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Study of Density Gradients in Certain Oil-in-Water Emulsions Using Multichannel Gamma Ray Analysis

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Abstract ☐ Variations in the attenuation of the 0.084 Mev. total absorption gamma photopeak of ¹⁷⁰Tm result when o/w emulsions exhibiting any separation (not necessarily visible) are placed in plastic parallel-sided containers and moved vertically between a radioactive source and a scintillation detector arranged horizontally. Slow raising or lowering of emulsion systems allows the making of an attenuation "map" of the system when data are accumulated using a multichannel analyzer in multiscale mode, and read out *via* a tape printer. Curves showing log attenuation (and hence density) *versus* channel number, their first differences, and equations are presented.

Keyphrases ☐ Density gradients oil-in-water emulsions—analysis ☐ Analysis, multichannel gamma ray—density gradient ☐ Emulsions, curves—Pearl-Reed *versus* Gompertz

The application of the photoextinction method (1, 2) to the state of matter through which visible and other radiation passes has been explored in detail. It has the obvious limitation that unless relative transparency to the incident radiation exists, it is insensitive. Disperse systems are, in general, opaque to visible light,

equally nonconducting to UV radiation, and, since they usually contain some water, are not amenable to IR evaluation unless attenuated total reflectance techniques are employed. Gamma photons of appropriate energy (0.01–0.10 Mev) are a usable source of radiation for the study of disperse systems of pharmaceutical interest whose optical properties forbid the use of visible light, and whose phase densities vary by not more than 0.20 grams per milliliter (3). Studies using scintillation detectors and monoenergetic gamma photons have been carried out (4) which indicate that the logarithm of the radiation intensity attenuation by the intervening system is proportional to the logarithm of the density or the specific gravity of that system. Thus, the ratio of the logarithm of the attenuated or reduced activity to the logarithm of the density of a given system is a constant. This study is concerned with the activity attenuation profiles of certain systems and their relationship to (*a*) position of maximum change within the system; (*b*) time dependency of attenuation change, and (*c*) the rate at which the attenuation change occurs at a given instant or position within a system.
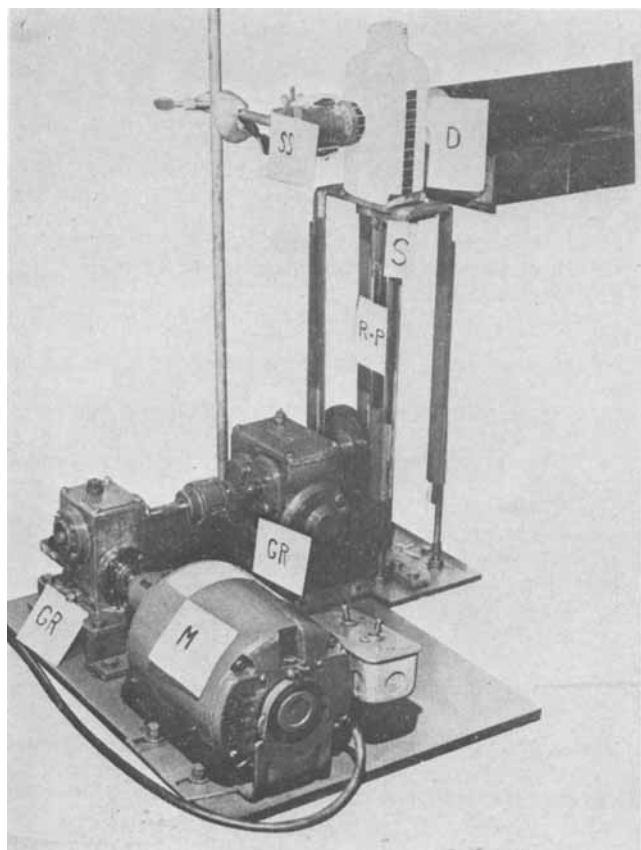
Figure 1—*Apparatus for study of density gradients in emulsions. Key: D, detector; SS, sealed source; S, stage; R + P, rack and pinion gear; GR, gear reduction boxes, M, motor.*

