Evaluation of Emulsion Stability by Diffuse Reflectance Spectroscopy

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Abstract □ A new method is described for evaluating the stability of emulsion bases and active components contained within such emulsions. Diffuse reflectance spectroscopy (DRS) is a technique that has the capability of detecting changes in particle size, surface properties, or drug quality of emulsions as a function of time without disturbance of the system. Such physical or chemical changes are monitored by changes in the visible and UV wavelength spectral characteristics of the emulsified systems. Four basic emulsion systems were prepared and analyzed for physical stability for 6 months by three techniques: visible coalescence, particle counting measurement, and DRS. Two drugs, aspirin and ascorbic acid, were then incorporated within stable emulsion bases, and the chemical stability of these drugs was monitored by DRS for 6 months. Results were compared with concomitant quantitative drug assay procedures. Good agreement was observed when data from DRS and analytical measurements were compared. The DRS technique may be used as a supportive method, offering simplicity and expedience, with other methods of evaluating emulsion stability and drug stability within emulsified systems.

Keyphrases □ Emulsions—system stability and stability of incorporated drugs, evaluated by diffuse reflectance spectroscopy, compared to visible coalescence and particle counter techniques □ Spectroscopy, diffuse reflectance—evaluation of stability of emulsions and active components in emulsions, compared to visible coalescence and particle counter techniques □ Aspirin—stability in emulsions, evaluated by diffuse reflectance spectroscopy □ Ascorbic acid—stability in emulsions, evaluated by diffuse reflectance spectroscopy

The stabilization of a thermodynamically unstable emulsified system presents a challenging proposition to the developmental pharmacist. The intimate dispersal of two immiscible liquids is prone to instability due to the natural tendency of like molecules to coalesce.

A literature survey shows that various techniques have been employed to evaluate emulsion stability. Most of these methods were reviewed previously (1). Size–distribution analysis of the emulsion as a function of time is the physical property most commonly measured, but other emulsion physical properties evaluated include particle charge, viscosity, creaming rate, and interfacial tension.

Lloyd (2) reported that optical methods to evaluate emulsion stability had received minimal attention and showed that the following relationship exists for oil-in-water emulsions:

$$R = \frac{c}{D^k} \qquad \text{(Eq. 1)}$$

where R is the reflectance at the wavelength at which the colored internal phase partially absorbs the incident light, D is the surface mean particle diameter:

$$D = \frac{\Sigma n_i d_i^3}{\Sigma n_i d_i^2}$$

and c and k are constants characteristic of the emulsion system. It was demonstrated that reflectance techniques can be applied to evaluate different emulsion stabilizers and to study the kinetics of emulsion coalescence.

Although Lloyd's reflectance technique has been utilized (3), few published papers relate to this subject. The reflectance technique known as diffuse reflectance spectroscopy (DRS) was utilized to study solid–solid interactions between drugs and formulation ingredients (4–7). DRS was sensitive to changes occurring at the surfaces of solid drug molecules due to interactions with other solid molecules. It was assumed that DRS might also detect surface changes due to the coalescence of particles in emulsions. In addition, since DRS gives spectra that closely resemble transmittance spectra, it should be possible to monitor the stability of an active ingredient formulated within an emulsified system.

Four 50% oil-in-water emulsions were prepared, each containing a different stabilizer, and analyzed for physical stability as a function of time using this DRS technique. Subsequently, aspirin and ascorbic acid were incorporated into the emulsion bases shown to be stable, and DRS was applied to ascertain the chemical stability of these drugs as a function of time. Thus, the intent of this investigation was to show the application of DRS as a sensitive tool for evaluating emulsion stability and drug stability in an emulsified formulation.

EXPERIMENTAL

Reagents—The stabilizers used were gum arabic[1] USP, polyoxyethylene sorbitan monooleate[2], sorbitan monopalmitate[2], sorbitan monolaurate[2], and sodium lauryl sulfate[3] USP. The two drugs used were aspirin[4], mp 133–135°, and L-ascorbic acid[5], reagent grade, mp 190–193°.

Preparation of Emulsions—All oil-soluble components were dissolved in the oil phase; heat was used if necessary, but precaution was taken not to use excessive temperatures. Water-soluble components were dissolved in the aqueous phase. Equal volumes of oil and aqueous phase were combined and triturated by a mortar and pestle to form a coarse emulsion. The emulsion was then emulsified for 2 min[6].

Composition of Emulsions—All emulsions were 50% oil-in-water emulsions except for emulsions containing gum arabic, which were 40% (Table I). Heavy mineral oil[7] was used as the oil phase. The percentage of stabilizer in these oil-in-water emulsions is given in Table I.

For the drug-containing emulsions, 6% (w/v) aspirin was formulated into Emulsion 1. The drug was dissolved in the oil phase. L-Ascorbic acid was incorporated into two different emulsion formulations: (*a*) 11.7% ascorbic acid in Emulsion 1, and (*b*) 9.33% ascorbic acid in Emulsion 2.

[1] S. B. Penick & Co., New York, N.Y.
[2] Atlas Chemical Industries, Wilmington, Del.
[3] E. I. du Pont de Nemours and Co., Wilmington, Del.
[4] Mallinckrodt Chemical Works, St. Louis, Mo.
[5] Fisher Scientific Co., Fair Lawn, N.J.
[6] Eppenbach colloid mill, Gifford-Wood Co., New York, N.Y.
[7] Paraffin oil, heavy, Fisher Scientific Co., Fair Lawn, N.J.

