18-26 nm) non-enveloped parvovirus and X-MuLV, Xenotropic Murine Leukemia Virus is a moderately large (80-120 nm) enveloped retrovirus. The virus titers pre- and post-purification on WorkBeads 40 TREN were measured and compared to control samples that showed the amount of virus applied to the columns. A logarithmic reduction value (LRV) was calculated. This work was performed by Vironova Biosafety AB, Stockholm, Sweden.

Prior to loading the feed, the packed columns were equilibrated with 20 column volumes (CV) 50 mM sodium phosphate, pH 7.4. 40 mL feed spiked with the respective virus was then loaded at a flow rate of 150 cm/h (residence time, 4 minutes). The flow through was collected and analyzed for virus content.

The capacity of WorkBeads 40 TREN resin for reduction of virus in the flow-through was high for both viruses tested. The average logarithmic reduction factor (LRV) of the parvovirus MVM in two runs was 4.89 Log10 TCID50 units which is deemed effective removal. The average LRV of X-MuLV in two runs was >3.67 Log10 TCID50 units. This is moderately effective to effective removal. See Table 1 below.

Table 1. Virus removal using WorkBeads 40 TREN.

Virus type	Reduction of MVM (Log_{10} $TCID_{50}$)	Reduction of X-MuLV (Log_{10} $TCID_{50}$)
Run 1	4.87	3.44
Run 2	4.91	3.82
Average	4.9	3.7

Host cell DNA, cell proteins and HMWS removal

To study the positive effects of WorkBeads 40 TREN as a pre-treatment also for removal of host cell DNA, cell proteins and high molecular weight species (HMWS), a prepacked GoBio™ Mini TREN 5 mL column was placed upstream of the WorkBeads affimAb column.

Inline purifications, where both the WorkBeads 40 TREN column and the WorkBeads affimAb column were positioned in series, as well as offline purifications, where the flow through (FT) was collected and analyzed after the WorkBeads 40 TREN column before loading onto the WorkBeads affimAb column, were performed.

Two different batches of a mAb expressed in CHO cells were used for inline (Batch 1) *vs.* offline (Batch 2) purifications. The inline setup is more suitable for lab-scale purifications, whereas the offline setup is more suitable in production scale purifications. The expression level of IgG was approximately 1 mg/mL for both batches.

For the inline purification, clarified CHO cell supernatant was loaded onto GoBio Mini TREN 5 mL in FT mode and thereafter directly captured on a column packed with WorkBeads affimAb. The GoBio Mini TREN column was disconnected and the WorkBeads affimAb column was washed prior to elution. See Table 2 for running conditions and experimental setup. The flow through was subsequently analyzed for host cell DNA (HCD) and host cell protein (HCP) contents and compared to an experiment conducted under identical conditions but in which the GoBio Mini TREN step was excluded. The elution conditions used in this purification had been optimized prior to start (see "Optimization of elution buffer").

For the offline purifications, clarified CHO cell supernatant was loaded onto two GoBio Mini TREN 5 mL connected in series. All flow through material was collected, analyzed and compared to the starting feed for impurity removal prior to loading on the WorkBeads affimAb column. See Table 2 for a description of running conditions and experimental setup.

As seen below, 99% of host cell DNA (HCD) was removed with GoBio Mini TREN using both methods, but the removal of HCP differed between the two experimental methods and batches with a span between 40–95%. Notable is that the HCP level in the two CHO feed batches varied from 0.1 mg HCP/mL (Batch 2) to 0.43 mg HCP/mL (Batch 1), showing two different HCP profiles.

Removal of HCD was measured using Quant-iT™ PicoGreen™ dsDNA assay kit (Invitrogen), and HCP removal was measured using CHO HCP ELISA 3G kit (Cygnus). The eluted mAbs post WorkBeads TREN were also analyzed with an analytical size exclusion chromatography column (SEC) showing the removal of high-molecular weight species (HMWS), see Figure 3.