APPARATUS

Radioactive Source and Container—Ten millicuries of ^{170}Tm (as the chloride in solution) were transferred in 500-μl. amounts to a cylindrical lead container 6.35-cm. diameter $\times$ 10.16 cm. high (2.5-in. diameter $\times$ 4 in. high) holding a force-fitted solid plastic insert into which a cylindrical hole 5.08 cm. deep $\times$ 0.31-cm.
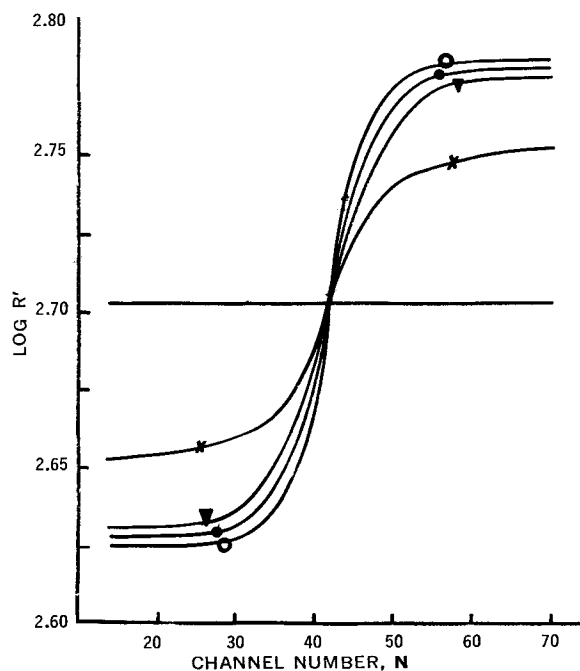

Figure 2—*Log attenuated activity profiles for O/W emulsion as a function of channel number. Key: $\bigcirc$, t = 90 days; $\bullet$, t = 28 days; $\blacktriangledown$, t = 14 days; $\times$, t = 7 days; and horizontal, t = 0.*

diameter (2 in. deep $\times$ 0.125-in. diameter) had been drilled. After each transfer, the source and container were dried under IR light to concentrate and produce a point source. To collimate the gamma radiation, a piece of lead sheeting 0.31 cm. (0.125 in.) thick with a slit 2.0 mm. wide was placed over the mouth of the container.

Detector—A thallium-activated sodium iodide crystal 3.18 cm. $\times$ 2.54 cm. (1.25 in. $\times$ 1 in.) and accompanying photomultiplier tube (Tracerlab, model P-51) served as detector. Lead sheeting [0.31-cm. (0.125-in.) thick] with a 2.0-mm. slit placed across the face of the crystal served as further collimation for incident radiation.

Stage—A 1760-r.p.m. motor with two gear-reduction boxes allowed the raising and lowering of systems being studied. These were placed on a metal stage 6.35 cm. (2.5 in.) wide and 15.24 cm. (6.0 in.) long, connected by rack and pinion to the shaft of the last gear reduction box. Gear reductions and tooth ratios were calculated so that the stage could be elevated or lowered 30.0 cm. in 5.00 min. so that a uniform velocity of 1.0 mm. per second could be maintained (see Fig. 1).

Analyzer and Readout—A channel analyzer (Nuclear Data 128, model ND-110) was used to store counting data. Readout was accomplished visually using an oscilloscope (model ND-410), and digitally using a printer (Victor, model ND-315).

MATERIALS

Emulsions—Oil-in-water emulsions containing varying quantities of mineral oil[1] (average viscosity, 75 cks. at 25°), sorbitan monopalmitate,[2] polyoxyethylene sorbitan monopalmitate,[3] and distilled water were prepared and homogenized by being put through a hand homogenizer twice. Concentrations of the ingredients were varied to give apparent stability for periods from 1 week to 1 year.

Standards—Hydroalcoholic solutions were prepared whose densities varied from 0.800–0.998 g. per ml. Their densities were determined using a Mohr-Westphal balance and were corrected to 25°.

Containers—Parallel-sided 1-pint plastic bottles served as containers for both standards and systems under study. These were used because they attenuated the radiation much less than did glass bottles of equal volume.

