Rapid Method of Obtaining the Clear Aqueous Filtrate of an Oil/Water Emulsion

Sir:

In most reports on experiments requiring the assay of one or both phases of an emulsion, the technique used to separate these phases involves centrifugation. Very often this technique is useless without the aid of a high-speed (or ultra-) centrifuge. Due to the nature of centrifugation, it is almost impossible to perform any short-term kinetic studies dealing with the partitioning of a drug from one phase of an emulsion to the other.

The authors have found in these laboratories that most o/w emulsions can be filtered, yielding a clear filtrate of the aqueous phase. The technique makes use of a vacuum pump, membrane filter assembly, and membrane filters, such as those manufactured by the Millipore Filter Corp., Bedford, Mass. The pore size required varies according to the droplet size of the internal phase and the interfacial tension between the drop and the external phase. For emulsions of very small particle size ($< 1\ \mu$), it was found that passing the emulsion through a .22-μ filter, and then passing the filtrate through a 100-mμ filter was adequate in most cases. It is difficult to filter large quantities, due to clogging (we assume) of the pores of the filter. This is overcome by changing the filter. Prefilters were tested, but proved ineffective.

In the filtering of preparations containing high amounts of surface-active agents, foaming occurs, but can be controlled by judicious use of the vacuum. Pressure filtration was not attempted. Emulsions (o/w) prepared from nonionic, anionic, and cationic emulsifiers were all capable of being filtered. When the per cent of internal phase was about 8–10%, clogging occurred faster than with more dilute emulsions.

The equation of Young and Laplace (1), $\Delta P = 2\gamma/r$, where ΔP is the pressure difference, inside and out of the drop, γ is the interfacial tension, and r is the radius of the droplet, can be used to determine the filtering requirements. If ΔP of the emulsion is greater than 1×10^6 dynes cm.$^{-2}$, and if the pore of the filter has a significantly smaller diameter than that of the droplet, the droplet will not be appreciably distorted, and can be filtered from the external phase.

This method is currently being employed in studying the rate of transport of a drug from the aqueous phase to an emulsified oil phase. The oil content is about 2%, with the droplet size being approximately 1.5 μ in diameter. The emulsion is sampled initially at 60-sec. intervals, and the disappearance of the drug from the aqueous phase is measured.

It was also determined that the oil phase, if external, can be obtained with the internal phase (water) being left on the filter.

This filtration method was also tested as a means of rapidly determining partition coefficients. Reese *et al.* (2) reported in 1964 a nonemulsion method for determining partition coefficients. They reported the True Partition Coefficient of benzoic acid in cyclohexane as being 1.18; the Apparent Partition Coefficient (their method) was 1.05, with 6 hr. required to be within 1% of equilibrium. Repeating their work, using an emulsion prepared by ultrasonification for 20 min., gave an Apparent Partition Coefficient of 1.27.

This method of filtering emulsions carries with it the limitations of membrane filters, *i.e.*, sorption and/or leaching of the filter materials. This may be minimized by use of the fluorinated hydrocarbon filters. It also permits assay of only the external phase, with the implicit assumption that what is not in the external phase is in the internal.

(1) Adamson, A. W., "Physical Chemistry of Surfaces,' Interscience Publishers, New York, N. Y., 1963.
(2) Reese, D. R., Irwin, G. M., Dittert, L. W., Chong, C. W., and Swintosky, J. V., *J. Pharm. Sci.*, **53**, 591(1964).

ARTHUR H. GOLDBERG
GEORGE ZOGRAFI
WILLIAM I. HIGUCHI

College of Pharmacy
University of Michigan
Ann Arbor 48104

Received October 24, 1966.
Accepted for publication December 5, 1966.

This investigation was supported by a fellowship from the Eli Lilly Foundation, in part by fellowship 1-F1-GM-34,237-01 from the National Institute of General Medical Sciences, and in part by grant GM-13368-01 from the National Institute of General Medical Sciences, U. S. Public Health Service, Bethesda, Md.