Column: Superdex™ 200 Increase 10/300 GL (Cytiva)
Running buffer: PBS, pH 7.4
Sample: 50 µl CHO cell supernatant, pre- and post-treatment with WorkBeads 40 TREN
Flow rate: 0.4 mL/min

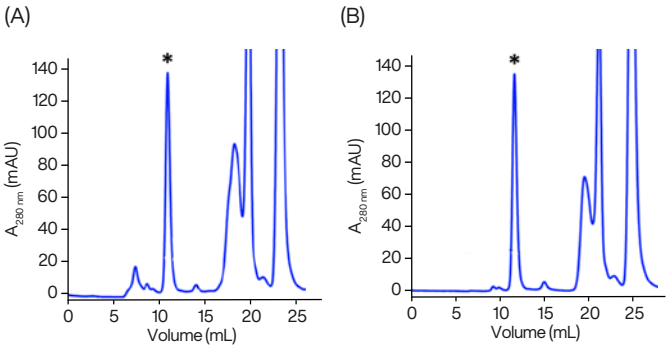

Figure 3. Analytical SEC profiles of CHO cell supernatants. (A) Before pre-treatment with WorkBeads 40 TREN and after (B). The asterisk (*) highlights the target mAb.

Table 2. Properties of WorkBeads 40 TREN.

	Inline	Offline
Columns	GoBio Mini TREN 5 mL + WorkBeads affimAb, 3.4 mL	2 × GoBio Mini TREN 5 mL
Binding buffer	50 mM sodium phosphate, pH 7.4	50 mM sodium phosphate, pH 7.4
Elution buffer	50 mM sodium phosphate, 1 M NaCl, pH 7.4	50 mM sodium phosphate, 1 M NaCl, pH 7.4
Elution gradient	5 CV 100% elution buffer in one step (to remove bound impurities)	5 CV 100% elution buffer in one step (to remove bound impurities)
Flow rate	0.6 mL/min	0.9 mL/min
Sample volume	20 mL	70 mL
Batch # (HCD/HCP levels)	Batch 1: 8 µg HCD/mL, 0.43 mg HCP/mL	Batch 2: 6 µg HCD/mL, 0.1 mg HCP/mL
Collected material for analysis	Flow through after WorkBeads affimAb[1]	Flow through containing mAbs was collected[2]

[1] Flow through was analyzed for HCD and HCP levels.
[2] Flow through was analyzed for HCD and HCP levels. This flow through contained mAbs to be further purified in next step

This means that the majority of HCD, HMWS and HCP were adsorbed to the WorkBeads 40 TREN and thus removed from the sample before it was loaded onto the WorkBeads affimAb column. No significant yield loss of mAbs was detected. The HCP and HCD results of the mAb purifications are shown in Figure 4 where the feed values are set to 1.

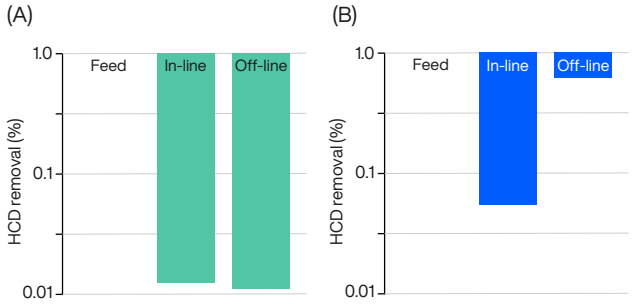

Figure 4. Removal of host cell impurities. (A) HCD removal pre- and post-WorkBeads 40 TREN for inline *vs.* offline purifications. Feed value is set to 1. (B) HCP removal pre- and post-WorkBeads 40 TREN for inline *vs.* offline purifications. Feed value is set to 1.

Step 2:
Capture on WorkBeads affimAb

Currently, the most widely used mAb purification technique is affinity chromatography with protein A resins. This technique gives high yield of antibodies with a relative high purity for most mAbs. WorkBeads affimAb is an alkali-stable protein A resin from Bio-Works designed for efficient mAb purification. The high binding capacity at high flow rates (short residence times), allow high productivity in downstream bioprocesses. This resin also allows a greater purity of eluted mAbs from cell supernatants than market-leading resins, see figures 5 A-B below.

