

Mimetic Ligands™

- Broad range of specific applications
- Screen for new applications
- Extremely favorable process economics
- High binding and flow rate performance
- Robust and caustic stable (up to 1M NaOH)
- Custom ligand/adsorbent development available



Mimetic Ligand™ Affinity Chromatography improves protein purification processes

By synthetically “mimicking” and enhancing the natural molecular affinity of binding ligands toward targeted biomolecules our innovative Mimetic Ligand™ adsorbents provide better separation at higher yields to help you conquer your toughest protein purification challenges.

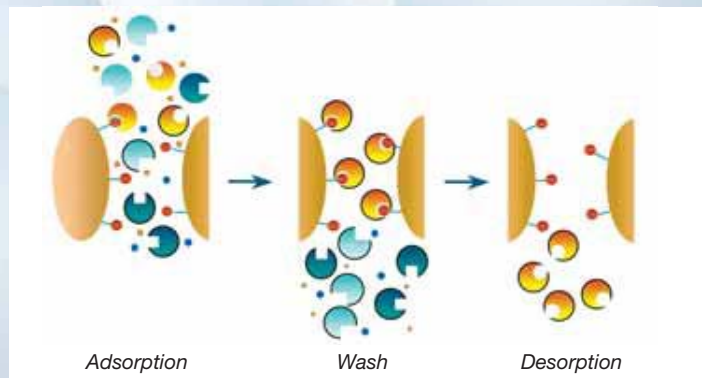
You can leverage the tremendous power of affinity chromatography by choosing a ligand from our standard range, or challenge us to create a custom solution from our extensive Chemical Combinatorial Library™.

Don't wait. Let us help you conquer your next purification challenge more efficiently, in less time than your regular process.

About Affinity Chromatography

Affinity chromatography is used principally for the separation and isolation of proteins. The technique relies upon the ability of proteins to recognize and bind to other molecules (ligands) in a specific and reversible manner. The ligand is normally bound by the protein at a "specific" site often within a fold of the protein.

Affinity chromatography uses an adsorbent comprising a porous support matrix to which the ligand is attached. The attachment or bonding is performed so that the immobilized ligand is still able to interact with the protein. If the ligand is relatively small a spacer arm is often incorporated between ligand and matrix, allowing the immobilized ligand to interact more effectively with the protein.



Schematic Diagram of Affinity Chromatography

An affinity separation is then performed by passing the starting protein solution over the adsorbent, incorporating the ligand, so that the target protein is adsorbed while allowing contaminants (other proteins, lipids, carbohydrates, DNA, pigments, etc.) to pass through without hindrance. The adsorbent is normally contained within a chromatography column, though the adsorption stage can be performed equally well by using the adsorbent as a stirred slurry in batch binding mode. Following adsorption, the adsorbent is washed with buffer to remove residual contaminants and then the bound protein is eluted in pure form. Elution is normally achieved by changing the buffer composition so the protein can no longer interact with the immobilized ligand.

Why Use Affinity Chromatography?

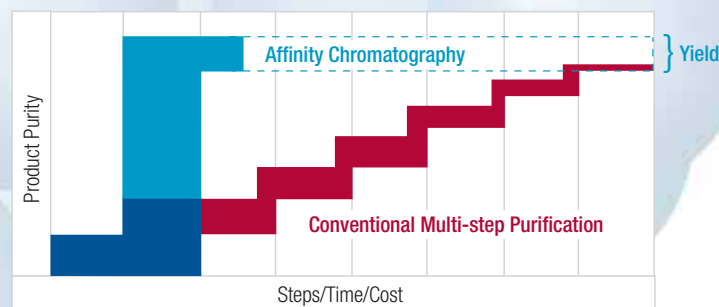
Affinity chromatography offers the user several major advantages compared to other protein purification techniques:

Selective Binding and Elution

- results in very pure product in a single unit operation
- provides high yields of purified product
- greatly reduced processing time
- cost reduction with economical affinity adsorbents
- high concentrations of material leave the column

Protein adsorption and concentration of purified protein make affinity chromatography ideal for

- large scale use
- stabilization of bound protein



Mimetic Ligand benefits: Fewer steps, faster process, higher purity, higher yields

