



Ion Exchange Resins for Active Pharmaceutical Ingredients (APIs) and Excipients in Pharmaceutical Applications

Learn the role of Purolite™ Resins as APIs and functional Excipients.

ECOLAB®

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Introduction

Ion Exchange resins (IEX resins) are known in many applications within the pharmaceutical industry and Drug Product Formulations such as make up process water, medical water, extraction and purification of biologics. This document addresses the uses of IEX resins as APIs for specific therapeutic indications, and as functional Excipients.

Ecolab's pharmaceutical grade products have been developed to meet the demands of multiple regulatory bodies, including the American (USP), European (Ph.Eur.), British (BP) and Japanese (JP) pharmacopeias. Drug Master Files and regulatory support are available to our partners globally.

Active Pharmaceutical Ingredients

Polymeric IEX resins used as APIs and Excipients are insoluble and, when taken orally, pass through the human digestive system without being adsorbed. Therefore, ingestion of specific resins has no side effects on the human body (that is, they are non-systemic). The properties of IEX resins used specifically as APIs are well documented, and their characteristics are clearly defined in various pharmacopeias.

Ecolab has DMFs (Drug Master Files) for all three APIs listed in this brochure: Sodium Polystyrene Sulfonate, Calcium Polystyrene Sulfonate and Cholestyramine.

- Sodium and Calcium Polystyrene Sulfonate are used to control blood Potassium levels in Hyperkalemia.
- Cholestyramine is a Bile Acid Sequestrant used to reduce elevated blood cholesterol in Hypercholesterolemia.

Ecolab provides value to these mature markets through its global footprint, operational expansions, regulatory acceptance and security of supply.



Ecolab's APIs and Excipients portfolio is produced in our FDA inspected, cGMP certified facilities in Victoria, Romania and King of Prussia, Pennsylvania, USA.

TABLE 1 Purolite Resins APIs

APIs	Product Code	Description
Sodium Polystyrene Sulfonate	C100MRNS	Strong acid cation exchange resin with Sulfonic groups. Used for the reduction of high Potassium levels in Hyperkalemia, topical microbicide and spermicide and as a controlled release carrier.
Calcium Polystyrene Sulfonate	C100CaMRNS	
Cholestyramine	A430MR	Strong base anion exchange resin in Chloride form. Acts as Bile Acid Sequestrant, used for the reduction of elevated serum Cholesterol in Hypercholesterolemia and for the relief of pruritus with Partial Biliary Obstruction.

Polystyrene Sulfonate: Hyperkalemia Treatment

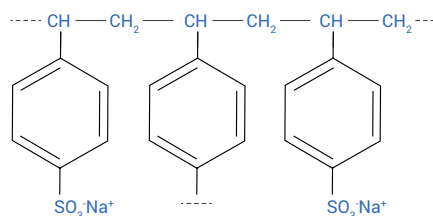
Hyperkalemia is one of the most common complications in end-stage renal disease patients. It could cause serious abnormality in the heart, such as cardiac arrhythmias, thereby being involved in heart failure and sudden death in patients with advanced Chronic Kidney Disease (CKD).

Polystyrene Sulfonate resin, a cation exchange resin, is the most commonly used drug to treat Hyperkalemia. The resin can be used in Calcium (Ca) form and Sodium (Na) form Polystyrene Sulfonate. Thus, Hyperkalemia can be treated with C100MRNS or C100CaMRNS. The Sodium or Calcium in the resin is exchanged for the Potassium in the body.

FIGURE 1

Typical Structure of Main Repeating Units

C100MRNS



Ecolab's Sodium and Calcium Polystyrene Sulfonate support the global Pharmaceutical and Nutraceutical communities, leading advanced development partnerships.



Cholestyramine: Bile Acid Sequestrant Used in Hypercholesterolemia Treatment

Hypercholesterolemia is the presence of elevated Low-Density Lipoprotein (LDL) cholesterol in the blood. Cholesterol is the precursor of Bile Acids. Cholestyramine exchanges its Chloride anions with Bile Acids salts present in the gastrointestinal tract and form an insoluble resin complex which is excreted in the feces. This results in a partial removal of Bile Acids from the enterohepatic circulation, and hence, a reduction of blood cholesterol levels.