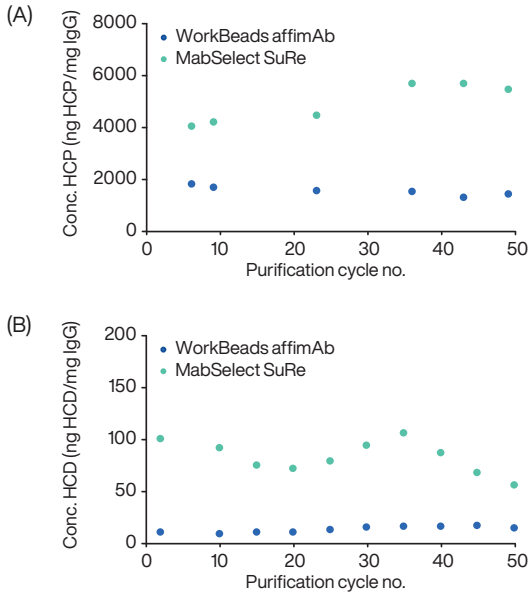

Figure 5. HCP and HCD levels in eluates in 50 consecutive purification cycles. 18 mL CHO cell supernatant was loaded onto a 6.6 x 50 mm column packed with either WorkBeads affimAb (blue) or MabSelect SuRe™ (Cytiva) (red) and eluted with 100 mM glycine-HCl, pH 2.7. Eluted mAbs were analyzed using ELISA and PicoGreen assays.

Optimization of elution conditions

Prior to conducting the experiments, optimization of the elution conditions was performed. IgG is generally eluted from a protein A column using, for example, a glycine or citrate buffer at a pH around 3.0–3.5. An acidic pH is needed to break the strong interaction between protein A and antibodies for elution, but this may have a negative impact. Due to conformational changes that may occur within the antibodies at low pH, it tends to cause aggregation of the antibodies. This is problematic since aggregation can lead to inactivation of the protein or to immunogenic responses. Therefore, as mild an elution condition (high pH) as possible is desired.

To investigate the optimal elution pH for this mAb, different elution buffers with a pH range from 2.7 to 4.2 were tested. As seen in figure 6, the harsher elution conditions with a pH of 2.7–3.0 generated the peak with the highest resolution and yield, whereas milder elution conditions led to peak broadening and loss in yield. Based on these experiments the following two elution buffers were used, 100 mM glycine-HCl, pH 2.7, and 50 mM sodium citrate, pH 3.0.

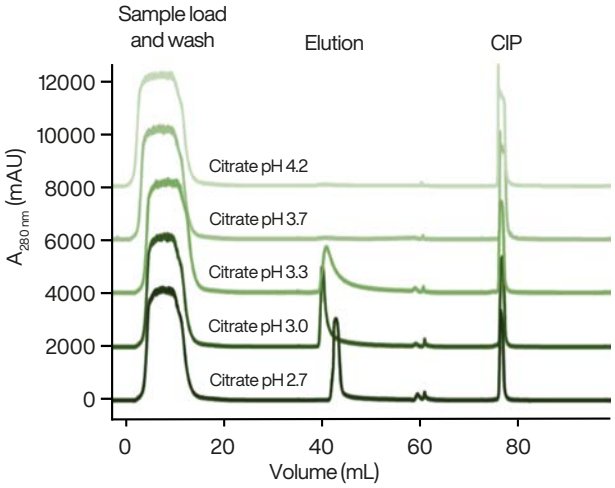

Figure 6. pH dependence of mAb elution, a pre-study of different elution buffers in the pH range of 2.7–4.2.

Inline *vs.* offline mAb purifications

Figure 7 shows the chromatogram from the inline purification, where the feed was first pre-treated with WorkBeads 40 TREN for impurity removal before capture on WorkBeads affimAb without any fractionation between the two steps. After a 20 CV wash with binding buffer, the mAbs were eluted in a 10 CV step with 100 mM glycine-HCl, pH 2.7. The collected mAbs were analyzed for both HCD and HCP removal.

Columns:	1. GoBio Mini TREN 5 mL 2. WorkBeads affimAb, 3.4 mL
Binding buffer:	50 mM sodium phosphate, pH 7.4
Elution buffer:	100 mM glycine-HCl, pH 2.7
Sample:	20 mL CHO cell supernatant
Flow rate:	Column 1: 0.6 mL/min, 25 cm/h Column 2: 0.6 mL/min, 100 cm/h
Gradient:	100% elution buffer in 10 CV

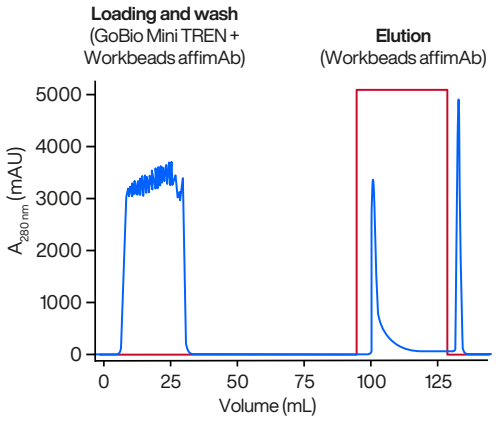

Figure 7. Chromatogram of mAb purification using GoBio Mini TREN and WorkBeads affimAb connected in series (inline). UV trace at 280 nm (blue) and concentration of elution buffer (red).

