AMBERLITE™ IRP69
Pharmaceutical Grade Cation Exchange Resin
(Sodium Polystyrene Sulfonate USP)

Description

AMBERLITE™ IRP69[1] resin is an insoluble, strongly acidic, sodium form cation exchange resin supplied as a dry, fine powder. AMBERLITE IRP69 Resin is suitable for use in pharmaceutical applications, both as an active ingredient and as a carrier for basic (cationic) drugs. It can be used for sustained release applications with compatible coating technologies.

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

Regulatory Status

A Drug Master File for AMBERLITE IRP69 is maintained with the United States Food and Drug Administration. Letters of authorization granting access to the file by FDA in support of NDA and ANDA submittals will be provided upon request. Similar help can also be offered in support of the registration of formulations containing AMBERLITE IRP69 in many other countries world-wide. AMBERLITE IRP69 is manufactured in accordance with Good Manufacturing Practices (cGMP) for bulk pharmaceutical chemicals.

Typical Physical and Chemical Properties

AMBERLITE IRP69 complies with the compendial specifications for Sodium Polystyrene Sulfonate USP when tested in conformance to the compendial test methods presented in current USP/NF.

Ionic form	Sodium
Particle size	
> 0.075 mm	10.0–25.0%
> 0.150 mm	1.0% maximum
Heavy metals content [1]	≤ 10 ppm
Potassium exchange capacity [1]	110–135 mg/g
Water content [1]	10.0% maximum
Ammonia salts [1]	Negative to litmus paper
Sodium content [1]	9.4%–11.5%
Styrene content [1]	1 ppm maximum

[1] Appears in current USP/NF

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Identification

AMBERLITE™ IRP69 can be identified by infrared spectroscopy, as shown in the example Figure 1.

Figure 1. AMBERLITE IRP69 Resin IR Spectrum

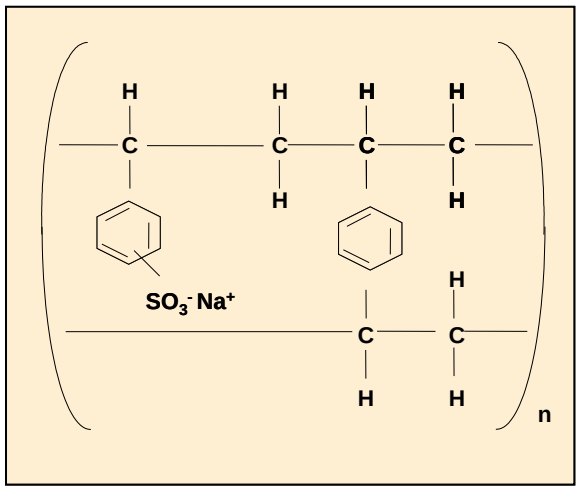
Chemical Properties

AMBERLITE™ IRP69 is derived from a sulfonated copolymer of styrene and divinylbenzene. The mobile, or exchangeable, cation is sodium; this can be exchanged for, or replaced by, many cationic (basic) species.

Since AMBERLITE IRP69 is an insoluble salt of a strong acid and a strong base, its ability to exchange ions is virtually independent of pH.

The chemical structure for AMBERLITE IRP69 is shown in Figure 2.

Figure 2. AMBERLITE IRP69 Resin Chemical Structure



Applications

Applications for AMBERLITE IRP69 include:

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

When used as a drug carrier, AMBERLITE IRP69 provides a means for binding medicinal agents onto an insoluble polymeric matrix. This can afford an effective means for minimizing problems of taste and odor which may be associated with the drug substance. 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 reaches equilibrium with the high electrolyte concentrations which are typical of the gastrointestinal tract.

As an active ingredient, AMBERLITE™ IRP69 can be used as a therapeutic agent to lower potassium levels in the treatment of hyperkaliemia.

Drug Loading

Batch equilibration is the preferred practice when loading a drug or other sorbate into finely divided ion exchange resin powders.

The total cation exchange capacity (~5 meq/g) represents the maximum achievable capacity for exchanging cations. The capacity which will be realized when loading a drug onto AMBERLITE IRP69 Resin will be less than this ideal; typically loadings will normally be between 5% and 75% of this maximum.

