

Pharmaceutical Products

This report deals with pharmaceutical products that require the use of homogenizing and dispersing equipment for proper preparation. Some of these products contain medicinal ingredients that must be dispersed in a vehicle in which they are not soluble, or they contain ingredients that must be incorporated into a base for application to the skin. Other types of products require emulsification to facilitate their injection and use in the body.

Creams, ointments and lotions can consist of medicinals dispersed in a continuous-phase vehicle or medicinals incorporated into oil-in-water (o/w) or water-in-oil (w/o) emulsions. Except for the medicinal ingredients, the base vehicles in creams, ointments and lotions are quite similar in formulation to cosmetic preparations. It has been found that properly formulated pharmaceutical emulsions and dispersions provide more accurate control of the dosage. They will also furnish a method of combining many immiscible ingredients into a single, stable product, and this improves the ease of application. The proper formulation and control of particle size and stability bring about the controlled release of the active ingredients.

When preparing these emulsions and dispersions, Gaulin and Rannie equipment provides the best control over the desired qualities of particle and droplet size and stability. Research work at Purdue University demonstrated that for certain types of pharmaceutical emulsions, such as liquid petrolatum and cod liver oil emulsions, the Gaulin homogenizer..."was the most effective of all the equipment studied...one pass through the homogenizer produced a much greater particle-size reduction than any other piece of equipment used."¹ The equipment studied included a Wall mixer, a Waring blender, an Eppenbach homo-mixer, a Tri-Homo disperser, an Eppenbach colloid mill and a Gaulin homogenizer. Another research paper showed that the Gaulin homogenizer, again, was the most effective piece of equipment for dispersing the suspending agents, bentonite U.S.P. and Veegum[®] HV. These suspending agents thicken a pharmaceutical preparation and impart the desired stability characteristics to the product.²

The following pharmaceutical products have been prepared using the Gaulin and Rannie homogenizers:

aloe lotion	cod liver oil emulsions	mineral oil emulsions
analgesic creams	intravenous emulsions	penicillin
antacid	laxatives	pharmaceutical creams
artificial blood	liposomes	vaccine emulsions
benzoyl peroxide	medicinal soaps	Veegum [®] dispersions
calamine lotion	milk of magnesia	vitamins
		zinc oxide dispersions

Because of the diversity of pharmaceutical products processed with Gaulin and Rannie equipment, it would require considerable space to detail each application; however, some general remarks can be made regarding the use of this equipment

The **homogenizer** is most effective under the following conditions: with oil-in-water emulsions, where the Newtonian oil viscosity is less than 500 cP; with oil-in-water emulsions, where the oil level is less than 50%; for dispersing solids such as benzoyl peroxide and antacid preparations (usually in the pressure range of 3000-5000 psi); and for generating very small droplet-size emulsions (all droplets less than one micrometer) with uniform size distribution.

Two special applications of homogenization are perfluorochemical emulsions and intravenous emulsions for nutritive therapy. (Also, see Process Report entitled "Intravenous Emulsions".)

The emulsions of perfluorochemicals have been called artificial blood, because they have been used as a blood substitute in animals and humans³. A more accurate description for these products is temporary oxygen carriers. These emulsions consist of a perfluorochemical emulsified in water. The water phase contains an emulsifier, salts and other additives. The perfluorochemicals are gas carriers, which dissolve large amounts of gases, are chemically inert and are generally nontoxic. In a pure form these compounds would cause immediate embolism; therefore, they must be emulsified in water. The droplet size of the emulsion must fall in the range of 0.1 μm to 0.6 μm , because "acute toxicity was found to increase rapidly with the proportion of particles larger than 0.4 μm ."⁴ To satisfy the small-droplet-size-range requirement, a high-pressure Gaulin or Rannie homogenizer is used. Normally, more than one pass through the homogenizer is required, because multiple passes generate a more narrow size distribution.

Intravenous emulsions for nutritive therapy are used when a patient is not able to take food or accept vascular administration of nutrition. These emulsions consist of oil, such as soybean oil, an emulsifier, such as a phospholipid, and a balanced blend of amino acids in a continuous phase of distilled water.⁵⁻⁸ These emulsions are injected into the vein and provide a means of administering a nutritive fluid to the patient. The droplet size of the oil must be kept small, usually below 0.6 μm with an average size of about 0.3 μm . Again, the Gaulin or Rannie high-pressure homogenizer is used with multiple passes to generate a small particle size and a narrow size distribution.

References:

1. Peck, G.E., H. G. DeKay and G. S. Banker, "A Comparative Study of Pharmaceutical Emulsification Equipment", *Journal of American Pharm. Assoc.*, **49**, No. 2, 75 (1960).
2. Simon, T.H., H. G. DeKay and G. S. Banker, "Effects of Processing on the Rheology of Thixotropic Suspensions", *Journal Pharmaceutical Sci.*, **50**, No. 10, 880 (1961).
3. Riess, J.H. and M. LeBlanc, "Perfluro Compounds as Blood Substitutes", *Angew. Chem. Int. Ed. Eng.*, **17**, No. 9, 621 (1978).
4. Simon, op cit.
5. Suzuki, A., H. Miura, K. Sawada and Y. Koida, (to Tanabe Pharmaceutical Co., Ltd.), "Process for Producing a Synthetic Nutritive Fluid for Therapy", Japanese Patent 7492 (1978).
6. Wretlind, A.J., "Method of Preparing Intravenously Injectable Fat Emulsions Free from Side Reactions or Complications", U. S. Pat. 3,169,094, Feb. 9, 1965.
7. Davis, S.S., J. Hadgraft and K.J. Palin, "Medical and Pharmaceutical Applications of Emulsions", Chapter 3, *Encyclopedia of Emulsion Technology*, Vol. 2, P. Becher, ed., Marcel Dekker, Inc., N.Y. (1985).
8. Pandolfe, W., "Homogenisation – An Overview", *European Pharmaceutical Contractor*, May 1998, pp. 72 – 78.

APV, An SPX Brand
Phone: 1-888-278-4321 Email: answers.us@apv.com

For more information about our worldwide locations, approvals, certifications, and local representatives, please visit www.apv.com.

SPX reserves the right to incorporate our latest design and material changes without notice or obligation. Design features, materials of construction and dimensional data, as described in this bulletin, are provided for your information only and should not be relied upon unless confirmed in writing.