For the offline purification, the following was conducted: 100 mL of collected pre-treated mAbs (flow through WorkBeads 40 TREN column) was applied onto a column packed with WorkBeads affimAb after an equilibration step with 50 mM sodium phosphate, pH 7.4. The mAbs were subsequentially washed with binding buffer before being eluted with 8 CV 50 mM sodium citrate, pH 3. See Figures 8 A-B for the purification chromatograms.

When an upstream WorkBeads 40 TREN is included, the mAb eluates in both experimental setups contained reduced HCP levels; 224 *vs.* 83 ppm which reflects the different initial HCP levels in the feed. These levels should be compared to feed that had not been pre-treated with a WorkBeads 40 TREN step and that had significantly higher HCP levels, 3 - 10 times higher (see Table 3).

The HCD analysis (PicoGreen assay) also showed reduced levels of HCD contaminants in WorkBeads affimAb eluates pre-treated with WorkBeads 40 TREN compared to the controls, with a ppm level of approximately 1 for both experiments compared to 2–4 without any pre-treatment (see Table 3).

The eluted mAbs from WorkBeads affimAb had a high degree of purity, but a final polishing step is needed to reduce the level of mAb aggregates, remaining HCP, and any potentially leached protein A.

Columns:	(A) WorkBeads affimAb, 3.4 mL (6.6 x 100 mm) (B) Superdex™ 200 Increase 10/300 GL
Binding buffers:	(A) 50 mM sodium phosphate, pH 7.4 (B) PBS, pH 7.4
Elution buffer:	(A) 50 mM sodium-citrate, pH 3.0
Samples:	(A) 100 mL pre-treated CHO cell supernatant (B) 50 µL of eluted mAbs
Flow rates:	(A) 0.9 mL/min (150 cm/h) (B) 0.4 mL/min
Gradient:	(A) 100% elution buffer one step in 8 CV

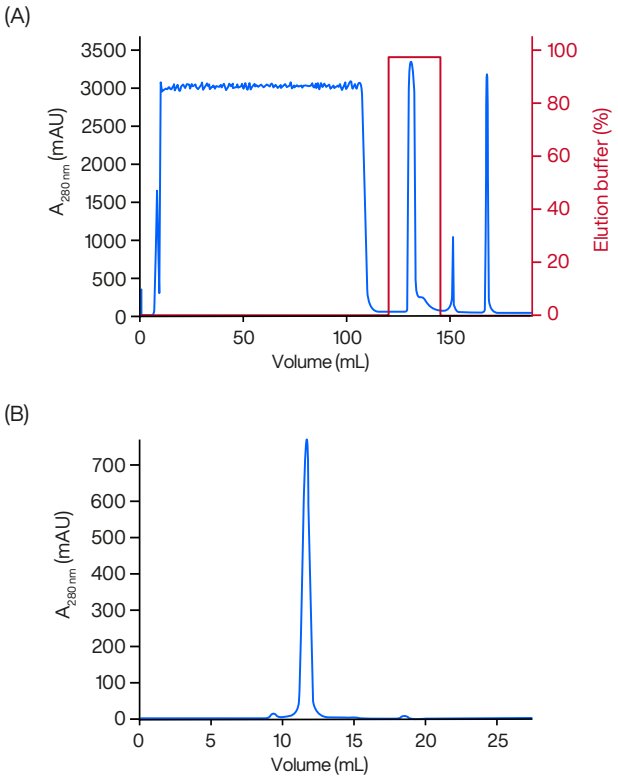

Figure 8. Chromatograms of mAb purification using WorkBeads affimAb with WorkBeads 40 TREN pre-treated feed. (A) Chromatogram from WorkBeads affimAb. (B) Analytical SEC of eluted mAb. UV trace at 280 nm (blue) and concentration of elution buffer (red) is shown.

Table 3. HCD and HCP levels in mAb eluates.

