ELEVATED TEMPERATURE AS AN ARTIFICIAL BREAKDOWN STRESS IN THE EVALUATION OF EMULSION STABILITY

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Since emulsion stability is dependent upon the mechanical strength of the interface, the stability may be estimated by the rate of coalescence of the dispersed globules. Many factors can lead to low stability, but they are effective only in so far as they modify the properties of the adsorbed film at the oil/water interface. When a pharmaceutical, cosmetic, or confectionery emulsion is prepared on a large scale in industry, the formulation has often been developed as the result of long storage tests involving examinations for deterioration at intervals of weeks or months. These emulsions must have a relatively high degree of stability, hence the breakdown is slow. Attempts have been made to find some means of evaluating stability rapidly. The storage period should be reduced considerably. This condition would require an artificial breakdown stress which should have a relationship to shelf storage. The addition of electrolytes, acids, or alkalis usually increases the breakdown rate, but this fact is not reliable as a basis for tests. The addition of these substances changes the constitution of the preparation, and we should in fact be examining a product which varies from the original. Cockton and Wynn[1] have used centrifugal force to apply a standard artificial breakdown stress, although as they pointed out, there does not appear to be any simple relationship between the behaviour of an emulsion in a centrifuge and under normal storage conditions. Centrifuging exaggerates the value of "g" in Stokes equation. Thus, a stable emulsion whose two phases have dissimilar densities may seem inferior to one that is less stable, but which has a smaller variation in the density between the two phases. It was decided in the work described here, to make an initial attack on the problem of assessing the value of elevated temperature as an artificial breakdown stress. Provided the constituents are stable to heat, heating merely accelerates the normal mechanism of breakdown, and may therefore, be regarded as artificial ageing. Since emulsion degradation is a thermodynamic process, it may well be that the rate of decrease of the total area of the interface is directly related not only to time, but also to temperature. The first of these relationships has been shown by King and Mukherjee[2] to be linear. A further argument in favour of the use of elevated temperature for artificial breakdown is the fact that pharmaceutical emulsions should have as one of their criteria of suitability for large scale production, the ability to withstand a rise or fall in temperature within limits.

The term "stability of an emulsion" when used in this paper refers to the type of stability with respect to "cracking" and ignores the stability with regard to "creaming."

Much may be learned about the state of an emulsion at any given time

by performing a size frequency analysis, i.e., an examination of the relative proportions of globules falling into different size groups. This involves the counting of a large number of globules[3,4]. Size frequency analyses are, however, not simple determinations as they involve the counting and measurement of a large number of globules. Curves may be obtained by measuring about 400 globules, but the accuracy of the results increases if the number of globules measured is larger. In the past, this method has involved the use of microprojection apparatus. In the present work a simpler apparatus is described. A less tedious method than size frequency analyses proposed by Smith and Grinling[5] involves a direct count of a smaller number of globules, and eliminates the necessity for measurement. An important factor concerning this globule counting method, discussed by Cooper[6], is the fact that in certain emulsions a portion of the dispersed phase may be "solubilised," or the globules may be so small that they may not be detected when examined microscopically. If this method were to be applied to such an emulsion, it would appear to be less stable than it actually is. In view of the fact, however, that Cockton and Wynn[1] have recently used this method with modifications to obtain reproducible results, it was decided to divide the present work into two parts, one making use of the globule counting method and the other in obtaining size frequency analyses.

Experimental Methods

(1) *Preparation of Emulsions*

(*a*) *Materials*

Internal phase. Heavy Liquid Petrolatum U.S.P. was used in each emulsion, the same sample being used throughout the experiments. The concentration of the dispersed phase was arbitrarily fixed at 25 per cent. v/v for all the experiments, except the one in which cetyltrimethylammonium bromide was used, when the concentration was 50 per cent. v/v. It is hoped to extend this investigation at a later date to emulsions prepared with a vegetable oil, thereby giving data for two types of oils commonly encountered in pharmaceuticals and cosmetics.

External phase. Distilled water was used. Each sample was examined for freedom from microscopically suspended material.