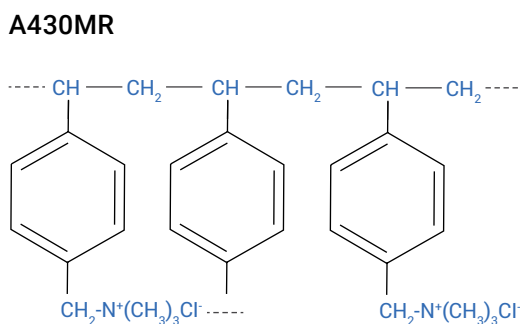
Cholestyramine's Bile Acid Sequestrant properties have extended its treatment area to pruritus associated with partial biliary obstruction and diarrhea resulting from Bile Acid malabsorption, as well as diaper rash (topical), and certain toxins removal (both human and veterinary used).



Ecolab's Cholestyramine supports the global Pharmaceutical, Nutraceutical and Veterinarian communities, leading various formulations success.

FIGURE 2

**Typical Structure of
Main Repeating Units**



Excipients

Pharmaceutical Excipients are substances other than the APIs that have been appropriately evaluated for safety and are intentionally included in a drug delivery system.

Unlike APIs, pharmaceutical Excipients are substances used in drug product formulations, that do not impose a biochemical affect to the body. These substances are used as part of the drug delivery system, and as such, are being regulated and validated for human consumption.

IEX resins are the ideal Excipients for the following delivery systems:

- Abuse Deterrence
- Controlled Release
- Deliquescence
- pH Buffering
- Polymorphism
- Solubility Enhancement of BCS class II and IV drugs
- Stabilization of Non-Stable API's
- Tablet Disintegration
- Taste Masking

TABLE 2 Purolite Resins Excipients

Excipients	Product Code	Description
Polistirex (Sodium Polystyrene Sulfonate)	C100MRNS	Strong acid cation exchange resin used for drug loading to control the release, taste masking and stability of APIs in oral dosage forms.
Cholestyramine	A430MR	Strong base anion exchange resin for the loading and delivery of acidic formulations for controlled release, taste masking and stability of APIs in oral dosage forms.
Polacrillex	C115HMR	Weak acid cation exchange resin in Hydrogen form. Used as a controlled release carrier or as pH adjuster in oral dosage forms. Also suitable for taste masking applications.
Polacrilin Potassium	C115KMR	Weak acid cation exchange resin in Potassium form. Acts as disintegrant in tablets and orally disintegrating tablets. Also suitable for taste masking applications.

Excipient Applications

Abuse Deterrence

IEX resins control the release rate of APIs when the original dosage form is tampered with, regardless of which illicit use route is chosen. If the active is sought out for dose dumping, an IEX resin-API complex (resinate) can control the release, keeping both the abuser and manufacturer safe from overdosing.

Controlled Release

The delayed, extended or sustained release action technique is prevalent in the pharmaceutical market. It permits a controlled quantity of the API to be released gradually into the body (over several hours), thus reducing the number of doses and increasing the acceptability of the drug product.

The rate of release of an API from the IEX resin depends on the resin properties such as the exchange capacity, the degree of cross-linkage, particle size, chemical structure, functional group pK, porosity, swelling and purity.

C115HMR weak acid cation exchange resin is used for the complexation and formation of the API Nicotine Polacrilex. The resinate complex is comprised of Nicotine and Polacrilex, a Polymethacrylic Acid resin.

The resinate complex is added to flavored chewing gums and hard lozenges used for smoking cessation programs. The use of the polymer for controlled release maximizes the amount of Nicotine released and absorbed by buccal mucosa during chewing, when saliva acts as a solvent for elution of the Nicotine from the resinate complex. C115HMR can be offered in different grades depending on the formulation and dose form.

Deliquescence

Using a resin to eliminate the deliquescent properties of an API can help with flow properties of these drugs during the formulation process. Loading a drug possessing this property onto a functional resin can reduce water uptake of the API, making a free-flowing resinate that is easy to formulate.

pH Buffering

Using IEX resins in formulations and medical devices as part of a buffering aid have been successfully used. Not all formulations are stable in a system with fluctuating pH. Adding an IEX resin like C115HMR can greatly stabilize a formulation or device.

Polymorphism

APIs can exhibit various crystalline forms and can result in a difference in bioavailability. These types of drugs are not easily controlled; however, creating a resinate with this API can stabilize it to reduce high variability in its dissolution profile.