Experiment	+/- WorkBeads 40 TREN	HCP[1] (ppm)	Purity increase factor for HCP	HCD[2] (ppm)	Purity increase factor for HCD
Inline/Batch 1	+ WorkBeads 40 TREN - WorkBeads 40 TREN	224 667	3	1 4	4
Offline/Batch 2	+ WorkBeads 40 TREN - WorkBeads 40 TREN	83 728	8	1 2	2

[1] CHO HCP ELISA 3G kit, Cygnus
[2] Quant-iT PicoGreen dsDNA assay kit, Invitrogen

Step 3:
Polishing on WorkBeads 40S

The final polishing step is constituted by a strong cation exchanger (CIEX) resin. After mAb elution from WorkBeads affimAb, a virus inactivation step at low pH is usually performed during which many mAbs tend to form aggregates. To remove these aggregates (here referred to as HMWS) a polishing step with WorkBeads 40S was added. WorkBeads 40S is a high-capacity, agarose-based strong cation exchange chromatography resin (it is completely ionized over a broad pH range, 2–12) derivatized with sulfonate ligands.

Determination of binding capacity

To obtain an estimate of the capacity of WorkBeads 40S, a dynamic binding capacity (DBC) measurement for IgG was performed. The DBC_{IgG} was determined by frontal analysis at 10% breakthrough of IgG at residence times from 2 to 6 minutes in a column packed with WorkBeads 40S. As can be seen in Figure 9 the DBC was stable over a wide range of flow rates/residence times giving a DBC of 70 mg IgG/mL at a residence time of 3 minutes.

Column:	WorkBeads 40S, 3.4 mL (6.6 × 100 mm)
Binding buffer:	50 mM sodium acetate, pH 5.5
Elution buffer:	50 mM sodium acetate, 1 M NaCl, pH 5.5
Samples:	2 mg polyclonal IgG/mL in binding buffer
Flow rates:	0.6, 0.9, 1.1 and 1.7 mL/min (100–300 cm/h)

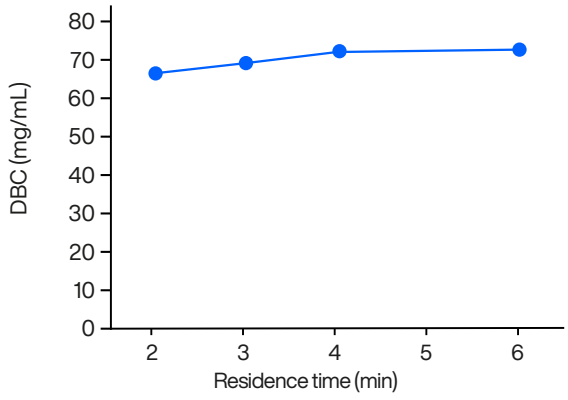

Figure 9. Loading capacity for WorkBeads 40S using pure IgG as target.

Optimization of polishing step

Purifications of mAbs usually require optimization of the running conditions to obtain the required purity and yield. While the gradient elution strategy has the advantage of higher resolution, the stepwise strategy is usually preferred in process scale due to faster performance and lower buffer consumption.

To determine which part of the peak should be collected, a monomer *vs.* aggregate/HMWS analysis needs to be performed. This analysis, using a linear gradient, is shown in Figures 10 A-B. The eluted mAbs were collected in 0.5 mL fractions and assessed with an analytical SEC to estimate the amount of monomeric mAbs *vs.* mAb aggregates in each fraction.

As seen in Figure 10A, there is an overlap between the monomeric mAbs and their corresponding aggregates, meaning that the peak must be cut to obtain an eluate with desired monomeric mAb purity. This will be at the expense of the yield, as is visualized in Figure 10B. This trade-off between purity and yield is dependent on the application and its purity requirement. In this experiment, the HMWS were efficiently removed from the monomers with a linear salt gradient, *i.e.* reduced to 1%, with a yield of 85%.

A pre-study of step elution conditions for WorkBeads 40S to determine the optimal separation between monomeric and aggregates was also conducted. The pH range was 4.9 to 7.4 and both separation as well as resolution was studied. The study showed an optimum at pH 5.9 for this specific mAb. At lower pH the broadening of the peaks was too great.

Using the optimised elution buffer at pH 5.9 in a 20 CV 20% elution buffer, a very good purity could be obtained with less than 0.5% HMWS at a yield of 86%, see Figure 10C.

Dependent on the application, a gradient elution optimization or a step elution optimization must be conducted as described above, where excellent compromises between purity and yield can be obtained using WorkBeads 40S resin.