Emulsifying agents. The following were used, the concentrations varying with different emulsions examined:—

(1) Polyethylene glycol 400 monostearate U.S.P., 1 and 2 per cent. w/v.
(2) Acacia, 5 and 6·25 per cent. w/v.
(3) Polysorbate 80 U.S.P., 0·1 per cent. w/v.
(4) Castile soap N.F. (amend white powder), 0·5 and 1·0 per cent. w/v.
(5) Cetyltrimethylammonium bromide, 2 per cent. w/v.
(6) Sodium lauryl sulphate, 0·5 per cent. w/v.

The emulsifying agents were selected so as to provide examples of different types (anionic, cationic, non-ionic, and a natural gum).

(*b*) *Method of preparation* (Quantities of 1000 ml.).

Equipment

(1) *Waring blender.* This is a cylindrically-shaped blender of approximately 1500 ml. capacity. Agitation of the liquids is brought about by rapidly rotating steel blades assembled in the base of the container. The speed of rotation is controlled by means of a variable resistance.

(2) *Club aluminium hand homogeniser.* This is a simple hand-operated lever-type of machine. The pumping action forces the emulsion from a bowl, through a fine orifice under high pressure. At the same time the movement of the handle lever agitates the liquid in the bowl by means of a beater.

Method

In all cases the required weight of the emulgent was dissolved in, or mixed with water and then made up to the calculated volume and then added to the oil. The liquids were premixed in the Waring blender at approximately 3000 r.p.m. for 10 minutes. The emulsion so formed was then passed through the homogeniser once at a temperature of 21° to 23° C. This method gave some degree of standardisation. Since the primary object of this work was to study the breakdown of various emulsions, and not to compare stabilities, a higher degree of standardisation was not considered necessary.

(2) *Storage of Emulsions*

(*a*) *Equipment.* A refrigeration unit, incubators, and hot air ovens were used to give a range of temperatures usually varying from 4° to 85° C.

(*b*) *Storage.* It was observed that at high temperatures small volumes (approx. 10 ml.) of an emulsion cracked before larger volumes (approx. 100 ml.) of the same emulsion. Hence, it was decided that each sample was to be 100 ml. in volume. This volume of the emulsion was distributed to each of a number of wide-mouth jars which were firmly closed by means of screw-caps. A sample of each emulsion was stored at different temperatures for the stated periods of time.

(3) *Examination of Emulsions*

(A) *Method of globule counting*

Equipment

(*a*) *Hæmacytometer cell.* The depth of the cell was 0·1 mm. The diluted emulsion was run in by capillarity after the cover-glass had been fixed in position. Errors due to unequal sedimentation were reduced by this quick method of filling. A hæmacytometer cell was preferred to a Helber counting cell which is 0·02 mm. in depth. It was believed that the latter type of cell would introduced a certain amount of selective sedimentation, i.e., the larger globules would tend to settle against the bottom of the cell or against the cover-glass, and not be drawn in with the rush of liquid at the same rate as the smaller globules. An additional objection to the Helber cell is that globules of a diameter greater than 20μ are encountered. This is greater than the depth of the Helber cell, which would then cause distortion and filtration of the larger globules. The Helber cell would,

however, permit thorough searching of the ruled area with less focussing than would a hæmacytometer. The difficulty of focussing was overcome by using a diluting fluid of high specific gravity. The oil globules would, in the course of 10 minutes, rise to the top of the cell, and would then lie in the same plane. When the microscope was focussed on this plane, it meant that the hæmacytometer rulings were out of focus. In order to compensate for this, a ruled ocular disc was placed in the eyepiece. These rulings were in the form of a block of 16 squares corresponding exactly to the 16 small squares of the hæmacytometer rulings. This procedure obviated the use of the hæmacytometer rulings altogether, the cell being used simply as a cell of convenient depth.

