



AMBERLITE™ IRP69

Pharmaceutical Grade Cation Exchange Resin

(SODIUM POLYSTYRENE SULFONATE USP)

PRODUCT DATA SHEET

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.

Regulatory Status

A Drug Master File for AMBERLITE IRP69 resin 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 submissions 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 resin is manufactured in accordance with Good Manufacturing Practices (cGMP) for bulk pharmaceutical chemicals.

Typical Physical Properties

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

Identification

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

AMBERLITE IRP69 IR Spectrum

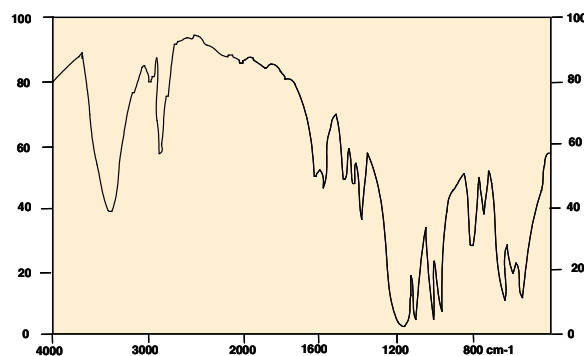


Figure 1

^[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.

TABLE I : TYPICAL PHYSICAL PROPERTIES

| | |
|--|--------------------------|
| Ionic form _____ | Sodium |
| Particle size _____ | |
| > 0.075 mm ^[2] _____ | 10.0 - 25.0 % |
| > 0.150 mm ^[2] _____ | 1.0 % maximum |
| Heavy metals content ^{[2] [3]} _____ | ≤ 10 ppm |
| Potassium exchange capacity ^{[2] [3]} _____ | 110 to 135 mg/g |
| Water content ^{[2] [3]} _____ | 10.0 % maximum |
| Ammonia salts ^{[2] [3]} _____ | Negative to litmus paper |
| Sodium content ^{[2] [3]} _____ | 9.4 % to 11.5 % |
| Styrene content ^[2] _____ | 1 ppm maximum |

^[2] Contractual value

^[3] Appears in current USP/NF.

CHEMICAL PROPERTIES

AMBERLITE™ IRP69 resin 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 resin 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.

AMBERLITE IRP69 Chemical Structure

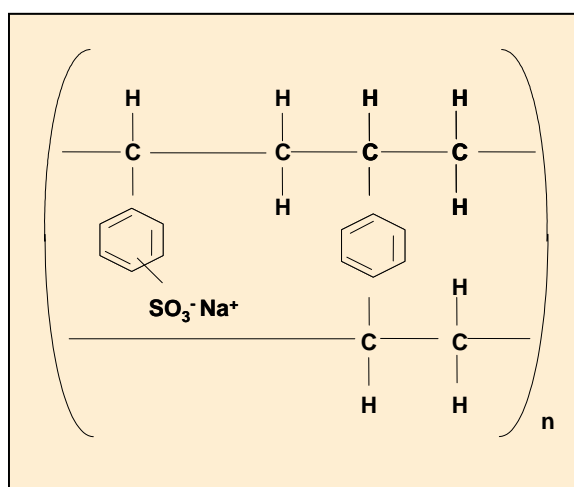


Figure 2

APPLICATIONS

Applications for AMBERLITE IRP69 resin include:

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

When used as a **drug carrier**, AMBERLITE IRP69 resin 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 resin is used as a therapeutic agent to lower potassium levels in the treatment of hyperkalemia.

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 resin 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 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.

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.

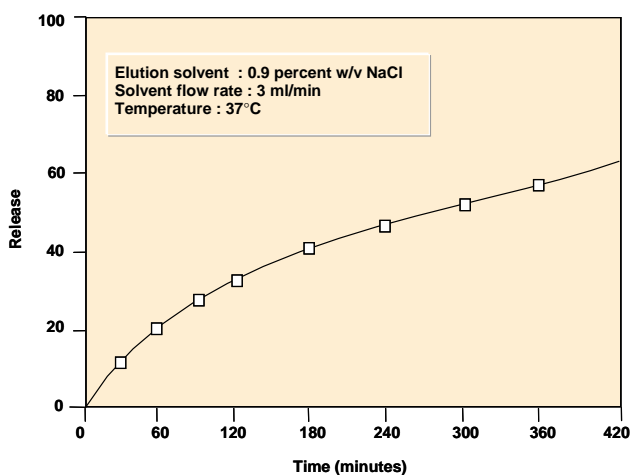
An example of this might be the presence of a transition metal in the structure of the sorbate molecule which can result in considerable selectivity through the formation of a coordination compound with the resin.

The following table and Figure 3 show the drug release properties for AMBERLITE™ IRP69 resin

Drug Release Characteristics of Amberlite IRP69 Resin

| Time, minutes | % Drug released in 0.1N HCl | | | |
|---------------|-----------------------------|-------------------|------------------|-----------|
| | Phenyl-propranolamine | Dextro-methorphan | Pseudo-ephedrine | 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)



AMBERLITE IRP69 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 phenylpropranolamine 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.

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 resins. Patent GB2,184,731.

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

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

Material Safety Data Sheets (MSDS) are available for all Rohm and Haas products. These sheets contain pertinent information that you may need to protect your employees and customers against any known health or safety hazards associated with our products.

We recommend that you obtain copies of our MSDS by calling 1-800-RH-AMBER before using our products in your facilities. We also suggest that you contact your suppliers of other materials recommended for use with our products for appropriate health and safety precautions before using them.

Caution: Acidic and basic regenerant solutions are corrosive and should be handled in a manner that will prevent eye and skin contact. In addition, the hazards of other organic solvents should be recognized and steps taken to control exposure.

Nitric acid and other strong oxidizing agents can cause explosive reactions when mixed with ion exchange resins. Proper design of process equipment to prevent rapid build up of pressure is necessary if use of an oxidizing agent such as nitric acid is contemplated. Before using strong oxidizing agents in contact with ion exchange resins, consult sources knowledgeable in the handling of these materials.

Note: Ion exchange resins and polymeric adsorbents, as produced, contain by-products resulting from the manufacturing process. The user must determine the extent to which organic by-products must be removed for any particular use and establish techniques to assure that the appropriate level of purity is achieved for that use. The user must ensure compliance with all prudent safety standards and regulatory requirements governing the application. Except where specifically otherwise stated, Rohm and Haas Company does not recommend its ion exchange resins or polymeric adsorbents as supplied as being suitable or appropriately pure for any particular use. Consult your Rohm and Haas technical representative for further information

All our products are produced in ISO 9001 certified manufacturing facilities.

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