Solubility Enhancement of BCS Class II and IV Drugs

The dissolution of a formulation has a direct effect on the API's bioavailability. The presence of IEX resins can increase the solubility of some APIs. API resinate complexes have a faster rate of dissolution. Some IEX resin matrices are relatively hydrophilic and can allow aqueous solutions to penetrate the dimensional resin structure, increasing the dissolution rate.

Stabilization of Non-Stable APIs

Some APIs present reduced effectivity due to their poor stability under storage conditions. Stability can be improved by complexing the API with a Carboxylic IEX resin such as C115HMR without reducing the therapeutic effect of the API. One example is vitamin B12. The resinate complex formed in this way is just as effective as free vitamin B12.

Tablet Disintegration

The efficiency of a compressed tablet to release API at a certain rate is one of the critical attributes of a solid oral dose formulation. C115KMR is a super disintegrant that can help formulators achieve this goal.

Taste Masking

Taste is a key organoleptic factor in the development of oral dosage forms. Taste can affect the patient's acceptability of a drug. Whether the drug is bitter or acidic, when dissolved in saliva, a taste is quickly developed. Drug molecules interact with taste receptors on the tongue to give a taste that can be bitter, sweet, acidic, alkaline, or salty.

Many Alkaline drug products are known to be quite bitter. Thus, their formulation requires an Excipient with the ability to mask the taste while oral drug product is in the mouth. Weak Acid Cation-exchange resins such as C115KMR can be used in these formulations. Due to its pK, the formulation is not dissociated in the mouth under the alkaline conditions of the saliva, thus masking the taste and releasing the API once in the acidic environment in the stomach.

Other Applications

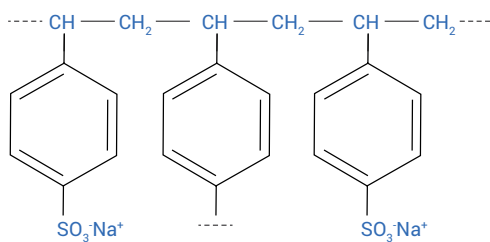
IEX resins are also used in several controlled drug release applications such as nasal and ophthalmic drug release or the sustained release of antidepressants.

No preconditioning is needed for the use of our products.

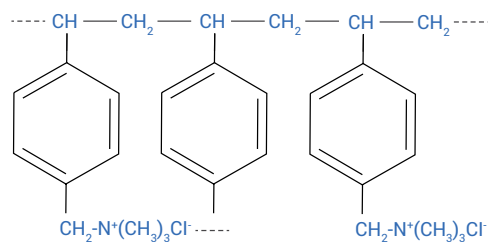
FIGURE 3

**Typical
Structure of
Main Repeating
Units**

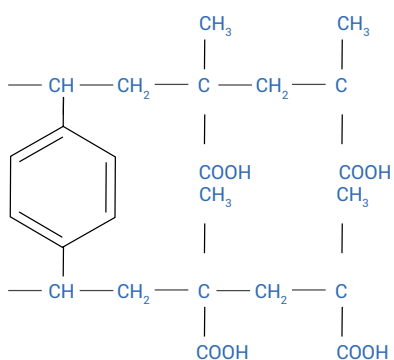
C100MRNS



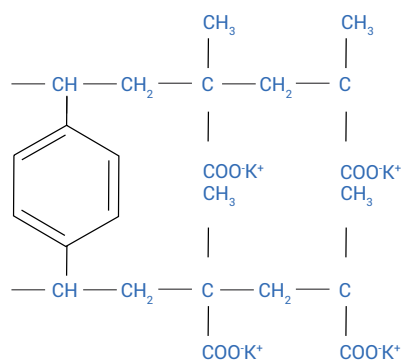
A430MR



C115KMR



C115HMR



Regulatory Support

When applying for a new drug application or changing your primary supplier to Ecolab, we will provide all pertinent regulatory information available for our APIs and Excipients, as well as samples to support your application.

Available documentation includes GMP certification, ISO certification, FDA inspection reports, FDA Product and Facility Registrations, Applicant's Part of the DMF (Drug Master File) designed to meet your drug product target market, a series of contaminant declarations and other necessary documents.