Method

The emulsion was first diluted to such an extent that when the cell was filled, a countable number of globules (10 to 20) was contained in each small square of the eye-disc. The microscope used was a binocular fitted with a × 20 objective and a × 10 eyepiece. Generally the degree of dilution varied between 1 in 500 and 1 in 1000. Sampling was carried out after gently rotating the container to obtain an even dispersion. 1 ml. of the emulsion was withdrawn from the centre of the sample by means of a 1 ml. pipette, and transferred to a sufficient quantity of 50 per cent. aqueous propylene glycol to produce one-half the final volume, after which a further quantity of the aqueous propylene glycol was added with thorough stirring to produce the final volume. The aqueous propylene glycol was selected because it possessed the following advantages at the concentration used: (1) it prevents Brownian movement of the globules; (2) it allows the globules of oil to rise to the top of the cell in about 10 minutes; (3) it is chemically stable and has a standard viscosity; (4) it has no intrinsic emulsifying action and thus eliminates the risk of additional emulsification of the oil; (5) it was shown experimentally that the risk of breakdown of the emulsions upon dilution was absent; an exception was the case of the emulsion using cetyltrimethylammonium bromide as the emulsifier, but this emulsion was only examined by the size frequency analysis method.

The reasons discussed under (2), (3), and (4) clearly show the value of this diluting fluid over acacia or gelatin solutions which have been used in the past. For the emulsion prepared with cetyltrimethylammonium bromide, a 40 per cent. aqueous glycerin solution was used as the diluting fluid.

After the counting chamber containing the dilution of the appropriate strength had been prepared, it was allowed to stand for 10 minutes before being examined to ensure that the distribution of the globules was uniform. If not, the chamber was cleaned and refilled. When the distribution was satisfactory, the globules contained in blocks of 16 small squares in 5 different fields (total of 80 small squares) were counted. In order to avoid counting the same globules twice, the count for each square included all those globules which lay on or touched the top and left-hand side of the square, and excluded all those which lay on or touched the bottom and

right-hand side. After making each count, the chamber and the coverglass were washed with sodium lauryl sulphate solution, rinsed with distilled water, and dried with a soft tissue.

In the light of the experience gained in the present work the authors are of the opinion that the squares counted should be done so in blocks rather than by selecting them at random. Since each determination is one of a series, the approximate number of globules that each square should contain is known to the worker. If the first portion of the squares do not conform to this approximation, there is a risk during random selection of unwittingly selecting squares to compensate for irregular counts. The number of globules per square was found to conform to a normal frequency distribution pattern.

(B) *Size frequency analyses*

Equipment

(*a*) *Hæmacytometer cell.* This cell was used again in order to give a cell of suitable depth. The rulings were ignored. The cell was filled with the same precautions as were exercised in Method A.

(*b*) *Camera lucida.* A Bausch and Lomb camera lucida was used. This accessory is fitted with assemblies for adjusting illumination from both the image and the drawing paper. The microscope was fitted with a $\times$ 90 oil-immersion objective and a $\times$ 20 eyepiece. This combination was adjusted so that 1μ in the image corresponded to 2 mm. on the paper.

Method

The emulsion was diluted to such an extent that when the cell was filled and the globules allowed to rise, the individual globules could be seen with a reasonable amount of space between them. The degree of dilution was far less than that necessary in Method A. It was not required to prepare the dilutions with any great degree of accuracy as was necessary in the former method. In practice the dilution was 1 in 10 or 1 in 20. Sampling was carried out with the same precautions that were exercised in the first method, and a period of 10 minutes was again allowed to elapse between filling the cell and the next stage in the procedure. The angle of the camera lucida was adjusted to avoid distortion on the paper. The outlines of the globules were traced on to sheets of paper. The outlines of all the globules in a given area were traced. The field was varied on a number of occasions for each sample. This procedure was repeated until a large number of outlines were so traced, the number varying from 400 to 800 per determination. After some practice this operation could be performed in less than 45 minutes. Measurements were made upon the diameter of each outline traced, and were recorded in groups, viz., under 1 mm., 1 to 2 mm., 2 to 3 mm., etc.

RESULTS

(A) *Method of globule counting*

Calculation. From the total number of globules counted in a given number of squares, the following values can be calculated:—

(*a*) "H" which expressed the number of millions of globules into which

1 cu. mm. of oil has been subdivided. If the number of small squares counted is 80, then the volume under 80 small squares in the hæmacytometer is $(80 \times 1/10 \times 1/20 \times 1/20) = 1/50$ cu. mm.