The actual amount of a drug loaded onto AMBERLITE IRP69 will be influenced by such factors as:

- the inherent selectivity of the sulfonic exchange groups for the drug.
- the drug's concentration in the loading solution.
- the concentration of competing cations also present in the loading solution.
- the choice of solvent
- the molecular size of the drug

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 cationic sorbate onto AMBERLITE IRP69, 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.

Carefully controlled laboratory experiments are required to establish precise loading and elution conditions.

Drug Release

The rate and completeness of drug desorption in vivo will be affected by:

- The diffusion rate of the drug through the phase of the resin.
- The selectivity of the drug for the resin.
- The nature and concentration of electrolytes in the bulk phase during desorption.

More hydrophobic drugs will usually elute from the resin at a lower rate, owing to hydrophobic interactions with the aromatic structure of the cation exchange system.

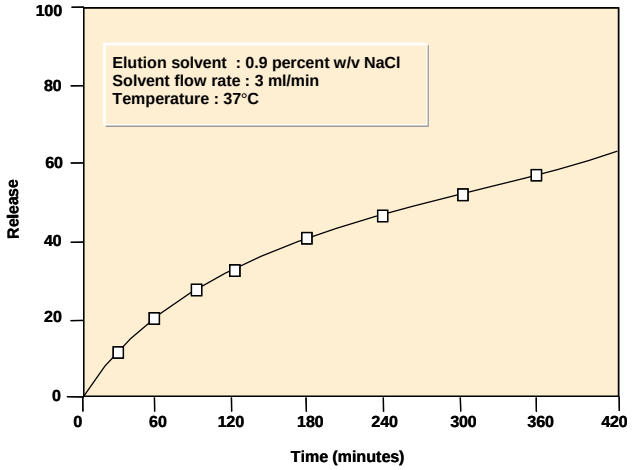
An example of this might be the presence of a transition metal in the structure of the sorbate molecule which can result in considerable selectivity through the formation of a coordination compound with the resin.

The following table and Figure 3 show the typical drug release properties for AMBERLITE™ IRP69 Resin.

Drug Release Characteristics of AMBERLITE IRP69 Resin

% Drug released in 0.1N HCl				
Time, minutes	Phenylpropanolamine	Dextromethorphan	Pseudoephedrine	Ephedrine
15	82	21	64	63
30	88	43	66	66
60	92	60	67	68
90	95	71	68	69

Figure 3. Dextromethorphan Release from AMBERLITE IRP69 Resin (0.9% w/v NaCl)



Controlled / Sustained Release

Amsel, L.P., O.N. Hinsvark, K. Rotenberg, and J.L. Sheumaker, 1983. recent advances in sustained release technology utilizing ion exchange polymers. Proc. Pharm Tech. Conf. '83: 251-266.

Ferro, M.T., and F.C. Mondelo, 1987. Preparation of (-) eburnamenin-1,4(1,5H)-one resinates. Patent GB2,184,731.

Raghunathan, Y., 1980. Prolonged release pharmaceutical preparations. Patent US 4,221,778.

Applications Reference List

Raghunathan, Y., L.P. Amsel, O.N. Hinsvark, and W. Bryant, 1981. Sustained-release drug delivery system I: Coated ion exchange resin system for phenylpropanolamine and other drugs. J. Phar. Sci. 70 (4): 379-384.

Raghunathan, Y., 1983. Sustained-release liquid pharmaceuticals containing ionic components. Patent US 532,864.

Raghunathan, Y., 1989. Controlled release pharmaceutical preparations. Patent US 4,487,077

Sheumaker, J.L, 1988. Liquid prolonged release pharmaceutical formulations containing ionic constituents. Patent US 4,762,709.

Taste-Masking

Martel, J., J. Tessler, P. Girault, and P. Grandadam., 1981. Acid type ion exchange resins and their use as medicines and compositions containing them. Patent EP 27,768.

Quinlan, J. M., 1980. Diethylcarbamazine resinate and Strylpyridinium resinate-diethylcarbamazine resinate edible anthelmintic tablets for companion animals. Patent GB 2,055,575.

Safe Handling Information

Before using this product, consult the Material Safety Data Sheet (MSDS)/Safety Data Sheet (SDS) for details on product hazards, recommended handling precautions and product storage.

Product Stewardship

Dow 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 Dow products - from the initial concept and research, to manufacture, use, sale, disposal, and recycle of each product.

Customer Notice

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

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.

DOW™ Ion Exchange Resins
For more information about DOW™ resins, call the Dow Water & Process Solutions business:
North America: 1-800-447-4369
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