Fractogel® EMD Chromatography Resin:
Capture your target with speed and efficiency
Introduction

For over 300 years, Merck KGaA has developed cutting-edge, high-quality products and services for the chemical and pharmaceutical industry. Merck Millipore, the life sciences division of Merck KGaA, continues this tradition with a long-term commitment to research and development. Our investment has yielded game-changing innovations that have been proven time and time again. From discovery through manufacturing, Merck Millipore provides a complete suite of innovative solutions and support services, designed to give you a performance edge at every step in the biopharmaceutical manufacturing process.

Chromatography Media from Merck Millipore

When it comes to chromatography, we understand the challenges of efficiently purifying your target product, while minimizing costs and speeding time to market. Product titers are steadily increasing, placing even greater demands on downstream processing. The development of appropriate purification strategies is an important factor to success. The chosen chromatographic media and techniques must be robust and should remove impurities to help you get a highly purified target molecule.
Fractogel® EMD Media: The Reliable Chromatography tool

The matrix
Fractogel® EMD media consist of synthetic methacrylate based polymeric beads providing excellent pressure stability resulting in high flow rates. Depending on your application, we can offer medium sized M-type beads with a particle size of 40–90 μm and small S-type beads with a particle size in the range of 20–40 μm.

The tentacles
The unique composition of Fractogel® EMD media creates a powerful tool for your purification strategy. Tentacles are long, linear polymer chains that carry the functional ligands. All tentacles are covalently attached to hydroxyl groups of the Fractogel® EMD matrix. This configuration provides a high surface area for biomolecules to bind accessible ligands without steric hindrance. A variety of ligands is available for different chromatography applications, including ion exchange, affinity, hydrophobic interaction, and size exclusion.

Properties of Fractogel® EMD media types:

<table>
<thead>
<tr>
<th>Property</th>
<th>S-type: 20–40 μm</th>
<th>M-type: 40–90 μm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Particle size</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pore size</td>
<td>about 800 Å</td>
<td></td>
</tr>
<tr>
<td>Matrix</td>
<td>crosslinked polymethacrylate</td>
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</tr>
<tr>
<td>Working range</td>
<td>pH 2–12</td>
<td></td>
</tr>
<tr>
<td>Pressure limit</td>
<td>8 bar</td>
<td></td>
</tr>
<tr>
<td>Storage</td>
<td>20% ethanol, 150mM NaCl</td>
<td></td>
</tr>
</tbody>
</table>
Advantages of Fractogel® EMD Chromatography Media

One of the main advantages of tentacle media is their greater accessibility and minimized steric hindrance between the functional group and the target molecule. Tentacle media provide higher binding capacities compared to conventional methods, especially for large proteins, antibodies, viruses, and plasmids. Target biomolecules are more tightly bound, but during the elution phase the reversible interaction can be neutralized.

Better production yields
A result of the unique surface modification technique is the high binding capacity of all Fractogel® EMD media. Due to the tighter binding of the target molecule, very often the capture step using Fractogel® ion exchange resins is more efficient than other resins. This more efficient capture results in greater overall yield than with other types of chromatography media.

Safer product
In contrast to carbohydrate based media, Fractogel® EMD media are resistant to microbial degradation. Thus, the risk of contamination with endotoxins is greatly reduced. In addition, the ability to clean Fractogel® EMD media multiple times extends its lifetime. This is an important feature especially when recombinant proteins, produced from micro-organisms, are purified.

Lower operating costs
Due to the chemical resistance of Fractogel® EMD media, a high number of cycles can be achieved. Resin lifetime is extremely long and replacement frequency is minimized, resulting in lower operating costs.

Benefits
- Reliable purification of macromolecules
- Efficient capture of target protein, and removal of viruses, DNA and endotoxins
- Excellent yield and high throughput
- Superior stability and quality
- Allowing multiple cycles of column regeneration and sanitization
- Tangible time and cost savings
Choosing the right Fractogel® EMD Media

Merck Millipore offers a variety of Fractogel® media for different chromatographic techniques. All Fractogel® media are designed for manufacturing of biomolecules. For example, native or recombinant proteins like blood plasma factors and monoclonal antibodies are processed on different Fractogel® ion exchangers with high throughput rates. For capture steps, M-type Fractogel® ion exchange media are widely used, whereas final polishing can be achieved using S-type ion exchange media. Final polishing can also be achieved with Fractogel® EMD BioSEC size exclusion columns. For certain application areas, metal chelate affinity chromatography can be used efficiently.
For Fractogel® EMD Chelate, iminodiacetic acid has been chosen as the functional affinity ligand. This ligand is very suitable for the coordination of metal ions. Free coordination sites of the metal ions are used to bind different proteins and peptides.

**Main application areas for Fractogel® EMD Metal Chelate Affinity Media**
- Ideal for separation of recombinant, histidine-tagged proteins
- Separation of peptides
- On-column re-folding

Ion exchange chromatography (IEC) is a robust, efficient technique for separating molecules based on charge. Two exchange types are differentiated: basic (positively charged, or cationic) and acidic (negatively charged, or anionic). They in turn can be divided into those with weakly basic or acidic or strongly basic or acidic functional groups. With the latter, the functional groups are always present in ionized form, independent from the pH value in the specified operating range. Ion exchange chromatography can be operated in either binding or flow-through mode.