If N is the number of globules counted in this volume of a 1 in Z dilution of an emulsion containing 25 per cent. v/v of oil then,

$$\text{"H"} = N \times 50 \times Z \times \frac{100}{25} \times 10^{-6}$$

(*b*) "S" is the total area of the interface given by 1 ml. of the emulsified oil. This is a value related to "specific interface." The latter expression is defined as the total area of interface given by 1 g. of the internal phase.

The volume of a globule (assumed spherical) $= 4\pi r^3/3$

$$= \frac{\pi d^3}{6}$$

$$= \frac{1}{\text{"H"} \times 10^6}$$

$$\text{Therefore d (in mm.)} = \sqrt[3]{\frac{6}{\text{"H"} \times 10^6 \times \pi}}$$

The surface of 1 droplet $= \pi d^2$ sq.cm.

Therefore "S" $= \pi d^2 \times$ "H" $\times 10^3$.

Tabulated data. A typical series of globule counts is given in Table I, using an emulsion prepared from liquid petrolatum and polysorbate 80 U.S.P. "S"values after various periods of storage at various temperatures are given for four additional emulsions in Table II.

TABLE I

EMULSION OF LIQUID PETROLATUM WITH 0·1 PER CENT. OF POLYSORBATE 80 U.S.P.
(By Globule Count Method)

	3 days			6 days		
Temperature °C.	N	"H"	"S"	N	"H"	"S"
30	332	66·4	19,590	311	62·2	19,150
37	332	66·4	19,590	301	60·2	18,950
45	326	65·2	19,450	164	32·8	15,400
50	308	61·6	19,080	128	25·6	14,100
55	285	57·0	18,600	126	25·2	14,030
60	238	47·6	17,500	115	23·0	13,600

N = Number of globules counted in 80 squares in a dilution of 1:1000.

(B) *Size frequency analyses*

(*a*) *The variation of distribution of sizes.* This was calculated for each sample examined as follows: The recordings of the measurements were expressed as actual diameters of the globules and the average size for each group was calculated. Thus, the average for the group falling under 0·5μ was taken as 0·25 μ, and the average of the group falling between 0·5 and 1 μ was taken as 0·75 μ. In the same way each of the successive size groups were expressed as the average of their actual size. The very large globules were assumed to have an arbitrarily fixed diameter of 15 μ. This assumption was made because large globules occur in small numbers, and

TABLE II

TOTAL AREA OF INTERFACE 'IN SQ. CM./CU. MM.' OF LIQUID PETROLATUM IN 4 EMULSIONS AFTER VARYING PERIODS OF STORAGE AT VARIOUS TEMPERATURES
(By Globule Count Method)*

Emulsion	Emulsion A			Emulsion B		Emulsion C	Emulsion D				
Period of storage	1 day	2 days	3 days	1 day	4 days	4 days	1 day	1·5 days	2 days	2·5 days	3·5 days
Temperature °C.											
4	—	—	—	—	—	—	19,950	18,270	16,200	14,900	12,650
30	23,100	22,690	21,980	17,940	19,750	28,800	19,700	17,800	16,090	14,830	13,880
37	22,130	21,520	21,230	19,680	19,130	28,800	18,930	17,600	17,690	17,050	17,260
45	22,120	21,170	20,500	19,250	18,430	25,250	18,260	17,600	15,590	15,000	—
50	21,770	20,750	20,420	18,050	18,950	24,900	—	—	—	—	—
55	20,570	20,500	20,100	19,100	17,830	24,950	17,830	17,200	15,480	14,560	13,000
60	20,250	20,200	19,780	17,700	17,330	24,850	—	—	—	—	—
65	—	—	—	—	—	—	17,350	—	14,560	13,900	—
75	—	—	—	—	—	—	—	14,210	13,990	14,300	—
85	—	—	—	—	—	—	14,380	13,770	14,490	14,370	12,930
"S" before storage	23,320			20,000		28,000	22,530				

Emulsion A. 6·25 per cent. of acacia as emulsifier.
,, B. 1 per cent. of polyethylene glycol monostearate 400 U.S.P. as emulsifier.
,, C. 2 per cent. of polyethylene glycol monostearate 400 U.S.P. as emulsifier.
,, D. 0·5 per cent. of castile soap N.F. (amend white powder) as emulsifier.
* The values given are the results of a single determination or an average of 2 determinations.

the frequency of their occurrence is not statistically reliable. The total number of globules in each size-group was determined and expressed as a percentage of the total number of globules.