The cation step is the third final polishing step in our mAb purification platform.

Columns:	WorkBeads 40S, 3.4 mL
Binding buffers:	20 mM sodium phosphate, pH 6.3
Elution buffers:	20 mM sodium phosphate, 0.5 M NaCl, pH 6.3
Samples:	4 mL mAbs eluted from WorkBeads affimAb
Flow rates:	1 mL/min (150 cm/h)
Gradients:	1. 0–65% elution buffer in 13 CV 2. 100% elution buffer in 6 CV

Columns:	GoBio Mini S 1 mL
Binding buffers:	20 mM sodium phosphate, pH 5.9
Elution buffers:	20 mM sodium phosphate, 0.5 M NaCl, pH 5.9
Samples:	0.75 mL mAbs eluted from WorkBeads affimAb
Flow rates:	0.3 mL/min (50 cm/h)
Gradients:	1. 20% elution buffer in 20 CV 2. 100% elution buffer in 7 CV

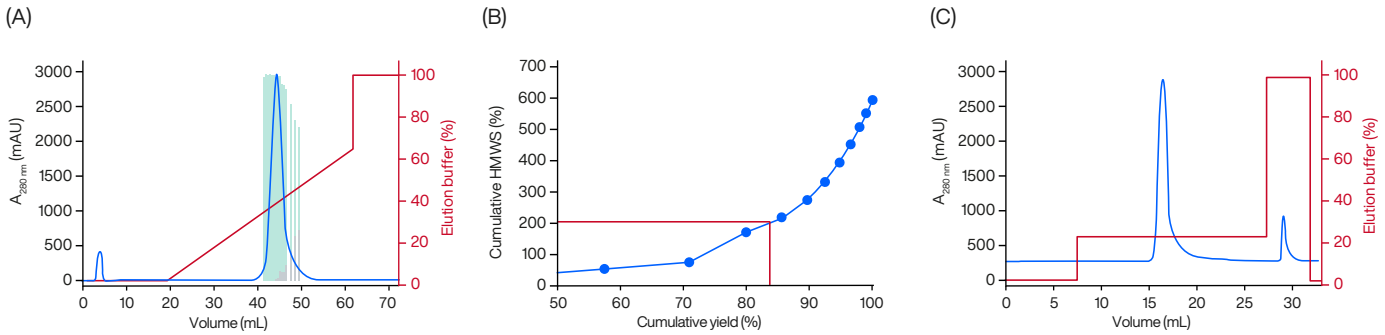

Figure 10. Linear and step elutions of mAbs. (A) Chromatogram of mAb purification on WorkBeads 40S with a linear gradient. The UV trace (blue) displays all proteins. The green bars represent the amount of monomeric mAbs and the grey bars represent mAb aggregates determined with an analytical SEC. (B) Monomeric mAbs *vs.* mAb aggregates in eluates in Figure 10A. A plot displaying the relationship between mAb aggregates *vs.* total mAb yield. Red lines show the yield obtained for an eluted mAb pool containing 1% mAb aggregates. (C) Chromatogram of mAb purification on WorkBeads 40S with a step gradient. The UV trace is in blue and concentrations of elution buffer is in red.

Summary three-step mAb purification

This combined three-step purification consisting of WorkBeads 40 TREN as a pre-treatment step, WorkBeads affimAb as the capture step and WorkBeads 40S as the polishing step generated a mAb product with a very high final purity and yield, as seen in Table 4. The experimental methods for this whole process are described in Table 5.

Table 4. Summary of three-step mAb purification

	Recovery[1]	HCP[2] (ppm)	HCD[3] (ppm)	HMWS[4] (%)	Monomer[4] (%)
Feed	100	107918	6009		
WorkBeads 40 TREN	93	74482	68		
WorkBeads affimAb	88	83	1	1.8	98
WorkBeads 40S	86	<35	7	<0.5	>99.5
Total	**70**	**<35**	**7**	**<0.5**	**>99.5**

1 Recover per step with exception of last row (total)
2 CHO HCP ELISA 3G kit, Cygnus
3 Quant-iT PicoGreen dsDNA assay kit, Invitrogen
4 Peak integration of analytical SEC peak using UNICORN™ software, Cytiva

Table 5. Experimental conditions used in platform purification steps 1 - 3.