Mimetic Ligand™ Adsorbents

Properties of Mimetic Ligand™ Adsorbents

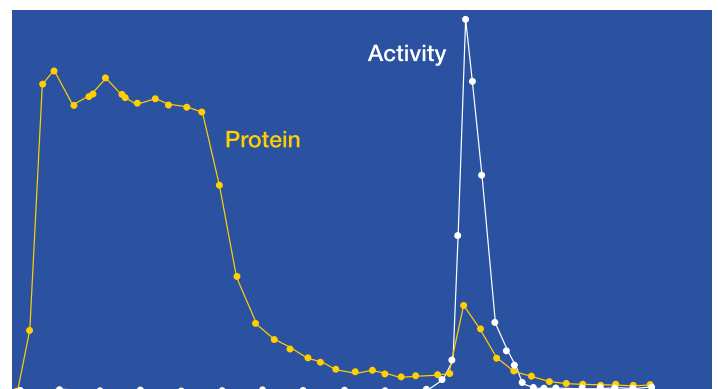
ROBUST - Mimetic Ligand adsorbents are biologically inert, very durable, have excellent liquid flow properties, and are resistant to most chemical treatments. Mimetic Ligand adsorbents are stable in the pH range 2 - 14, can be treated with denaturants (8M urea), detergents (Triton, SDS) and can be sterilized by autoclaving.

DEFINED STRUCTURE - Each ligand structure has been designed and synthesized in-house and is of known purity. These factors allow precise control of immobilized ligand concentration providing accurate batch reproducibility and hence chromatographic reproducibility.

HIGH CAPACITIES - In general, Mimetic Ligand adsorbent capacities are higher than other affinity adsorbents. Depending upon applied sample purity, type of protein and operational conditions, capacities can exceed 50mg protein per ml of packed gel.

LOW LIGAND LEAKAGE - Mimetic Ligands are immobilized by a defined and highly stable spacer-arm linkage which eliminates detectable ligand leakage across a wide pH range.

HIGH RECOVERIES - Protein absorption and desorption may be performed at physiological pH without the need for denaturants, leading to high recoveries of activity.



Purification of Morphine Dehydrogenase using Mimetic Orange 3

Advantages of Mimetic Ligand™ Adsorbents

UNIVERSALLY APPLICABLE - The Mimetic Ligand adsorbent range has been designed to enable purification of many proteins, providing a general technique that can replace ion-exchange, gel permeation and hydrophobic interaction chromatography, but with higher recovery and purity.

UNKNOWN OR UN-CHARACTERIZED TARGET PROTEINS - Mimetic Ligand adsorbents can be used without detailed information on the target protein (e.g. molecular weight or iso-electric point). Our Mimetic Ligand Screening Kits are ideal for adsorbent selection and method scouting.

BI-MODAL PURIFICATION - Purification may be achieved by positive binding (target protein bound; contaminants un-retarded) or negative binding (contaminants bound; target protein un-retarded).

ALKALI-STABLE ADSORBENTS - Enables cleaning, sterilization and depyrogenation with 1M sodium hydroxide, ensuring long operational lifetimes.



Our separation specialists are available to assist you in selecting the best adsorbents for your application or to design a custom solution.

- Broad range of ligand structures and specificities
- Robust and stable (pH 2-14)
- High Capacities (typically 20-50 mg)
- Excellent Recoveries
- High flow with PuraBead® cross-linked agarose

Since 1987 ProMetic has been pioneering design, development and manufacture of affinity purification technology for large scale bioprocessing as well as research and development at lab-scale in the biotechnology industry. Our patented Mimetic Ligand™ technology synthetically “mimics” and enhances the natural molecular affinity of binding ligands towards targeted biomolecules.

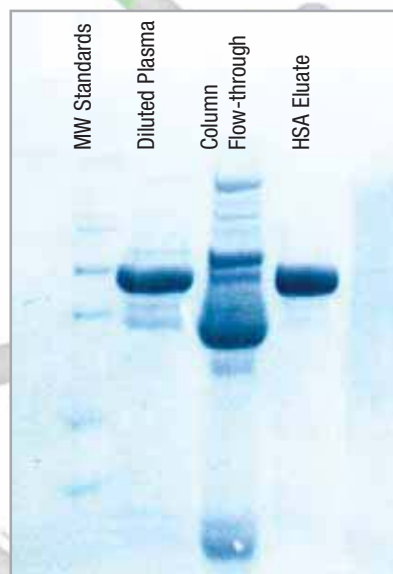
The Result: Optimized binding and yields for all your biomolecular purification needs. The key to our success in biomolecule purification lies in the development of an extensive Chemical Combinatorial Library™. Through years of dedication, research and development we have systematically screened countless ligand arrays and utilized our computer modeling processes to design new ligand structures.