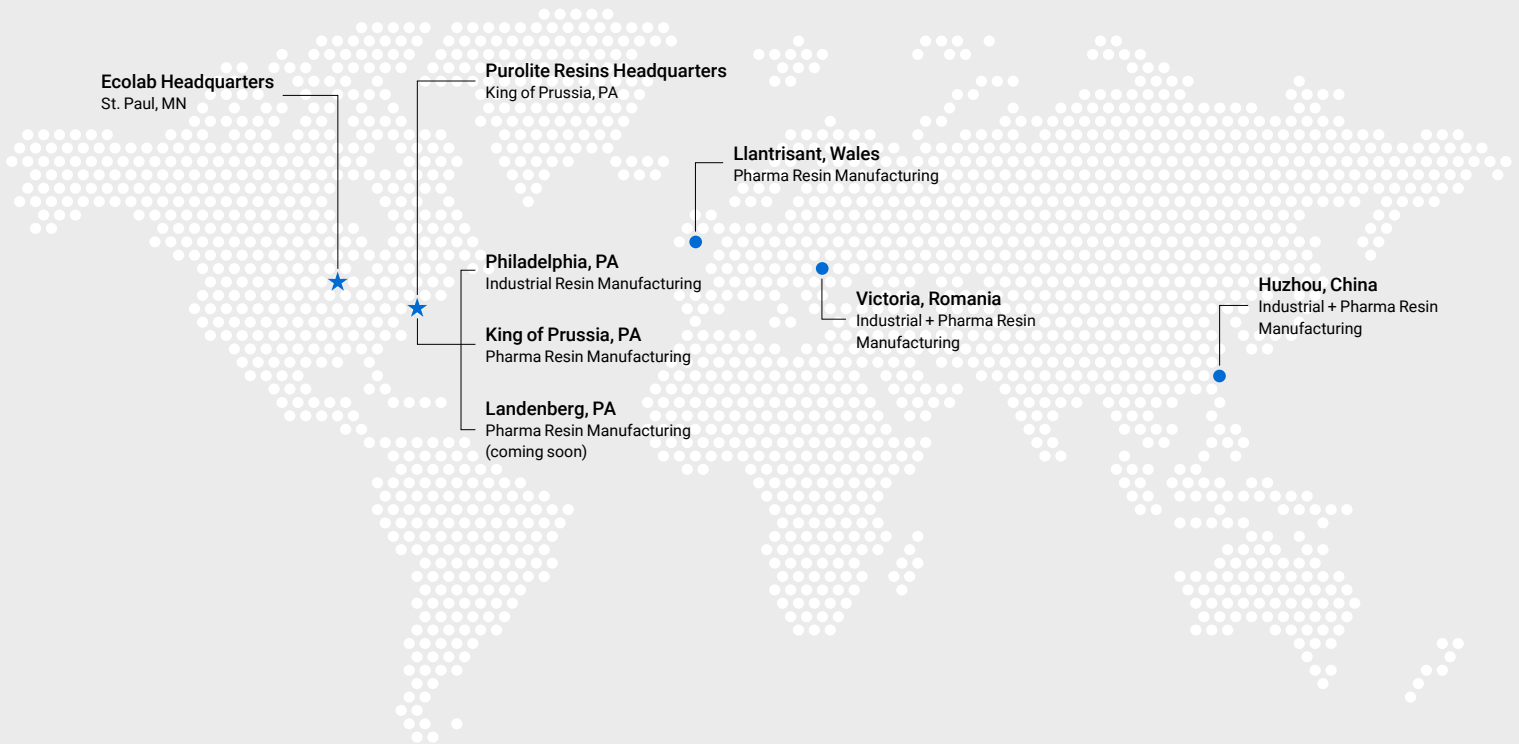
Ecolab's cleanrooms have been and will continue to be audited by pharmaceutical and biotechnology organizations, located worldwide.

As a leader in the Ion Exchange resin space, Ecolab is proud to support your drug product throughout its life cycle, adhering to quality guidelines and regulators in each of its target markets.

Ecolab is a global developer, manufacturer, and supplier of Purolite™ Resins including ion exchange, catalyst adsorbent and advanced polymers that make the world cleaner and healthier.



www.puroliteresins.com



We're ready to solve your process challenges.

For further information on products and services, visit www.puroliteresins.com or contact us at the addresses below.

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