Product Data Sheet

DUOLITE™ AP143/1083 Resin

Pharmaceutical Grade Anion Exchange Resin (Cholestyramine Resin USP)

For Advanced Release Technologies

Description

DUOLITE™ AP143/1083[1] resin is an insoluble, strongly basic, anion exchange resin in the chloride form supplied as a dry, fine powder. DUOLITE™ AP143/1083 is suitable for pharmaceutical applications either as an active ingredient or as a carrier for acidic (anionic) drug substances. A monograph for Cholestyramine Resin USP appears in the United States Pharmacopoeia/National Formulary. DUOLITE™AP143/1083 conforms to the compendial specifications.

A Drug Master File for this product is maintained with the United States Food and Drug Administration.

[1] The use of AMBERLITE™ and DUOLITE™ pharmaceutical grade ion exchange resins as components of drug formulations is subject to the Food, Drug, and Cosmetic Act as amended.

Typical Properties

Physical Properties	
Copolymer	Styrene-divinylbenzene
Type	Strong base anion
Functional Group	Quaternary amine
Physical Form	White to buff-colored, fine powder
Chemical Properties	
Ionic Form as Shipped	Cl^-
Loss on drying [1]	12.0% maximum
Identity (by IR spectrum) [1]	Identical to USP reference standard
Heavy metals [1]	0.002% maximum
pH of slurry [1]	4.0–6.0
Residue on ignition [1]	0.1% maximum
Dialyzable quaternary amine [1]	0.05%
Chloride content [1]	13.0–17.0%
Sodium glycocholate exchange capacity [1]	1.8–2.2 g/g
Organic volatile impurities <467>[1]	Meets requirements
Particle Size §	
< 425 microns	100% minimum
< 150 microns	85% minimum
< 75 microns	50% maximum

§[1] Appears in current USP/NF

Letters of authorization granting access to the file by FDA in support of NDA and ANDA submittals will be provided upon request. DUOLITE™ AP143/1083 Resin is manufactured in accordance with Good Manufacturing Practices (cGMP) for bulk pharmaceutical chemicals.

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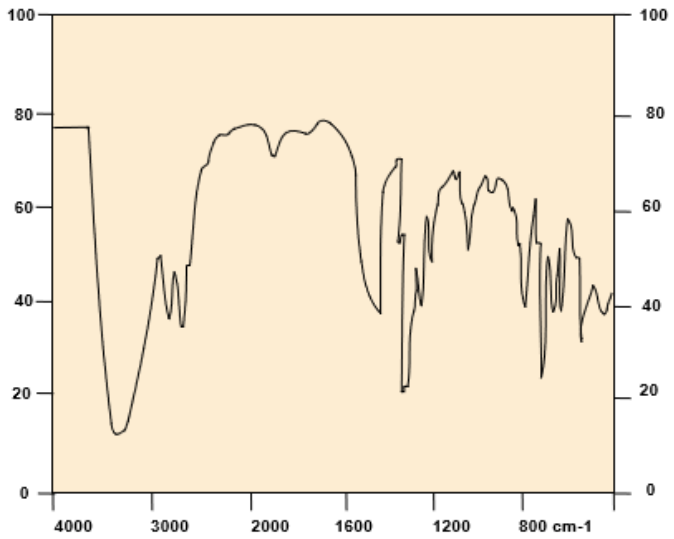
Typical Physical Properties

DUOLITE™ AP143/1083 complies with the compendial specifications for Cholestyramine Resin USP when tested in conformance to the compendial test methods presented in current USP/NF. The resin is described as a “White to buff colored, hygroscopic, fine powder. Is odorless or has not more than a slight amine-like odor. Insoluble in water, in alcohol, in chloroform and in ether.”

Identification

DUOLITE™ AP143/1083 can be identified by infrared spectroscopy, as shown in the example Figure 1.

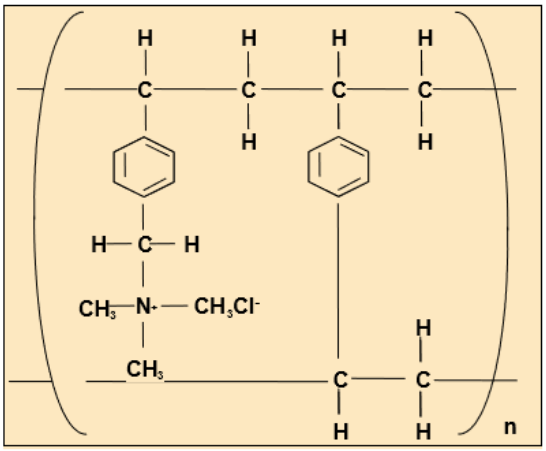
Figure 1. DUOLITE™ AP143/1083 IR Spectrum



Chemical Properties

DUOLITE™ AP143/1083 is derived from a copolymer of styrene and divinylbenzene with quaternary ammonium functionality. The mobile, or exchangeable, anion is chloride which can be exchanged for, or replaced by, virtually any anionic species. DUOLITE™ AP143/1083 Resin is an insoluble salt of a strong base and a strong acid; hence, its ability to exchange anions is largely independent of pH. The chemical structure of DUOLITE™ AP143/1083 is shown below in Fig. 2.