Table I—Composition of Emulsion Bases Used in This Study

Emulsion 1	40% mineral oil in water 10% (w/v) gum arabic 0.02% sorbic acid
Emulsion 2	50% mineral oil in water 4% (v/v) sorbitan monopalmitate and polyoxyethylene sorbitan monooleate, HLB = 10.85
Emulsion 3	50% mineral oil in water 4% (w/v) sorbitan monolaurate
Emulsion 4	50% mineral oil in water 4% (w/v) sodium lauryl sulfate

Reflectance Measurement—Diffuse reflectance spectra were measured using a spectrophotometer with a reflectance attachment[8]. Special Plexiglas cells (Fig. 1) were manufactured to contain the emulsion sample to be analyzed.

The emulsion sample was introduced into the cell through a hole on top with a disposable pipet until the entire shaded area was filled with sample. All cells were leakproof. The reflectance of emulsions was measured relative to a white standard such as magnesium oxide, while reflectances of drug-containing emulsions were measured relative to an identical emulsion base containing no drug. The instrument was zeroed in at 400 nm using two white standards, and the reflectance spectrum was measured from 700 to 200 nm. Precision of the technique was 0.1% R.

Measurement of Particle-Size Distribution of Emulsions—The particle counter[9], calibrated periodically with monosized ragweed pollen particles, was used to determine average particle size (d_m) of emulsions as a function of time. The emulsions were gently shaken prior to the withdrawal of a 2-ml sample, which was then diluted to 1 liter with distilled water. The 1-liter solution was vigorously shaken for 2 min, and then another 2-ml sample was withdrawn and diluted to 200 ml with 0.9% sodium chloride solution. Since the emulsion sample was diluted 50,000-fold, it was assumed that droplet sizes would not be affected significantly by using the saline vehicle rather than the appropriate surfactant vehicle.

To test this assumption and to check the reproducibility of the particle-size determination, Emulsions 1 and 2, triplicates and duplicates, respectively (Table I), were treated in this manner. The results are shown in Table II. The low standard error and percent error indicate that use of the saline vehicle did not cause irreproducible results.

Measurement of Coalescence—The same procedure as described by Rowe (8) was used immediately after preparation. A 50-ml emulsion sample was poured into a 50-ml graduated cylinder and stoppered. The volume ratio of the two phases was ascertained at room temperature as a function of time.

Methods of Drug Analysis—The aspirin emulsion was analyzed by determining the percent of salicylic acid formed as a result of aspirin partitioning from the oil to the aqueous phase and immediately hydrolyzed. A modification of the spectrophotometric method of Clayton and Thiers (9) was used for the assay of salicylic acid in the emulsion aqueous phase. A 20-ml emulsion sample was taken at the appropriate time intervals and centrifuged[10] for 15 min to separate the aqueous and oil phases. Aliquots of the aqueous phase were diluted with 2 N NaOH, filtered, and analyzed at 301 nm for salicylic acid[11].

Identical emulsions without drug were treated by the same procedure and used as reference blanks. A standard curve was obtained by dissolving known quantities of salicylic acid in the aqueous phase of the emulsion and using the same procedure.

The USP iodometric titration method was used to measure the degradation of ascorbic acid in emulsions. An emulsion sample equivalent to 400 mg of ascorbic acid was dissolved in a mixture of 100 ml of carbon dioxide-free water and 25 ml of dilute sulfuric acid. The solution was titrated at once with 0.1 N iodine solution

[8] Beckman model DB-G.
[9] Coulter counter, model B, Coulter Electronics Industrial Division.
[10] International centrifuge, No. 6404914.
[11] Gilford spectrophotometer model 240.

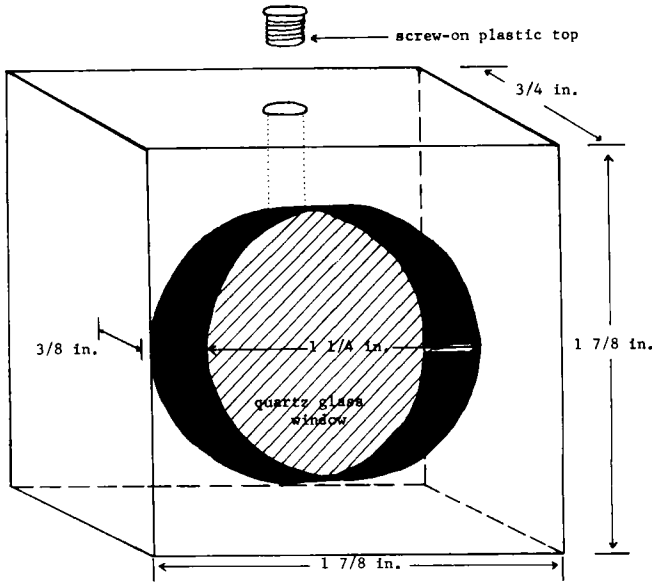

Figure 1—*Design of special Plexiglas cell used for diffuse reflectance measurement of emulsions.*

standardized with arsenious oxide; as the end-point was approached, a few drops of starch TS were added as an indicator. Each milliliter of 0.1 N iodine was equivalent to 8.8 mg of ascorbic acid.

