



AMBERLITE™ IRP64

Pharmaceutical Grade Cation Exchange Resin

(POLACRILEX RESIN)

PRODUCT DATA SHEET

AMBERLITE™ IRP64¹ resin is an insoluble, weakly acidic, hydrogen form, cation exchange resin supplied as a dry, fine powder. AMBERLITE IRP64 resin is suitable for use in pharmaceutical applications, primarily as a carrier for certain basic (cationic) drugs and related substances. It is also used to mask objectionable tastes associated with certain basic drugs. Commercial examples of its use include:

- Stabilization of Vitamin B12
- Sustained Release of Nicotine

A Drug Master File for this product 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 assistance can also be offered in support of the registration of formulations containing AMBERLITE IRP64 in many other countries. AMBERLITE IRP64 resin is manufactured in accordance with Good Manufacturing Practices (cGMP) for bulk pharmaceutical chemicals.

Identification

AMBERLITE IRP64 resin can be identified by infrared spectroscopy, as shown in the sample spectrum in Fig. 1.

Figure 1: AMBERLITE IRP64 IR Spectrum

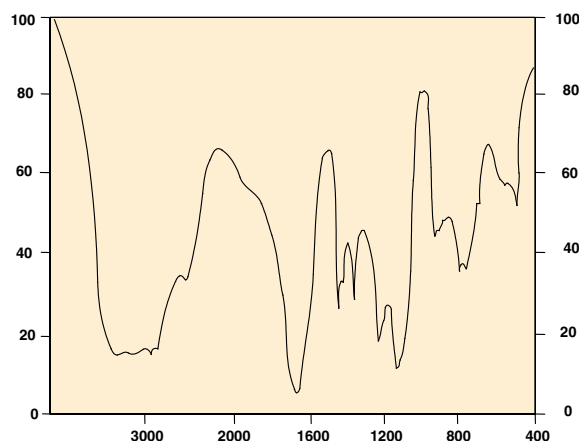


TABLE I : PRODUCT SPECIFICATIONS

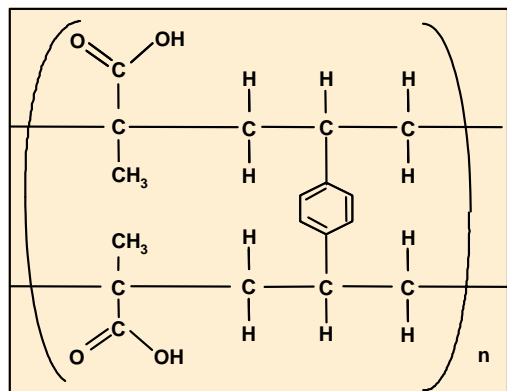
Ionic form _____	Hydrogen
Appearance _____	White to off white fine powder free of foreign matter and any agglomeration
IR Identification _____	Conforms to reference spectrum assay
Exchange capacity «as is» _____	Not less than 10.0 meq/g, on dried basis
Purify Testing	
Sodium _____	Not more than 0.20 %
Heavy metals _____	Not more than 0.001 %
Iron _____	Not more than 0.01 %
Methacrylic acid _____	Not more than 300 ppm
Water extractable impurities _____	Not more than 2.0 %
Physico-chemical Testing	
Loss on drying _____	Not more than 5.0 %
Particle size _____	
> 0.150 mm _____	Not more than 1.0 %
> 0.075 mm _____	15.0 to 30.0 %
< 0.050 mm _____	Not more than 70.0 %
Microbial Purity	
Total bacterial count _____	Not more than 100 cfu/g
Total mold count _____	Not more than 100 cfu/g

⁽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.

CHEMICAL STRUCTURE

AMBERLITE™ IRP64 resin is derived from a porous copolymer of methacrylic acid and divinylbenzene. The chemical structure of AMBERLITE IRP64 is shown in Figure 2.

Figure 2: AMBERLITE IRP64 Chemical Structure



APPLICATIONS

Applications for Amberlite IRP64 include:

- Taste Masking
- Drug Stabilization
- Carrier for Cationic Drugs
- Controlled Release Formulations

AMBERLITE IRP64 resin provides a means for binding medicinal agents onto an insoluble polymeric matrix. This affords an effective technique for overcoming problems of taste and odor in oral dosage formulations as well as providing a matrix upon which a sustained or controlled release formulation can be developed.

The high affinity of AMBERLITE IRP64 resin for the hydrogen ion results in ready desorption of adsorbed species by exposure to an acidic environment, such as that exhibited in the stomach. This accounts for the higher desorption efficiencies versus a strong acid cation resin like AMBERLITE IRP69.

Chemical instability problems can sometimes be resolved by adsorption on to AMBERLITE IRP64 resin. For example, complexes of AMBERLITE IRP64 resin with cyanocobalamin (Vitamin B12), a nonionic material, have been used for many years as a means of providing a stable oral dosage form of this vitamin.

Drug Loading

Batch equilibration is the preferred practice when loading a drug or other sorbate into finely divided ion exchange resins. resin powders. Due to its fine particle size, AMBERLITE IRP64 resin does not lend itself to conventional columnar operations normally used with ion exchange resins.

The mobile, or exchangeable, cation in IRP64 resin is the hydrogen ion. In acidic environments (generally below pH 4) AMBERLITE IRP64 resin exists as the free acid in an essentially nonionic state. Adsorption (loading) onto this cation exchange resin is usually carried out at pH 6 or higher.

The amount of drug loaded onto AMBERLITE IRP64 resin will be influenced by such factors as:

- the inherent affinity or selectivity between the ion exchange resin and the drug.
- the concentration of the drug in the loading solution.
- the concentration and selectivity of competing cations.
- the pH of 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 AMBERLITE IRP64 resin, it may be 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.

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 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 particularly in the hydrogen ion, in the desorption environment.

More hydrophobic drugs will usually elute from the resin at a lower rate, as will drugs with a relatively high selectivity for the carboxylic acid functional structure in the resin. Other resin-sorbate interactions are possible, and these can have a pronounced effect upon loading capacities and rates.

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.

SAFE HANDLING INFORMATION

Material Safety Data Sheets

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.

AMBERLITE™ IRP64 APPLICATIONS REFERENCE LIST

Controlled/Sustained Release

Leo Corporation, 1973. Smoking substitutes and method of production. Patent GB 1,325,011.

Taste-Masking

Douglas, S.J. Glaxo Group Research Ltd, 1990. Process for the preparation of a ranitidine resin absorbate. US 5219 563.

Astruc, J., and A. Sambot, 1970. Ion-exchange resin: spiramycin compositions. Patent GB 1,180,233.

Borodkin, S., and D.P. Sundberg, 1971. Chewable tablets including coated particles of pseudoephedrine-weak cation exchange resin. Patent US 3,594,470.

Other

Fretland, D.J., 1974. Use of ion-exchange resins for removing prostaglandins from human urine prior to radioimmunoassay. Prostaglandins 6 (5): 421-425.

Miles Laboratories, Inc., 1970 Detection device for enzymes and other factors in body fluids. Patent US 3,616,251.

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

Rohm and Haas/Ion Exchange Resins - Philadelphia, PA - Tel. (800) RH AMBER - Fax: (1) 215-409-4534
Rohm and Haas/Ion Exchange Resins - 75579 Paris Cedex 12 - Tel. (33) 1 40 02 50 00 - Fax : 1 43 45 28 19

WEB SITE: <http://www.rohmhaas.com/ionexchange/Pharmaceuticals>