METHODS

The hydroalcoholic solution standards were placed on the stage and passed vertically between source and detector, during which time counting data were accumulated. The plastic bottles were filled to three-quarters of their total volume to allow counts to be obtained in the air space above the liquid level. This allowed for about 15 channels of counting information which, when averaged, became the observed count rate (R_a) through the sample container and intervening air. Repeated counting data obtained with empty sample containers between source and detector indicated that this number of channels was sufficient to yield statistically significant information. The multichannel analyzer was set in the multiscale mode with a dwell time of 1 sec./channel. The rate of rise of the stage was 1.0 mm. per second, so the channel address changed each millimeter of scan and at 1-sec. intervals. Since the time required for change of channel address is of the order of microseconds, no correction for this was considered necessary. Thus data were accumulated in units of counts per second per channel (R_s) of counts per second per millimeter of scan. In the analysis to follow, various emulsion parameters are expressed as a function of channel number (N) as independent variable; however, the independent variable could as well have been time in seconds or scan distance in millimeters under the conditions of the experiment. In any case, either count rate or activity attenuation by standard solutions is (R_a − R_s). A plot of the linear relationship between log (R_a − R_s) and log density (slope, 1.62) was made, which indicated that (R_a − R_s) is proportional to (density)$^{1.62}$. Since this constant power relationship exists between activity attenuation and density, dependent variables

might be expressed either in terms of log density, or directly in terms of log attenuated activity. The latter coordinate was chosen, and emulsion systems, scanned in exactly the same way as were the standard solutions, were analyzed using log $(R_a - R_e)$, called log R', as ordinate and channel number (N) as abscissa. Where first differences (approximating first derivatives) are plotted as ordinate, $[\Delta(\log R')/\Delta N]$ is used.

Data were accumulated as the stage holding the standard or 7.62 cm. emulsion and container ascended. Since the source and detector (3.0 in. apart) were arranged horizontally and elevated, the radiation passed first through the container and air space above an emulsion, then through the oil-rich portion, across the interface, and finally into the aqueous portion, i.e., in the direction of increasing density.

Instrument stability was ascertained by daily counts made through the same container which held distilled water at $25 \pm 2°$. Statistical analysis by chi square and Chauvenet's criterion revealed no apparent nonrandom fluctuations in instrument behavior.

RESULTS AND DISCUSSION

The form taken by log R' as a function of channel number is illustrated in Fig. 2. The data were fitted by the least squares method of Bliss (5) to a logistic or Pearl-Reed curve (6), which in one of its simpler forms is

$$y = \frac{k}{1 + e^{-ax}} \qquad \text{(Eq. 1)}$$

which has k as upper asymptote and zero as its lower. The midpoint of this sigmoidal curve is at the vertical intercept which is $k/2$.

Translating the curve upward a distance y_0 and to the right a distance x_0 yields

$$y - y_0 = \frac{k}{1 - e^{-a(x - x_0)}} \qquad \text{(Eq. 2)}$$

Writing Eq. 2 in terms of activity attenuation and channel number, gives

$$\log R' = \log R_L' + \frac{\log R_U' - \log R_L'}{1 + e^{-a(N - N_0)}} \qquad \text{(Eq. 3)}$$

where log R_U' and log R_L' are, respectively, the upper and lower asymptotes, and N_0 is the channel corresponding to the midpoint of the curve. At this midpoint $(R_{1/2})$, the change in log R' per channel $[\Delta(\log R')/\Delta N]$ is maximal.

It may be seen that

as $\qquad N \rightarrow \infty, \log R' \rightarrow \log R_U'$,

as $\qquad N \rightarrow \infty, \log R' \rightarrow \log R_L'$

as $\quad N \rightarrow N_0, \log R' \rightarrow \dfrac{\log R_U' + \log R_L'}{2} = \log R_{1/2}'$,

and as $\quad N \rightarrow 0, \log R' \rightarrow \log R_L' + \dfrac{\log R_U' - \log R_L'}{1 + e^{aN_0}}$,

the vertical intercept.