Experimental Design—After preparation, the emulsions were allowed to stand for 1 day before initial measurements were taken. This period allowed the emulsion components to reach a pseudo-equilibrium state. Emulsions were subjected to coalescence measurement, particle-size analysis, reflectance measurement, and analysis of the active ingredient once each month for 6 months. The aspirin emulsions were subjected to these studies each week for the 1st month and then treated like the other emulsions for the remaining 5 months.

THEORY

When radiation is directed onto the surface of a solid or semisolid, two types of reflectance from that surface can result. The first type, called regular reflectance or "mirror reflection," is governed by the Fresnel equations. The second type, called diffuse reflectance, is interpreted by the Kubelka–Munk equation (10):

$$f(r_\infty) = \frac{(1 - r_\infty)^2}{2r_\infty} = \frac{k}{s} \qquad \text{(Eq. 2)}$$

where $f(r_\infty)$ is the remission function, r_∞ is the relative reflectance, k is the absorption coefficient, and s is the scattering coefficient. A portion of the radiant flux penetrates into the interior of a sample, and part of this radiation returns to the sample surface. The remaining part of the incident flux is absorbed and scattered at the boundaries of the individual particles comprising the sample.

Taking the logarithm of the remission function gives:

$$\log f(r_\infty) = \log k - \log s \qquad \text{(Eq. 3)}$$

Table II—Data Verifying the Reproducibility of Particle Counting Measurements Using Emulsion 1 (Triplicates) and Emulsion 2 (Duplicates)

	Emulsion 1		Emulsion 2	
Months	Mean d_m (n = 3)	Standard Error	Mean d_m (n = 2)	Percent Error
0	2.916	0.108	2.601	1.920
1	3.146	0.181	2.816	1.060
2	3.055	0.195	2.976	3.020
3	3.320	0.125	2.850	1.750
4	3.276	0.176	2.805	2.862
5	3.386	0.162	2.850	4.387
6	3.586	0.185	2.904	4.141

Table III—Stability Evaluation of Oil-in-Water Emulsion Bases Indicated by Changes[a] in Percent Coalescence ($\Delta\%C$), Changes[a] in Percent Mean Particle Diameter ($\Delta\%d_m$), and Changes[a] in Percent Reflectance Intensity at Selected Wavelengths ($\Delta\%R\lambda$) as a Function of Time

	Emulsion 1				Emulsion 2				Emulsion 3				Emulsion 4			
Months	$\Delta\%C$	$\Delta\%d_m$	$\Delta\%R$, 500 nm	$\Delta\%R$, 320 nm	$\Delta\%C$	$\Delta\%d_m$	$\Delta\%R$, 500 nm	$\Delta\%R$, 300 nm	$\Delta\%C$	$\Delta\%d_m$	$\Delta\%R$, 500 nm	$\Delta\%R$, 300 nm	$\Delta\%C$	$\Delta\%d_m$	$\Delta\%R$, 500 nm	$\Delta\%R$, 300 nm
1	0	11.8	−3	−2	0	11.7	0	0	25	16.4	−4	−1	31	38.6	−4	+2
2	1	3.8	−3	0	0	20.4	−2	+3	31	34.0	−5	−4	31	52.7	−5	0
3	3	9.2	−4	0	0	9.8	−2	+3	36	51.3	−10	−6	31	42.6	−10	−5
4	9	16.0	−4	−2	0	6.6	−2	+3	37	41.0	−17	−11	31	54.0	−18	−18
5	10	18.5	−6	−2	0	6.6	−2	+5	38	61.9	−17	−13	31	71.1	−22	−17
6	10	20.2	−8	−7	0	9.0	−2	+4	38	68.8	−18	−16	31	76.2	−29	−24

[a] Changes relative to measurements taken at zero time.

Table IV—Correlation Coefficients (r) between Any Two of Three Dependent Variables Used to Evaluate Stability of the Four Basic Emulsions Monthly for 6 Months

Months	$\Delta\%d_m$ *versus* $\Delta\%R_{300}$	$\Delta\%d_m$ *versus* $\Delta\%C$	$\Delta\%C$ *versus* $\Delta\%R_{300}$
1	0.864	0.806	0.609
2	0.264	0.863	0.713
3	0.952	0.985	0.974
4	0.997	0.927	0.900
5	0.990	0.958	0.946
6	0.971	0.960	0.894

Thus, a plot of $\log f(r_\infty)$ *versus* wavelength results in a curve corresponding to the real absorption spectrum of the compound determined by $\%T$, except for a displacement of $-\log s$ in the ordinate direction. The value of s is a very complicated function of the ratio of the particle size to the wavelength used (11). In the experiments described in this paper, one or two representative wavelengths were selected and comparisons with time were made at these two wavelengths only. However, $\log s$ may not remain constant if the ratio of drop size to wavelength changes appreciably with time.

The intensity of reflectance at a selected wavelength can be related directly to the concentration of the absorbing species in the sample because of the following relationship (12):

$$f(r_\infty) = \frac{\epsilon c}{s} \qquad \text{(Eq. 4)}$$

where ϵ is the molar extinction coefficient, and c is the molar concentration.