**Main application areas for Fractogel® EMD Ion Exchange Media**
- Isolation of native and recombinant proteins from different sources (e.g. cell culture supernatant, microbial expression systems, inclusion bodies, plasma, plants, tissue, etc.)
- Efficient purification of peptides and low molecule weight substances (e.g. NADP, ATP, gangliosides, etc.)
- Excellent log reduction of DNA, endotoxins and host cell proteins
- Safe removal of viruses
- Well suited for efficient purification of monoclonal antibodies
Fractogel® EMD Media for Size Exclusion Chromatography

Size exclusion chromatography (SEC) is a method for polishing and usually there is no restriction in buffer selection. Native as well as recombinant proteins, viruses and plasma-derived bio-therapeutics can be purified on Fractogel® EMD BioSEC media. Due to its pressure stability Fractogel® EMD BioSEC media can easily be packed into high-performing production scale columns. The benefits include a shorter time to the market, with simple and straightforward transfer from lab-scale to production scale columns.

Main application areas for Fractogel® EMD BioSEC Media

- Efficient polishing step of blood plasma factors
- Removal of dimers and high molecular weight aggregates (e.g. monoclonal antibodies)
- Purification of viruses
- Determination of apparent molecular weights of proteins

Figure 3. Separation of a standard protein mixture on Fractogel® EMD BioSEC. The sample contains BSA (peak 1, dimer of BSA, peak 2 monomer of BSA), ovalbumin (peak 3) and cytochrome (peak 4). 500 µl of the sample were loaded on a 600 x 16 mm Fractogel® EMD BioSEC column at a flow rate of 1.0 ml/min (30 cm/hr) using 20 mM sodium phosphate buffer containing 0.1 M NaCl (pH 7.2) as the eluent.
Implementing Fractogel® EMD Media in your process

Fractogel® media are backed by Merck Millipore’s unmatched global expertise and customer support services. Our dedicated service organizations are available in 64 countries, providing technical and application expertise worldwide. Count on us to provide on-site training and support or, utilize one of our Biomanufacturing Science and Training facilities worldwide to leverage our expertise in your process.

Our goal is to help you:

- Move predictably and efficiently from bench scale to manufacturing scale processing
- Ensure production at planned rates, with desired yield and purity
- Create a robust, consistent and transferable process
- Ensure timely and successful startup and operation of plant
Manufacturing Excellence

Merck Millipore adheres to strict safety standards in the production and handling of process materials for biopharmaceutical production. Merck Millipore operates according to recognized international quality standards, with the goal of providing the highest product quality and safety. In addition to the established DIN ISO 9001:2008 or equivalent quality system, several GMP requirements are implemented into the production and handling of the Fractogel® EMD media product line.
<table>
<thead>
<tr>
<th>Description</th>
<th>Quantity [ml]</th>
<th>Particle Size [µm]</th>
<th>Capacity [per ml gel]</th>
<th>Catalogue No.</th>
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<td>Fractogel® EMD IEX media</td>
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<td>Fractogel® EMD weak cation exchanger</td>
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<td>Fractogel® EMD COD (M)</td>
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<td>Fractogel® EMD affinity media</td>
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<td>Fractogel® EMD SEC media</td>
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<td>Fractogel® EMD BioSEC</td>
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<td>20-40</td>
<td>5-1,000 kDa</td>
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</tbody>
</table>

SEC = size exclusion  Lys = Lysozyme  BSA = bovine serum albumin
Fractogel® EMD Media in Prepacked Columns

Chromabolt® is a family of prepacked chromatography columns containing our comprehensive chromatography resin portfolio. Chromabolt® columns have been optimized for early clinical stage manufacturing and are available in 3 sizes – 10, 20 and 32 cm inner diameter all with 20 cm bed heights. These prepacked columns have been intelligently designed for ease of use, ergonomics and transportation and will free up your valuable time and resources by eliminating manual packing and cleaning.

Learn more about Chromabolt® at:
www.merckmillipore.com/Chromabolt

Our Fractogel® EMD media are also available in prepacked, ready-to-use, disposable columns for research and lab development scale. The MiniChrom columns and RoboColumns® are the ideal tool for performing initial media screening, scaling and optimization studies. The easy-to-use, economical small scale columns can be used with any chromatography system.

For MiniChrom columns, please visit:
www.merckmillipore.com/MiniChromColumns

For RoboColumns®, please visit:
www.merckmillipore.com/RoboColumns
To place an order or receive technical assistance

In Europe, please call Customer Service:
France: 0825 045 645
Germany: 069 86798021
Italy: 848 845 645
Spain: 901 516 645 Option 1
Switzerland: 0848 645 645
United Kingdom: 0870 900 4645

For other countries across Europe, please call: +44 (0) 115 943 0840

Or visit: www.merckmillipore.com/offices

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www.merckmillipore.com/techservice