



Antibiotic purification

Adsorbent and ion exchange resins can be used in the purification process of antibiotics. They are well established in the purification of molecules like cephalosporins, glycopeptides and aminoglycosides.

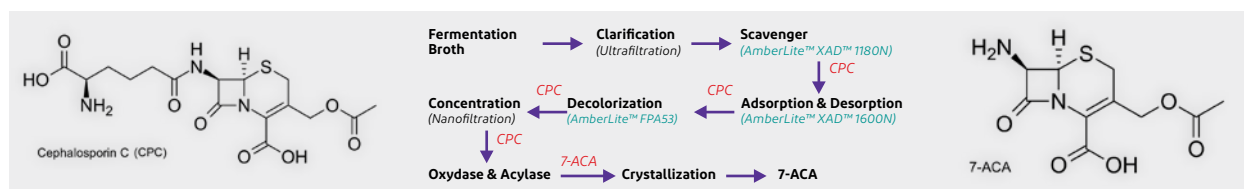
Cephalosporins

Cephalosporins are the most important antibiotics having β -lactam ring. They are obtained from the fungus *Acremonium chrysogenum*, also known as *cephalosporium* and they have a wide use against bacteria in various severe infections such as respiratory tract infection (RTI), skin infection and urinary tract infection (UTI). 7 Aminocephalosporanic acid (7-ACA) is made from Cephalosporin C (CPC) and is a key intermediate for synthesizing the four major classes of cephalosporin antibiotics.

After fermentation, the separation of biomass and antibiotic-containing broth is generally achieved by microfiltration by which the biomass is removed from the CPC containing filtrate. The filtered broth is then passed through large-scale hydro-

phobic interaction chromatography (HIC) columns to remove impurities, in particular proteins, peptides, salts and side products like deacetyl CPC (DAC) and deacetoxy CPC (DAOC).

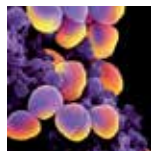
The first column, called a scavenger, is filled with an adsorbent, e.g. **DuPont™ AmberLite™ XAD™ 1180N**. The second column is filled with another adsorbent, e.g. **AmberLite™ XAD™ 1600N**. The remaining color is removed by percolating the CPC solution through a column filled with a weak anionic acrylic resin in acetate form, **AmberLite™ FPA53**. Then CPC is converted into 7-ACA by a two step cleavage with D-amino acid oxidase (DAO) and glutaryl acylase (GAC). A Merry Go Round column system is typically used for this process.



Vancomycin

Vancomycin is one of the glycopeptide antibiotics. It has bactericidal activity against aerobic and anaerobic Gram-positive bacteria and is used in the treatment of methicillin resistant staphylococcus aureus (MRSA). The initial purity of vancomycin in a fermentation broth of bacteria *S. orientalis* is around 32–35%, and the purity must be driven up to greater than 95% for pharmaceutical application.

The capture step can be performed on a strongly acidic resin, **AmberLite™ FPC23H**, decolorization and desalting of crude filtered vancomycin can be performed on



AmberLite™ XAD™ 16 or **AmberLite™ XAD™ 1600N** and the final purification step on **DuPont™ AmberChrom™ CG161M** enables >95% product purity.

Tobramycin

Tobramycin is an aminoglycoside antibiotic derived from *Streptomyces tenebrarius*. It is used to treat various types of bacterial infections, particularly Gram-negative infections. The product of microbial fermentation is carbamoyltobramycin, which is converted to tobramycin using ammonium hydroxide hydrolysis. Tobramycin is then recovered upon a carboxylic resin such as **AmberLite™ FPC3500** in the ammonium form and then decolorized upon an anionic resin such as **AmberLite™ FPA90 CL** or **AmberLite™ FPA40 CL**. A further separation of A, B and C components can be performed upon **AmberLite™ CG50 TYPE 1**. A similar process exists to produce other aminoglycoside antibiotics like Kanamycin, Netilmicin, Sisomicin or Gentamicin.

| Biomolecule | Application | Process steps | Resin |
|----------------|--|---|---|
| Cephalosporins | β-lactam for respiratory tract infection, Skin Infection, Urinary Infection | Scavenger Extraction Decolorization | AmberLite™ XAD™ 1180N AmberLite™ XAD™ 1600N AmberLite™ FPA53 |
| Vancomycin | Glycopeptide for Gram-positive bacteria MRSA | Capture Decolorization & desalting Final purification | AmberLite™ FPC23H AmberLite™ XAD™ 16N AmberChrom™ CG161M |
| Tobramycin | Aminoglycosides for gram negative infections | Capture Decolorization Final purification | AmberLite™ FPC3500 AmberLite™ FPA90 CL AmberLite™ CG50 (Type 1) |
| Streptomycin | Aminoglycosides for treatment of active tuberculosis | Conversion to sulfate form | AmberLite™ FPA40 |
| Oritavancin | Glycopeptide for Gram-positive bacteria | Capture Decolorization & desalting Final purification | AmberLite™ FPC23H AmberLite™ XAD™ 16N AmberChrom™ CG161M |
| Erythromycin | Macrolide antibiotic for respiratory tract infection, Skin Infection, STD | Capture and concentration Decolorization Desalting | AmberLite™ FPC3500 AmberLite™ FPA98 CL AmberLite™ XAD™ 16N |
| Geldanamycin | Ansamycin for broad spectrum antibiotic | Capture | AmberLite™ XAD™ 1600N |

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Water Solutions

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