The application of reflectance measurements to emulsion stability studies was first investigated by Langlois *et al.* (13). They found a direct relationship between the specific interfacial area of emulsions composed of nonabsorbing components and the transmission of light by emulsions relative to the continuous phase. The relative light transmission, I_0/I, was related to the interfacial area, A, by the following equation:

$$\frac{I_0}{I} = 1 + \beta A \qquad \text{(Eq. 5)}$$

The term β was a constant found to be a function of the ratio N_d/N_c, the refractive indexes of the disperse and continuous phases, respectively.

Lloyd (2) demonstrated the existence of an inverse relationship between the reflectances, r, of colored oil-in-water emulsions and the surface-average particle diameter, d, of their dispersed phases:

$$\log R = -k \log D + \log c \qquad \text{(Eq. 6)}$$

where k and c are constants characteristic of the emulsion system. The surface average particle diameter is inversely related to the specific interfacial area, A, of a given emulsion by:

$$D = \frac{6f}{A} \qquad \text{(Eq. 7)}$$

where f is the volume fraction of the dispersed phase. This equation is based on the implicit assumption that all drops are the same size. Thus, reflectance is proportional to the specific interfacial area of the emulsion raised to the k power:

$$R = C^1 A^k \qquad \text{(Eq. 8)}$$

where $C^1 = c/(6f)^k$.

Table V—Areas under the Percent Reflectance *versus* Wavelength Curves (AUC)[a]

Emulsion	Emulsifying Agent	AUC Zero Time, cm²	AUC 6 Months, cm²	Difference
1	Gum arabic	106	100	−6
2	Sorbitan monopalmitate/polyoxyethylene sorbitan monooleate	156	164	+8
3	Sorbitan monolaurate	144	116	−28
4	Sodium lauryl sulfate	158	112	−46

[a] AUC determined by the $K + E$ polar planimeter No. 62 0005 between 550 and 200 nm.

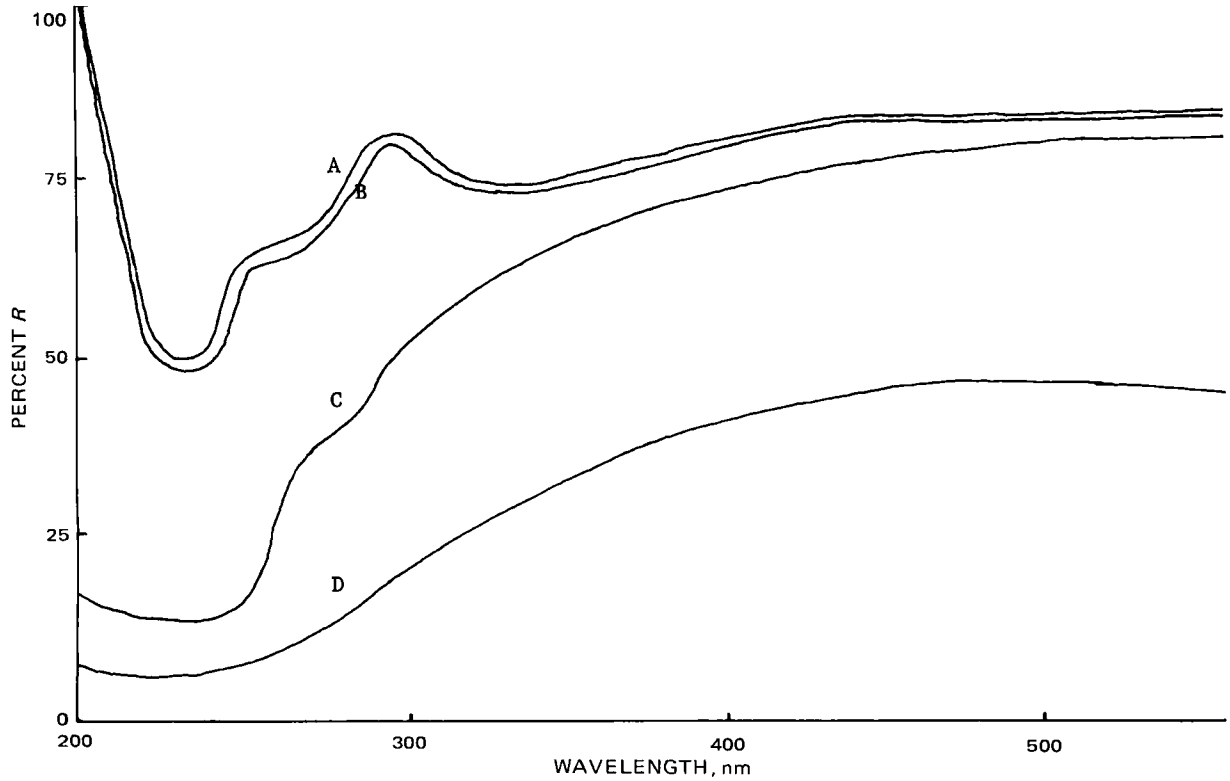

Figure 2—*Reflectance spectra of a stable 50% oil-in-water emulsion initially (curve A) and 1 month after preparation (curve B) and of an unstable 50% oil-in-water emulsion initially (curve C) and 1 month after preparation (curve D).*

Giovanelli (14) studied the influence of particle aggregation on the reflectance of nonhomogeneous media. In a uniform medium, R depends only on k/s (Eq. 2), which represents the fraction of light lost by scattering. In aggregated systems, represented by unstable emulsions, R depends on the attenuation coefficient K:

$$K = k + s \qquad \text{(Eq. 9)}$$

which represents all radiation lost by both absorption, k, and scattering, s. Although k/s may still be constant, R may be decreased by 30% if large aggregates are present. Previously, it was stated that the diffusely reflected component must be scattered by individual particles for reflectance to occur. As Giovanelli (14) indirectly showed, if aggregation of these individual particles occurs, the concentration of scattering centers and, consequently, the diffuse reflectance is reduced.