	Step 1. WorkBeads 40 TREN	Step 2. WorkBeads affimAb	Step 3. WorkBeads 40S
Columns/Resins	2 x GoBio Mini TREN 5 mL connected in series	WorkBeads affimAb 6.6 x 100 mm (3.4 mL)	GoBio Mini S 1 mL
Samples	70 mL clarified CHO cell supernatant (Batch 2)	100 mL mAb eluate from step 1	7 mL mAb eluate from step 2
Flow rates, mL/min	1.9	0.9	0.3
Residence times (min)	4	4	4
Binding buffer	50 mM sodium phosphate, pH 7.4	50 mM sodium phosphate, pH 7.4	20 mM sodium phosphate, pH 5.9
Elution conditions	–	50 mM sodium-citrate, pH 3.0	20 mM sodium phosphate, 100 mM NaCl, pH 5.9
Regeneration/ CIP	1 M NaCl; 1 M NaOH	0.5 M NaOH	0.5 M NaOH

Conclusion

We have presented the ECP concept, a three-step purification platform for efficient mAb purifications, where most impurities are removed very early in the purification process to prolong the lifetime of the protein A resin. One additional aspect is that the variability of the feed loaded onto the protein A resin is reduced using WorkBeads 40 TREN by removing most of the host cell DNA (99 %), potential viruses (Log 4–5) and a significant proportion of the HMWS and host cell proteins (40–95%). The eluted mAbs from WorkBeads affimAb undergo a final polishing with WorkBeads 40S to remove remaining HMWS that could have co-purified with the mAb or been generated during the virus inactivation step.

This proposed three-step purification platform using WorkBeads 40 TREN to bridge the transition between the upstream and downstream processes is a very useful and cost-effective new approach. This might be especially important for mAbs which are more difficult to purify, since the first step removes most impurities prior to the capture step. One additional important aspect regarding the positive effects of early removal of impurities is the possibility of stressing the cell culture further in order to obtain a very high mAb concentration but which also results in higher host-cell impurity levels due to cell death.

Figure 11 illustrates the workflow for this platform (as already seen in Figure 1) and how well it performs.

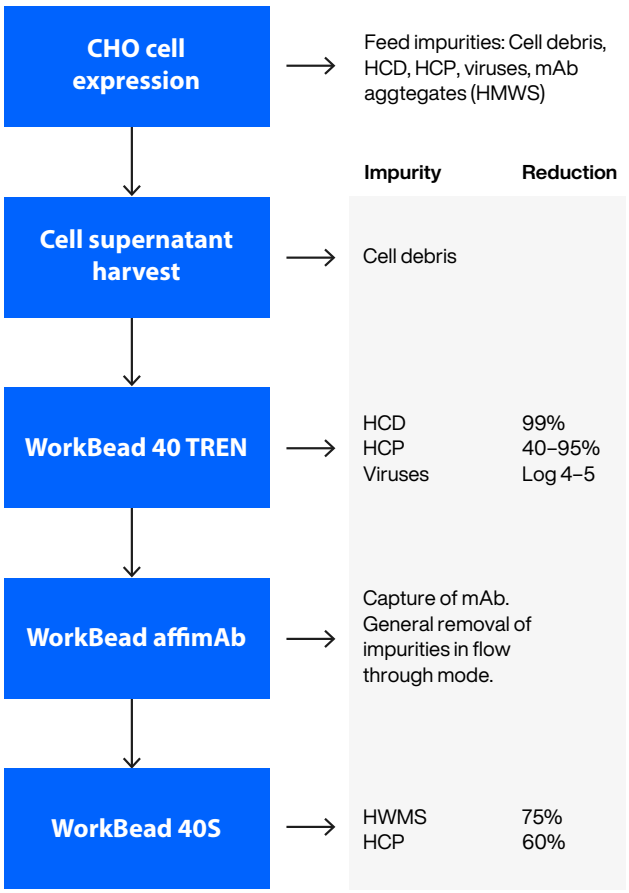

Figure 11. Three-step chromatographic purification platform consisting of WorkBeads 40 TREN, WorkBeads affimAb and WorkBeads 40S. The reductions of the major impurities in each subsequent step are shown in the highlighted box to the right

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Ordering information

Visit www. bio-works.com for information regarding all WorkBeads resins.

Orders: sales@bio-works.com or contact your local distributor.

For more information about local distributor and products visit www.bio-works.com or contact us at info@bio-works.com

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