Dedicated to ISO9001 quality and increased production efficiency

Quality and innovation go hand in hand, that's why we work hard to maintain and even exceed ISO9001:2000 standards. By staying close to our customers and their unique requirements, we enhance our ability to provide innovative solutions to meet the needs of the biopharmaceutical market. We collaborate with pharmaceutical and biotech companies to optimize bioseparation and purification processes. Our patented separation technology and expansive Chemical Combinatorial Library™ of synthetic ligand media increases production efficiency, reduces manufacturing costs and enables companies to strengthen market positions through continuous improvements in product purity and yield.

The Power of Affinity Chromatography with Mimetic Ligand™ Adsorbents

Mimetic Ligand adsorbents use highly stable, synthetic affinity adsorbents which are capable of interacting with a wide range of proteins. Unlike the crude textile dyes which have been used previously, Mimetic Ligands have purpose-designed structures which are synthesized and immobilized to solid supports by extremely stable spacer-arm linkages. They therefore offer higher degrees of purification, minimal ligand leakage and more reproducible separations. A diverse range of ligand structures have been developed, each of which incorporates features which mimic the protein-binding components of natural ligands. Consequently each Mimetic Ligand has a very different specificity allowing a wide range of proteins to be purified using this family of adsorbents.



Purification of HSA from plasma using Mimetic Blue SA

Typical proteins suited for purification by Mimetic Ligands™:

- Albumin • Proteases • Blood Proteins
- Oxidases • Dehydrogenases
- Ligases • Kinases • Antibodies
- Nucleases • Cytokines

Mimetic Ligands™

ProMetic BioSciences has developed a range of Mimetic Ligand Adsorbents, each offers different binding properties toward any given protein molecule:

Specific Application	Mimetic Red 2, 3	Mimetic Orange 1, 2, 3	Mimetic Yellow 1, 2	Mimetic Green 1	Mimetic Blue 1	Mimetic Blue SA	Mimetic Blue AP
Albumin (serum, plasma and recombinant) Albumin fusion proteins					■	■	
Human albumin (serum, plasma, and recombinant) Albumin fusion proteins						■	
NADP+ cofactor dependent proteins, e.g.: Glucose-6-phosphate dehydrogenase Aldehyde & Dihydrofolate reductases	■						
Various enzymes such as: Glucose oxidase Morphine dehydrogenase		■					
Chymosin Glucose oxidase			■				
Cytokines (e.g. Interferons, Interleukins, Growth Factors) NAD+ cofactor dependent proteins, e.g.: Alcohol and Lactate dehydrogenases					■		
Alkaline phosphatase DNA & RNA polymerases Restriction endonuclease							■
Screen for other proteins/enzymes, ATP/IMP/GTD dependent proteins, dehydrogenases, kinases, synthases, transferases, cyclases, and polymerases	■	■	■	■	■	■	■

Screening Kits

We have developed a range of convenient Mimetic Ligand adsorbent screening kits, designed to eliminate the arduous task of developing an optimized chromatographic procedure for protein purification without any prior knowledge of the physico-chemical properties of the molecules (e.g. iso-electric point, molecular weight, hydrophobicity, ligand specificity).

Advantages of our Screening Kits include:

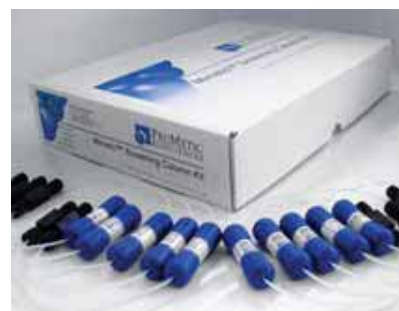
- Rapid screening to identify suitable adsorbents for your target molecule
- High level of certainty of identifying suitable adsorbents in a single experiment
- Easy optimization of binding elution and conditions (pH, ionic strength) following identification (method scouting)



PIKSI-M Kit

Integrated unit containing 1ml gravity columns of ten different Mimetic Ligand™ adsorbents, an integral buffer reservoir, and a detachable fraction collection rack. Ideal for use when access to sophisticated instruments is not possible.