Interpretations based on light scattering of dispersed systems may be complex. Additional confusion may be introduced by realizing that reflectance can be influenced by factors other than particle size, *e.g.*, wavelength, refractive index, and particle shape (10). However, to simplify the interpretations, the following things were done:

1. Simple emulsion compositions were used.
2. All emulsions were prepared in exactly the same manner, which initially provided nearly a constant particle size of all emulsions.
3. By using the Plexiglas cell (Fig. 1), equal emulsion volumes were measured, with distances and angles between radiation source and sample being identical.
4. Only one wavelength was monitored per emulsion, except for the determination of areas under the reflectance curves.
5. The experiments were duplicated.

RESULTS AND DISCUSSION

Emulsions are dynamic systems in which changes in the physical properties and/or phase composition of the components of the system are constantly occurring. In this paper, the mere separation of the two phases into a cream layer and aqueous phase is defined as an instability. With most analytical techniques, it is necessary to sample the emulsion and thus disturb the pseudoequilibrium state of that system. This disturbance possibly could affect the reproducibility of later analyses.

DRS offers the advantage that the stability of an emulsion can be evaluated without disturbance of the system. Once the freshly prepared emulsion sample is placed in the specially designed DRS Plexiglas cell, the cell is sealed and the emulsion is left undisturbed for the duration of the experiment. Theoretically, DRS should detect changes occurring in the microenvironment within the surfaces of emulsion systems which cannot be seen visually.

Figure 2 shows general characteristics of DRS curves. Wavelength regions in the visible and UV spectra are scanned, and reflectance intensities from 0 (100% absorbance) to 100 (0% absorbance) are recorded as a function of wavelength. As certain physical and chemical changes occur in particle size, shape, color, or chemical structure, the DRS technique manifests the changes in the reflectance intensities or shifts in the spectral peaks (15). The curves in Fig. 2 indicate that minimal changes in DRS spectra occur if the emulsion system remains stable (curves A and B, Fig. 2). However, unstable emulsions result in marked differences in reflectance curves after a period of time (compare curves C and D).

Four simple oil-in-water (o/w) emulsion bases were prepared, each differing in the type of emulsifying agent used (Table I). Table III presents the data obtained on these four emulsions after being evaluated for 6 months by three techniques. Generally, as the emulsions coalesced, indicated by an increase in percent C, the mean particle diameter of the emulsions also increased; this increase was accompanied by a decrease in the percent reflectance at the measured wavelength (300 nm).

Correlation coefficients among the measured parameters are presented in Table IV. The data indicate that good correlations were obtained among the three techniques at 3 months or later. The poor correlations during the first 2 months probably reflected both unfamiliarity with the particle counting technique and the very rapid coalescence of two of the four emulsions. This coalescence, measured in volumetric cylinders, was not so readily apparent in the small Plexiglas DRS cells. The good correlation seen in Table IV indicates that, despite the use of different methods to evaluate stability, which, admittedly, are probing different characteristics of the system, the results may be favorably compared and utilized to support one another.

