Application Notes

Liposome Characterization

Liposomes and vesicles have elicited great interest in a number of applications ranging from targeted drug delivery systems to cosmetics. This note concerns pharmaceutical liposome formulations, several of which are currently undergoing Phase II clinical trials at the U.S. Food and Drug Administration.

One of the most important parameters of a liposomal formulation is its size distribution, which in pharmaceutical applications, tends to be in the range of 80–200 nm. The combination of a cross-flow field flow fractionator (FFF) and a DAWN multi-angle light scattering instrument is ideally suited to the absolute characterization of particle sizes within this range.

Because of the absence of a stationary phase, FFF is able to separate a sample for subsequent light scattering analysis without the artifacts associated with size exclusion columns. The DAWN instrument, by virtue of its 18 scattering angles, provides *actual* size measurements *directly* from the angular variation of the light scattered by the particles. In this fashion, the *distribution* of liposome sizes may be quickly and accurately determined.

Unlike photon correlation spectroscopy (PCS), in which a sample is analyzed *without* separation, and attempts are made to deconvolve the size distribution from the signal, the FFF / DAWN system provides a *direct* size determination with *no assumptions.*

Using this combined instrument system, the size distribution of a pharmaceutical liposome formulation was determined. Figure 1 illustrates the rms radius versus volume, superposed over the 90° light scattering signal. Note that in contrast to GPC / SEC separation, the *smaller* liposomes elute *first* in FFF.

The distribution of liposome sizes is presented in Figure 2. The data show a distinct peak at about 95 nm, but the distribution is by no means monodisperse, as it has components up to at least 180 nm.

These data show the enormous power of the FFF / DAWN. Since the sample is separated into its individual size components, much more specific distribution information is produced—instead of relying on PCS and its generalized answers.

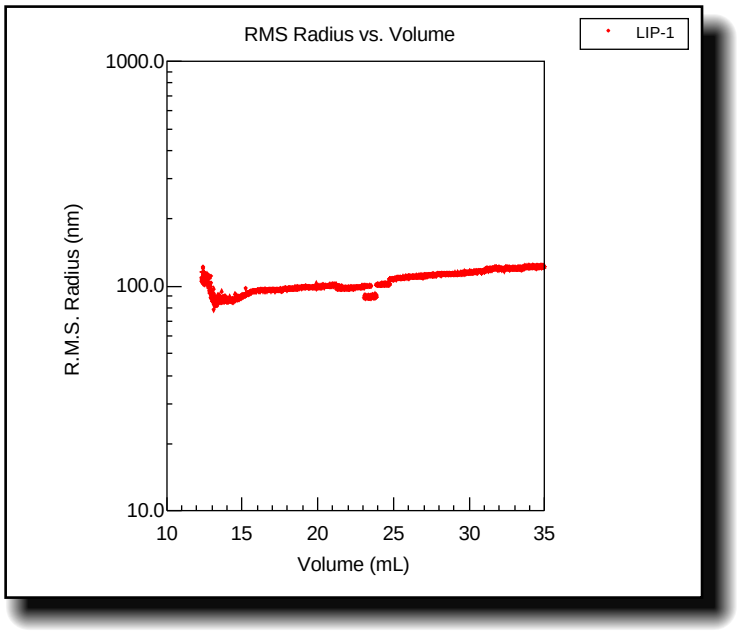

Figure 1. The RMS Radius vs. Volume is overlayed on the 90° light scattering signal.

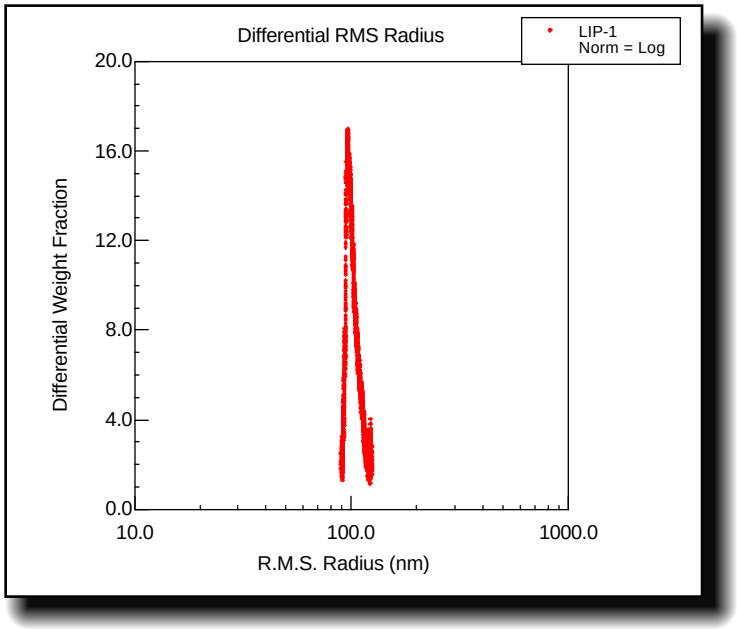

Figure 2. The Differential RMS radius is plotted showing the preponderance of liposomes sized around 95-100 nm.

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