Mimetic Ligand Screening Column Kit



Contains 1ml pre-packed columns of ten different Mimetic Ligand™ adsorbents, suitable for attachment to automated chromatography work stations. Industry standard connectors make these columns easy to attach and detach from your system.

Mimetic Ligand 96-Well Screening Kit



Ideal for "high throughput chromatography" making it possible to screen an array of adsorbents against a large number of samples, under a diverse range of conditions, in the fastest possible time. Each pack also contains a fraction collection plate. Choose from standard adsorbent arrays, or request a custom array for your specific requirements.

For ordering information on Mimetic Ligand Adsorbents and our Screening Kits see back cover or visit www.Ligands.discoverprometic.com

Mimetic Ligands™

Off-the-shelf Media

ProMetic's core technology is based on a family of unique and proprietary synthetic molecules called Mimetic Ligands™. These compounds can be compared to chemical hooks that selectively recognize and bind targeted proteins. By synthetically "mimicking" and enhancing the natural molecular affinity of binding ligands toward targeted biomolecules, we've created a family of synthetic affinity adsorbents that provide better separation at higher yields than your regular chromatographic processes.

Custom Media Development Programs

Alternatively, a Mimetic Ligand affinity adsorbent can be specifically designed, developed and manufactured for the purification of your product. Our Chemical Combinatorial Library™, combined with a rational ligand design approach, can give you a fully validated customized affinity adsorbent that is suitable for use in the production of therapeutic biopharmaceuticals.

International Sales and Technical Support:

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GENERAL SPECIFICATIONS: Mimetic Ligand™ Adsorbents

Ligand	Synthetic, aromatic triazine derivative
Matrix	6% cross-linked agarose (PuraBead® 6XL)
Particle size	100 ± 25µm (90%) (PuraBead® 6XL)
Immobilized ligand concentration	2.5 ± 0.3 mol/g moist weight; 36 ± 4 mol/g dry weight
Binding capacity	Typically in the range 20-50mg/ml resin
Flow rate	Up to 600 cm/hr (PuraBead® 6XL)
Operating pressure	1 bar (15 psi)
Operating pH	pH 2 - 14
pH stability	Long term (3 months): pH 3 - 13
Chemical stability	All commonly used aqueous buffers, also compatible with alcohols, esters, ketones and ethers
Sanitization	1M sodium hydroxide, 25°C
Sterilizability	Autoclavable: 121°C, 20 minutes
Storage	4°C in 24% EtOH/76% 0.1 M NaCl

ORDERING INFORMATION

MIMETIC LIGAND ADSORBENTS

Part Numbers	Suspension				Pre-Packed Columns	
	25ml	100ml	500ml	1000ml	5 x 1ml	1 x 10ml
Mimetic Red 2	0020-00025	0020-00100	0020-00500	0020-01000	1020-00001	1020-00010
Mimetic Red 3	0013-00025	0013-00100	0013-00500	0013-01000	1013-00001	1013-00010
Mimetic Orange 1	0030-00025	0030-00100	0030-00500	0030-01000	1030-00001	1030-00010
Mimetic Orange 2	0040-00025	0040-00100	0040-00500	0040-01000	1040-00001	1040-00010
Mimetic Orange 3	0050-00025	0050-00100	0050-00500	0050-01000	1050-00001	1050-00010
Mimetic Yellow 1	0060-00025	0060-00100	0060-00500	0060-01000	1060-00001	1060-00010
Mimetic Yellow 2	0070-00025	0070-00100	0070-00500	0070-01000	1070-00001	1070-00010
Mimetic Green 1	0080-00025	0080-00100	0080-00500	0080-01000	1080-00001	1080-00010
Mimetic Blue 1	3090-00025	3090-00100	3090-00500	3090-01000	4090-00001	4090-00010
Mimetic Blue SA	3120-00025	3120-00100	3120-00500	3120-01000	4120-00001	4120-00010
Mimetic Blue AP	0110-00025	0110-00100	0110-00500	0110-01000	1110-00001	1110-00010

Mimetic Ligand adsorbents can be supplied in any volume for your large-scale bioprocess. Please contact us to ask about your specific needs.

MIMETIC LIGAND ADSORBENT SCREENING KITS

Part Numbers	
PIKSI M Kit (10 x 1ml columns in integrated unit - gravity feed)	1000-00001
Mimetic Screening Column Kit (10 x 1ml pre-packed columns)	1003-00001
Mimetic Screening Kit - 96 Well	Contact us for information