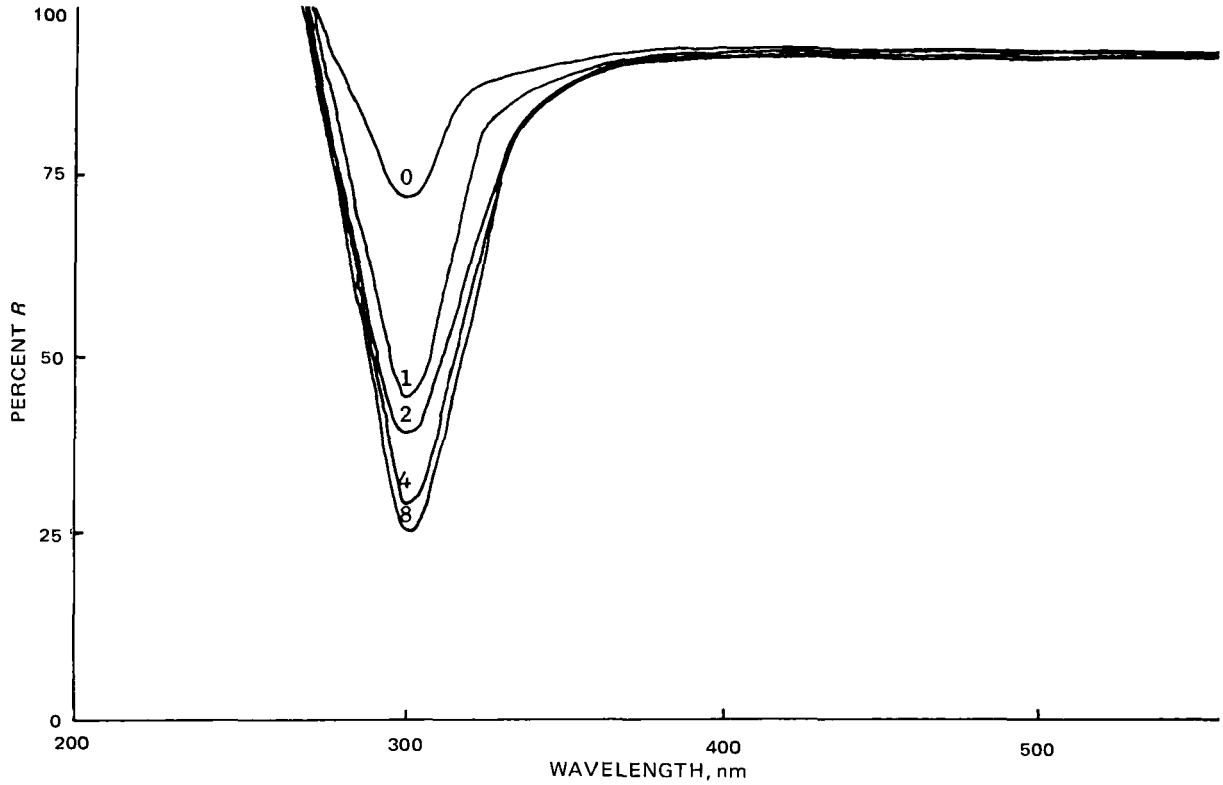

Figure 3—*Reflectance spectra of a 6% aspirin oil-in-water emulsion. The numbers on the curves correspond to the week after preparation.*

Vold and Mittal (16) discussed why confusion exists concerning the stability of emulsions. Reasons include: (*a*) different definitions of the term emulsion stability, particularly in the failure to distinguish clearly between creaming and coalescence; (*b*) insensitivity of some methods to detect subtle changes occurring in the emulsions; and (*c*) different methods of characterization that measure different properties of the emulsion, or emulsions that may be in different physical states in the various experiments.

In light of these reasons, it was realized that correlating reflectance with particle count and volume ratio data could generate serious arguments and confusion. However, Lloyd (2) showed the correlation of reflectance and particle size, and Rowe (8) showed the correlation of particle-size and coalescence measurements. It has been attempted here only to show some credibility for using the DRS technique for evaluating emulsion stability; accordingly, some older or more conventional technique must be employed to verify this credibility.

Another method of interpreting DRS evaluation of emulsion stability is to measure the area under the percent reflectance *versus* wavelength curves (*AUC*) as a function of time. The relative difference of the *AUC*, measured between the same two wavelengths, could further substantiate the application of DRS in evaluating emulsion stability.

Areas under the percent *R versus* wavelength curves for each of the four basic emulsions were measured at zero time and again 6 months later (Table V). The difference in the *AUC* after a certain

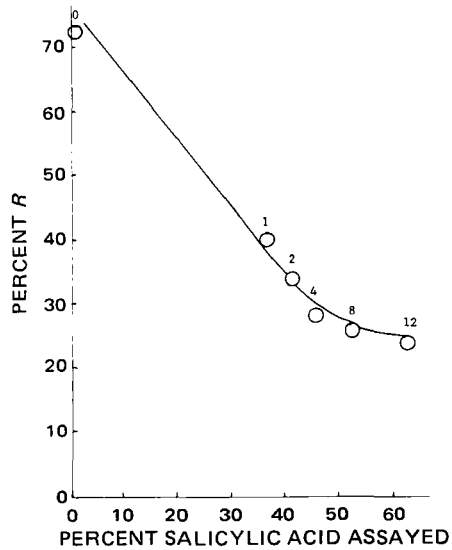

Figure 4—*Plot of percent reflectance* versus *percent salicylic acid assayed as a function of time. The percent reflectance was determined at 310 nm. The numbers correspond to the week after preparation of the drug-containing emulsion.*

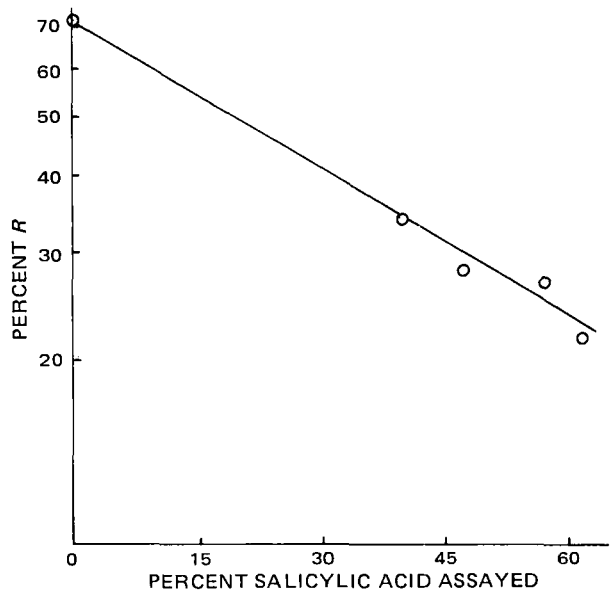

Figure 5—*Semilogarithmic plot of percent reflectance* versus *percent salicylic acid assayed using the points shown in Fig. 4.*