(*b*) *Average diameter.* The arithmetical mean was calculated from the formula, $d = \frac{\Sigma m,}{n}$

where m = the diameter of each globule,
and n = the number of globules measured.

(*c*) *Calculation of the value for "S".* "S" is the total area of the interface given by 1 ml. of the emulsified oil.

The volume of a globule (assumed spherical) $= \frac{\pi d^3.}{6}$

Therefore the number of globules per cm.^{3} $= \frac{6}{\pi d^3.}$

The surface of a globule $= \pi d^2$

Therefore "S" $= \pi d^2 \times \frac{6}{\pi d^3}$

$= \frac{6}{d}$

(*d*) *Tabulated data.* A typical series of size frequency analyses is given in Table III, using an emulsion prepared from liquid petrolatum and 0·5 per cent. w/v of castile soap N.F. "S" values calculated from various size frequency analyses are given in Table IV. Figures 1, 2, 3 and 4 show

size frequency curves obtained for various emulsions after storage at different temperatures.

CONCLUSIONS

1. The techniques described are capable of detecting relatively small degrees of deterioration in emulsions. These changes should provide a useful method of predicting changes on a macroscopic scale. Subsequent storage tests have roughly followed the pattern shown by the short-term tests.

TABLE III

EMULSION OF LIQUID PETROLATUM WITH 0·5 PER CENT. OF SODIUM LAURYL SULPHATE SIZE FREQUENCY ANALYSES BEFORE STORAGE AND AFTER 10 DAYS' STORAGE AT VARIOUS TEMPERATURES

	Before storage	4° C.	30° C.	37° C.	45° C.	55° C.	65° C.	75° C.	85° C.
Average diameter μ	per cent.	per cent.	per cent.	per cent.	per cent.	per cent.	per cent.	per cent.	per cent.
0·25	0·00	0·00	0·00	0·00	0·00	0·00	0·00	0·00	Oil Separated
0·75	0·68	0·30	1·59	1·60	0·22	0·00	0·00	0·00	
1·25	9·10	3·85	9·10	2·40	3·26	4·65	10·18	3·24	
1·75	31·14	28·00	31·60	24·00	17·82	18·40	24·69	21·27	
2·25	25·91	25·65	24·90	27·49	28·28	26·46	29·28	27·15	
2·75	11·58	16·00	11·37	15·48	16·09	16·08	10·43	16·39	
3·25	6·14	6·82	6·36	8·54	10·87	11·78	3·31	7·29	
3·75	4·55	5·63	3·64	4·54	6·74	5·00	4·07	3·85	
4·25	2·73	3·26	2·73	5·07	3·26	4·65	3·82	3·85	
4·75	2·27	2·22	1·82	3·21	2·49	2·50	0·76	1·82	
5·25	1·82	2·22	1·36	1·60	2·61	2·50	1·27	1·82	
5·75	1·59	1·33	1·14	0·53	1·74	1·07	1·02	1·62	
6·25	0·68	0·89	0·68	0·53	1·96	1·25	0·51	0·81	
6·75	0·23	0·59	0·68	1·33	0·65	1·43	1·27	1·23	
7·25	0·45	0·59	0·45	0·27	0·65	0·89	1·02	1·23	
7·75	0·23	0·74	0·45	0·80	0·87	0·89	0·76	1·01	
8·25	0·23	0·59	0·23	0·27	0·43	0·36	0·51	1·01	
8·75	0·23	0·30	0·23	0·27	0·22	0·00	0·51	0·40	
9·25	0·00	0·15	0·00	0·53	0·22	0·18	1·02	0·61	
9·75	0·23	0·15	0·00	0·27	0·00	0·18	1·02	0·81	
10·25	0·00	0·15	0·45	0·27	0·43	0·18	0·25	0·81	
10·75	0·00	0·30	0·23	0·27	0·00	0·00	0·51	0·81	
11·25	0·00	0·00	0·45	0·00	0·22	0·18	0·51	0·40	
11·75	0·00	0·00	0·00	0·00	0·00	0·36	0·76	0·40	
12·25	0·00	0·00	0·00	0·00	0·00	0·00	1·02	0·40	
12·75	0·00	0·00	0·00	0·00	0·22	0·36	0·51	0·40	
15·00*	0·23	0·30	1·59	0·80	0·87	0·72	1·02	1·23	
Total number of globules measured	440	675	441	375	460	563	393	494	
Average diameter μ	2·522	2·817	2·763	2·936	3·111	3·084	3·215	3·390	
"S"	24,350	21,630	22,510	20,900	19,720	19,800	19,000	17,910	

* All globules larger in size than 13 μ were placed in this group.