If $[\Delta(\log R')/\Delta N]$ becomes maximal for large N, then as $N \rightarrow 0$, log $R' \cong \log R_L'$, as would be expected.

Figure 2 shows five scans of an emulsion system which was essentially completely separated after a 3-month period. Values of $[\Delta(\log R')/\Delta N]$ were maximal in Channel 42 (see also Fig. 3). This corresponded to a log $R_{1/2}'$ value of 2.678, a lower asymptote at 2.600, and an upper asymptote at 2.755. Thus Eq. 3 becomes

$$\log R' = \log R_L' + \frac{\log R_U' - \log R_L'}{1 + e^{-0.476(N - N_0)}} \qquad \text{(Eq. 4)}$$

for this system.

The logistic, rather than the Gompertz curve (6) was considered to be the better fit for two reasons:

1. A plot of (log $R' - \log R_L'$)/(log $R_U' - \log R_L'$) $\times$ 100% versus channel number gave reasonably good fit (using least squares) when plotted on arithmetic probability paper (Fig. 4). The resemblance of Fig. 2 to a cumulative frequency distribution is evident,
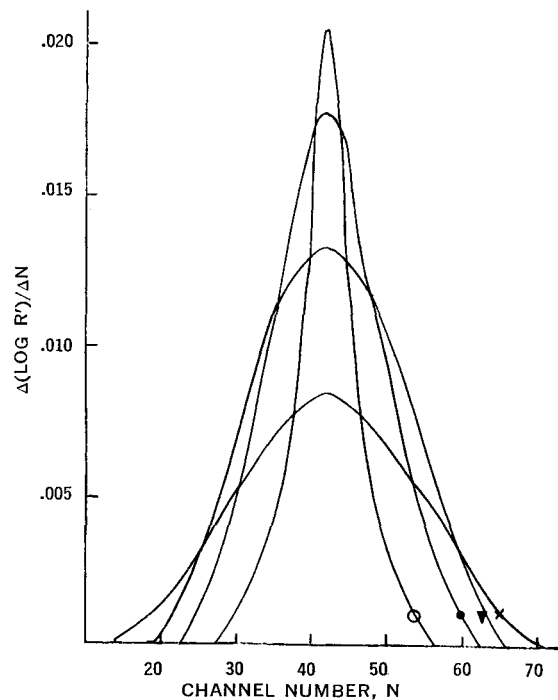

Figure 3—*Attenuated activity gradient shapes, illustrating variations in kurtosis with time. Key is that of Fig. 2.*

and a linear probability plot would indicate a symmetrical distribution, if not a normal one.

2. Inspection of Fig. 3 reveals a series of bell-shaped curves having varying degrees of kurtosis but no apparent skewness. Skewness in plots of $[\Delta(\log R')/\Delta N]$ versus N would indicate that a Gompertz curve would be the better fit (6).

An effective interface width may be evaluated if the best straight line (by least squares) is drawn through the inclined portions of Fig. 1, extrapolated through both asymptotes, and its slope determined. This slope may be written

$$m = \frac{\log R_U' - \log R_L'}{N_U - N_L} \qquad \text{(Eq. 5)}$$

(where N_U and N_L are channel numbers corresponding to the intersections of the extrapolated lines with the upper and lower asymptotes). Its numerator is a measure of density difference across the interface, and its denominator is a measure of the sharpness of separation. Values of the ratio should vary from zero (in the case of complete dispersion) to infinity (in the case of an infinitely sharp interface). In systems studied, values ranged from 0 to 0.155/8, or 0.0193 log units per channel. This corresponded to an average
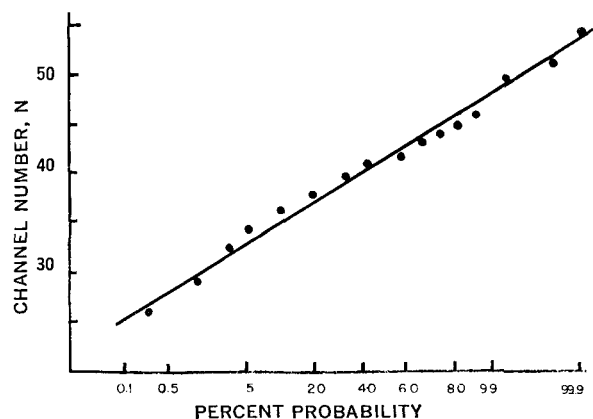