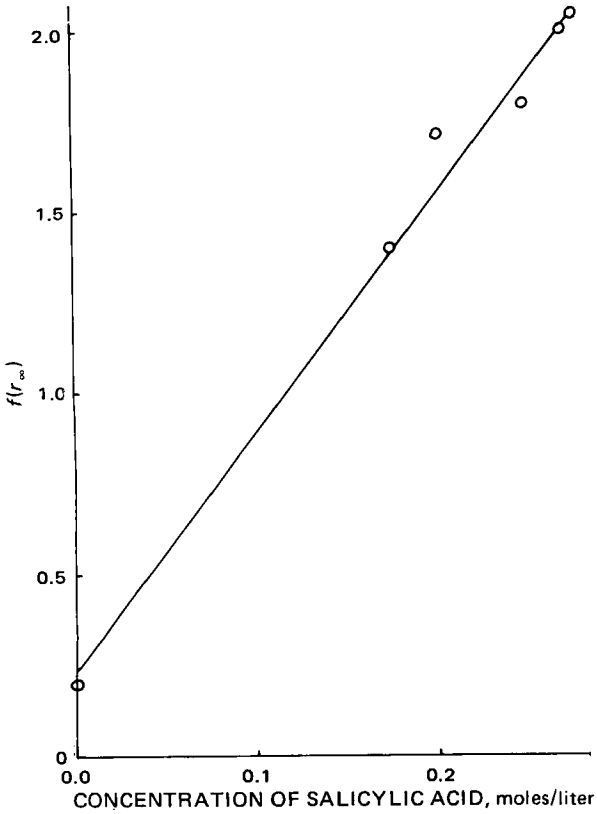

Figure 6—*Plot of remission coefficient* versus *molar concentration of salicylic acid in Emulsion 1.*

time can be a useful indicator for comparing the relative effectiveness of different emulsifying agents on producing stable emulsions. According to the data in Table V, the rank order of effective emulsifying agents would be sorbitan monopalmitate/polyoxyethylene sorbitan monooleate > gum arabic ≫ sorbitan monolaurate > sodium lauryl sulfate.

Since DRS compared favorably with the more established methods for emulsion stability evaluation, it was decided to study the ability of DRS to evaluate the chemical stability of an active ingredient incorporated into a stable emulsion formulation. The emulsion base was used as the reference material in the DRS measurements with the same emulsion base containing the drug as the sample. The two emulsions, with and without drug, were monitored simultaneously by coalescence, particle-size, and reflectance measurements to determine whether the emulsion base or the drug or both were causing the observed changes in the measured parameters. Since some drugs possess surface activity, the possibility does exist that a surface-active drug could affect the stability of the base emulsion.

Aspirin (6%) was dissolved in the oil phase of Emulsion 1. This emulsion was shown previously to be stable (Table III). Figure 3 shows the DRS results in analyzing the stability of aspirin in Emulsion 1.

Changes in the reflectance spectra occurred at the wavelength region where salicylic acid molecules are known to absorb light (approximately 310 nm). In Fig. 3, this change can be observed by the continual decrease in percent R at 310 nm. As salicylic acid formed, light was absorbed by the molecules, resulting in a decrease in the quantity of light reflected. Over a period of time, aspirin gradually degraded to salicylic acid; this change was monitored by a gradual decrease in percent R.

Figure 4 shows a plot of percent R at 310 nm *versus* the percent salicylic acid recovered in quantitative assay work over 12 weeks. A logarithmic relationship apparently existed between percent R and percent salicylic acid for this system (Fig. 5).

According to theory, the remission coefficient, $f(r_\infty)$, is directly proportional to the molar concentration of the absorbing species (Eq. 4). For the appearance of salicylic acid as a direct result of aspirin degradation, this proportionality appears to hold, as evidenced by the linearity seen in Fig. 6.

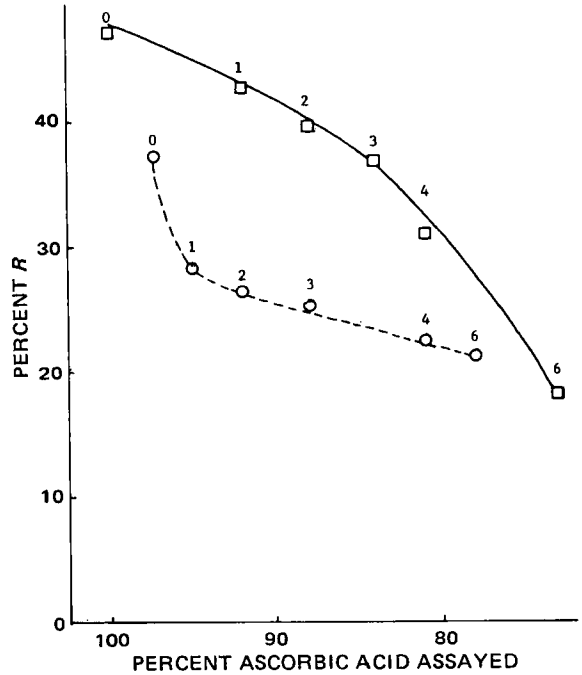

Figure 7—*Plot of percent reflectance* versus *percent ascorbic acid assayed as a function of time. The numbers correspond to the month after preparation of the drug-containing emulsion. Key:* □, *Emulsion 1, percent reflectance measured at 350 nm; and* ○, *Emulsion 2, percent reflectance measured at 320 nm.*

Aspirin was chosen as the drug for monitoring stability in emulsions by DRS because its hydrolytic degradation is well known, and it was felt that aspirin would be an ideal drug with which to test the DRS method. Since good correlation between reflectance and drug assay results indeed were seen, it seemed necessary to use a different drug that is formulated as an emulsion dosage form. Ascorbic acid was chosen, and its stability in two different stable emulsion systems (Emulsions 1 and 2) was analyzed.