2. In accord with the findings of previous workers, this work has shown that finer dispersions usually are more stable, although this cannot be stated as a general rule.

3. The degree of dispersion in an emulsion, when examined immediately after preparation, gives some indication of the emulsifying power of the emulgent used, if the method of preparation is standardised. Thus, 1 per cent. castile soap N.F. has better emulsifying power than 0·5 per cent. sodium lauryl sulphate in liquid petrolatum-water emulsions. See Tables III and IV. From Table IV, it will be seen that the emulgents

TABLE IV

TOTAL AREA OF INTERFACE (IN SQ. CM. CU. MM.) OF LIQUID PETROLATUM IN EMULSIONS AFTER VARYING PERIODS OF STORAGE AT VARIOUS TEMPERATURES CALCULATED FROM SIZE FREQUENCY ANAYLSES

Emulsion	E		F		G			
Period of storage	10 days		15 days		15 days		40 days	
Temperature °C.	N	"S"	N	"S"	N	"S"	N	"S"
4	565	24,550	380	18,100	410	21,200	230	19,900
30	360	24,040	475	19,920	826	26,480	350	22,600
37	525	24,680	416	20,710	741	26,750	350	19,900
45	460	23,750	410	18,350	818	25,590	472	18,610
55	555	22,910	405	18,020	490	21,200	608	17,300
65	630	21,600	336	17,860	709	19,800	C	—
75	540	21,590	478	16,800	C	—	C	—
85	C	—	C	—	C	—	C	—
"S" before storage	630	25,100	—	—	—	—	—	—

C—Oil separated. N—Number of globules measured.
Emulsion E—1·0 per cent. castile soap N.F. (amend white powder) as emulsifier.
Emulsion F—2·0 per cent. cetyltrimethylammonium bromide as emulsifier. This emulsion contains 50 per cent. liquid petrolatum.
Emulsion G—5·0 per cent. of acacia as emulsifier.

may be arranged in the following decreasing order of emulsifying power, relative to liquid petrolatum-water emulsions: (*a*) polyethylene glycol 400 monostearate U.S.P., 2 per cent.; (*b*) acacia, 6·25 per cent.; (*c*) castile soap N.F., 0·5 per cent.; (*d*) polyethylene glycol 400 monostearate U.S.P., 1 per cent.

4. The results obtained by both methods show that above 40° C., the rate of decrease of interfacial area increases with a rise in temperature.

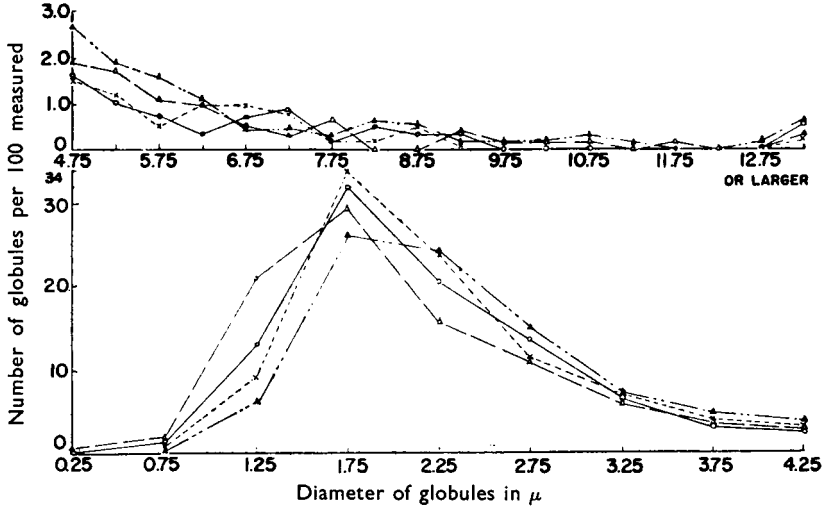

FIG. 1. Size frequency analyses. Liquid petrolatum emulsion with 1·0 per cent. w/v castile soap N.F. as emulsifier, before storage and after 10 days.