Figure 2. Chemical Structure



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Applications

- Taste Masking
- Drug Stabilization
- Controlled Release
- Active Ingredient

When used as a drug carrier, DUOLITE™ AP143/1083 provides a means for binding medicinal agents onto an insoluble polymeric matrix; this can be an effective technique to minimize taste and odor problems associated with the drug.

Controlled or sustained release properties can also be imparted to oral dosage formulations through the formation of resin-drug complexes (drug resinates). The drug is released from the resin in vivo as the drug resinate reaches equilibrium with the high electrolyte concentrations typically found in the gastrointestinal tract.

When used as an active ingredient, DUOLITE™ AP143/1083 binds bile acids; this leads to replenishment of the bile acids through increased catabolism of serum cholesterol, resulting in lowered serum cholesterol levels.

Drug Loading

Batch equilibration is the preferred practice when loading a drug or other sorbate into finely divided ion exchange resin powders. Due to its fine particle size, DUOLITE™ AP143/1083 Resin does not lend itself to conventional columnar operations used with ion exchange resins.

The total anion exchange capacity represents the maximum achievable capacity for exchanging ions, measured under ideal laboratory conditions. The capacity which will be realized when loading a drug onto DUOLITE™ AP143/1083 will be less than this ideal; typically loadings will normally be between 5% and 50% of this maximum. The actual amount of a drug loaded onto DUOLITE™ AP143/1083 will be influenced by such factors as the inherent selectivity of the anion exchange resin for the drug, the drug's concentration in the loading solution and the concentration of competing anions also present in the loading solution. The rate of loading will be affected by the activity of the drug and its molecular dimensions as well as the extent to which the polymer phase is swollen during loading.

When utilizing a batch or equilibrium contact to load a drug or other anionic sorbate onto DUOLITE™ AP143/1083, it is usually desirable to load as much as possible of the substance of value onto the resin. Complete transfer of the drug from the loading solution is not likely in a single equilibrium stage. Accordingly, more than one equilibration may be required in order to achieve the desired loading onto the resin. The use of two or more loading stages, separating the resin from the liquid phase between stages, is an effective means of achieving maximum loading of the drug onto the resin while maintaining minimum loss of drug from the liquid phase of the final stage.

Although carefully controlled laboratory experiments are required to establish precise loading and elution conditions, a few general principles can be used. High loading capacity will be favored by high charge density in the drug. A high loading rate is favored by lower molecular weight. Higher drug concentrations in the loading solution, with a minimum of competing anions, will also favor higher adsorption capacity.

Drug Release

The rate and completeness of drug desorption in vivo will be controlled by the diffusion rate of the drug through the polymer phase of the resin (usually a function of molecular weight), the selectivity of the drug for the resin and the concentration of electrolytes in the desorption environment.

Cholestyramine Applications Reference List

Irwin, W. J, R. MacHale, and P. J. Watts. (1990) Drug-delivery by ion exchange. Part VII: Release of acidic drugs from anionic exchange resinate complexes. Drug. Dev. Ind. Pharm. 16(6):883-898

Sriwongjanya, Mongkol; Bodmeier, Roland; Effect of ion exchange resins on the drug release from matrix tablets; College Pharmacy, Freie Universitaet Berlin, Berlin, D-12169, Germany; Eur. J. Pharm. Biopharm. (1998), 46(3), 321-327
Polli, Gerald P. and Shoop, Clyde E., (Merck and Co. USA), 1976. Palatable cholestyramine coacervate compositions. Patent US 3,974,272.

Brauns H. A., Polli, Gerald P and Shoop, Clyde E., (Merck and Co., USA), 1974. Cholestyramine containing coacervate. Ger. Offen DE 2,344,090.

Kunin, Robert; Blood cholesterol reducing pharmaceutical composition; 1998; Patent US 5840339.

Product Stewardship

DuPont has a fundamental concern for all who make, distribute, and use its products, and for the environment in which we live. This concern is the basis for our product stewardship philosophy by which we assess the safety, health, and environmental information on our products and then take appropriate steps to protect employee and public health and our environment. The success of our product stewardship program rests with each and every individual involved with DuPont products—from the initial concept and research, to manufacture, use, sale, disposal, and recycle of each product.

Customer Notice

DuPont strongly encourages its customers to review both their manufacturing processes and their applications of DuPont products from the standpoint of human health and environmental quality to ensure that DuPont products are not used in ways for which they are not intended or tested. DuPont personnel are available to answer your questions and to provide reasonable technical support. DuPont product literature, including safety data sheets, should be consulted prior to use of DuPont products. Current safety data sheets are available from DuPont.

Please be aware of the following:

- **WARNING:** Oxidizing agents such as nitric acid attack organic ion exchange resins under certain conditions. This could lead to anything from slight resin degradation to a violent exothermic reaction (explosion). Before using strong oxidizing agents, consult sources knowledgeable in handling such materials.
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