In Fig. 7, percent R is plotted *versus* percent ascorbic acid found

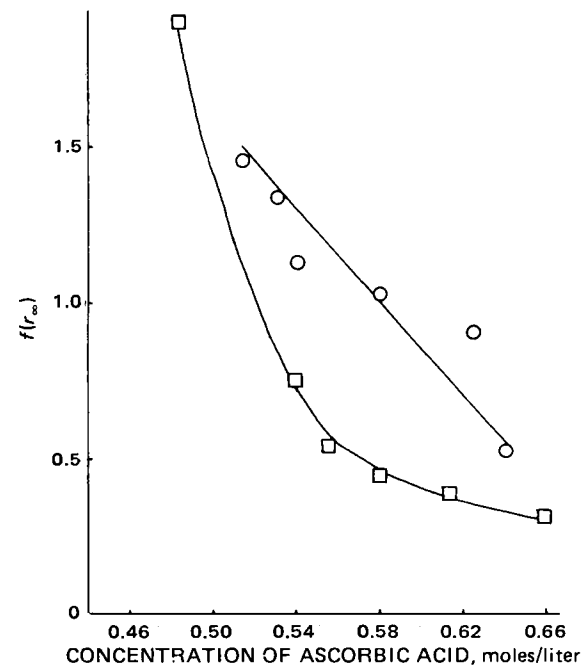

Figure 8—*Plot of remission coefficient* versus *molar concentration of ascorbic acid in two different emulsion bases. Key:* □, *Emulsion 1; and* ○, *Emulsion 2.*

when using a quantitative assay procedure. Ascorbic acid appeared to degrade to a greater extent in Emulsion 1 than in Emulsion 2. This finding agreed with the results of Bandelin and Tuschhoff (17), who found that vegetable gums added to produce liquids of greater viscosity seemed to accelerate the degradation of ascorbic acid. However, the main point to be emphasized once again is that drug degradation within a stable emulsion can be monitored at least semiquantitatively by DRS. Using DRS alone with no quantitative assay, one could conclude with little trepidation that ascorbic acid was unstable in these emulsion systems.

Figure 8 is shown to test the Kubelka–Munk hypothesis relating $f(r_\infty)$ directly to the concentration of the absorbing species. A linear relationship was evident for the drug in Emulsion 2 but not for the drug in Emulsion 1. Unfortunately for this drug emulsion system, no other wavelength could be used as an indicator of ascorbic acid degradation. However, the evidence indicates that ascorbic acid degradation in an emulsified formulation was monitored adequately by DRS.

SUMMARY AND CONCLUSIONS

DRS is a simple method and can be used in combination with other methods for evaluating emulsion stability. The method is sensitive and can detect subtle changes in the emulsion microenvironment, but it does not demand sampling or manipulation of the system. Should a semiquantitative estimate of an active component within an emulsion be desired, then the DRS method offers the unique advantage of estimating drug stability without disturbing the system.

Additional research is recommended to improve or define exactly the interpretation of the data obtained from reflectance measurements. These studies only show the application of DRS as a corroborative tool for the monitoring and evaluation of emulsion stability and drug stability within an emulsified system.

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Retardation of Dissolution and Growth of Calcium Oxalate Monohydrate

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Abstract □ The kinetics of dissolution and growth of calcium oxalate monohydrate were examined in the presence of small concentrations of pyrophosphate, chlorophyll, and other agents. Data presented show that the retardation in mass transport in both processes is controlled by the nature of the additive, its concentration, and the way the additives are combined in the dissolution medium. Dissolution was studied using a particle counter method, and growth was conducted in a gel system under the slow diffusion of the reacting ions. Results obtained show that chlorophyll is more active than other inhibitors studied and suggest a higher surface adsorption intensity on the primary sources of the crystal surface.

Keyphrases □ Calcium oxalate monohydrate—kinetics of dissolution and crystal growth, effects of various additives alone and in combination □ Dissolution—calcium oxalate monohydrate, kinetics, effects of various additives alone and in combination □ Crystal growth—calcium oxalate monohydrate, kinetics, effects of various additives alone and in combination □ Renal stone formation—calcium oxalate monohydrate, kinetics of dissolution and crystal growth, effects of various additives alone and in combination

Genesis and growth of calcium oxalate calculi are still unclear (1). To explain the ability of urine to remain supersaturated without precipitation, crystallization inhibitors should be studied. Equally important are the factors influencing the kinetics of dissolution of the stone components.

The complexity of urine in stone formation is certainly responsible for the slow progress in the area. The interaction of one compound with the others [*e.g.*, the action of magnesium on the solubility of calcium oxalate (2)] and the presence of material with a high epitaxial activity [such as organic material (3–