Figure 4—*Linear plot on arithmetic probability paper indicating activity gradient symmetry, and hence the applicability of the logistic curve to fitting attenuated activity profiles.*
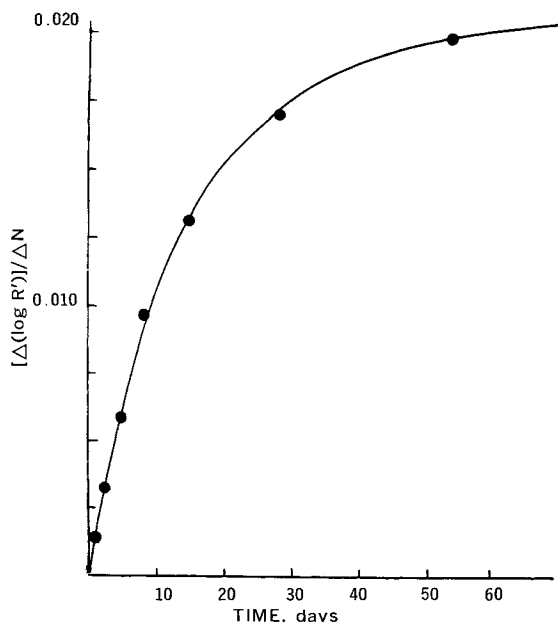
Figure 5—*Asymptotic growth curve illustrating the dependence of attenuated activity gradient maxima on time.*

density difference of 0.011 g./ml./channel at maximum emulsion separation. Figure 2, then, is a "map" of emulsion density; average density changes per channel may be graphically or numerically determined from it; but the actual shapes of density changes per channel are given by Fig. 4, which represents the spatial density gradient. Values of maximum change ranged from 0 to 0.0205 log units, corresponding to a maximum density change of 0.012 g./ml./channel (in the case where separation was substantially complete).

The shapes of spatial gradients are time-dependent, since emulsion separation is time-dependent. A plot, such as Fig. 5, which relates maximum density change per channel to time, then serves as a time gradient. The rate at which density change maxima increase with time indicates a rate of separation "growth." Figure 5 is an asymptotic growth curve (6), whose equation may be written in simplest terms (with y a function of t)

$$y = C(1 - e^{-nt}),$$ (Eq. 6)

with C as upper asymptote and n the growth constant.
In terms of attenuation gradient,

$$\frac{\Delta(\log R')}{\Delta N} = \frac{\Delta(\log R_{max}.')}{\Delta N} (1 - e^{-nt})$$ (Eq. 7)

Numerically, for the system under study, $[\Delta(\log R_{max}.')/\Delta N] = 0.0205$ and $n = 0.495$ (weeks)$^{-1}$.

Thus it can be seen that with the passage of time, density profiles of emulsions change, and that the change in density gradient is even more marked, not only in maximum value, but in shape as well.

Future work will include analysis of many more data points by computer. Investigations will include (a) emulsion systems such as those discussed here; (b) band and boundary sedimentation studies on suspensions of pharmaceutical interest; (c) the effects of emulsion and suspension composition and concentration on density gradient shapes; and (d) the applicability of the gamma-attenuation method to particle size and particle shape analysis. Here, it is felt that the computer will be a particularly useful tool.

SUMMARY

A sealed ^{170}Tm source acts as an emitter of gamma photons of suitable energy for the study of density profiles and density gradients in w/o emulsions. Samples and standards are placed on a slowly ascending stage and are passed between the source and a solid scintillation detector connected to a multichannel analyzer. Data are accumulated with the analyzer in the multiscale mode and are printed out on tape. Density profiles proved to be sigmoidal and density gradients bell-shaped. Gradient maxima relate to time by an asymptotic growth curve.

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