— — △ — — Before storage.
———○——— 4° C.
- - - -×- - - - 37° C.
— - -▲- - — 65° C.

Within the range of about 30° to 45° C., temperature has a less marked influence upon stability, but below a temperature of about 30° C., the stability usually decreases as the temperature falls to 4° C. This implies a

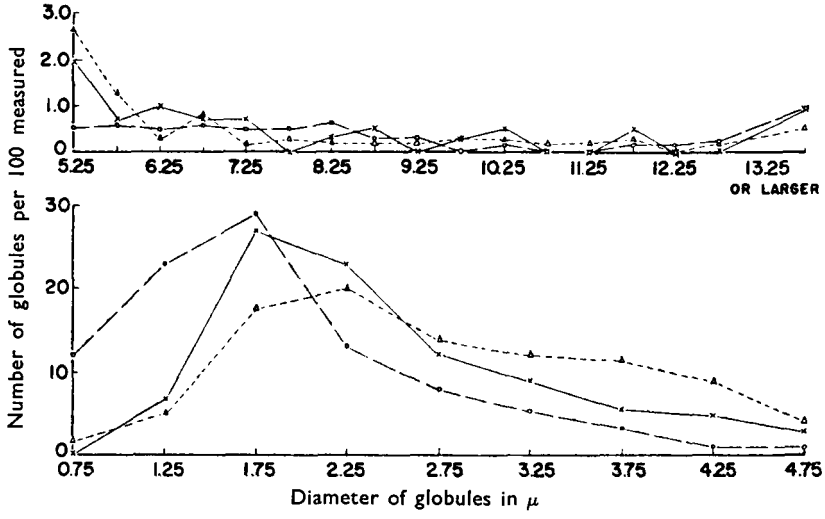

FIG. 2. Size frequency analyses. Liquid petrolatum emulsion with 5·0 per cent. w/v acacia as emulsifier. After 15 days storage.

——×—— 4° C.
— — ○ — — 37° C.
- - - - △ - - - - 65° C.

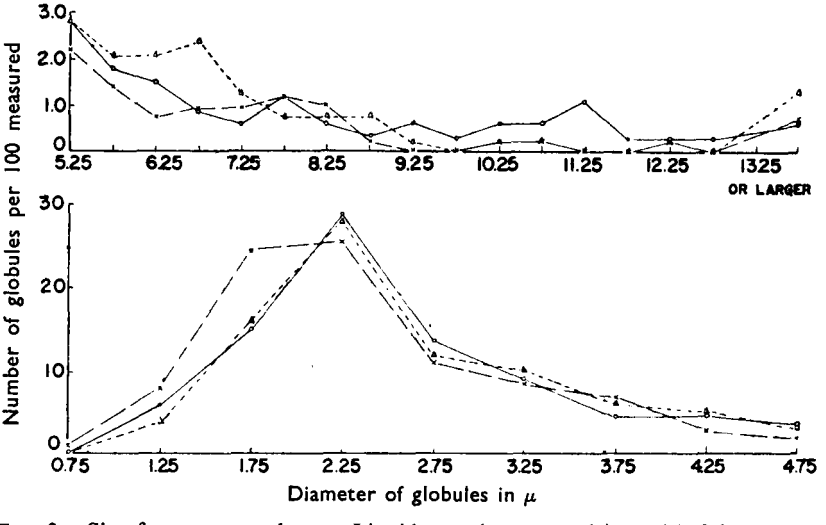

FIG. 3. Size frequency analyses. Liquid petrolatum emulsion with 2·0 per cent. w/v cetyltrimethylammonium bromide. After 15 days storage. This emulsion contains 50 per cent. v/v of dispersed phase.

- - - - △ - - - - 4° C.
— — × — — 37° C.
—— ○ —— 65° C.

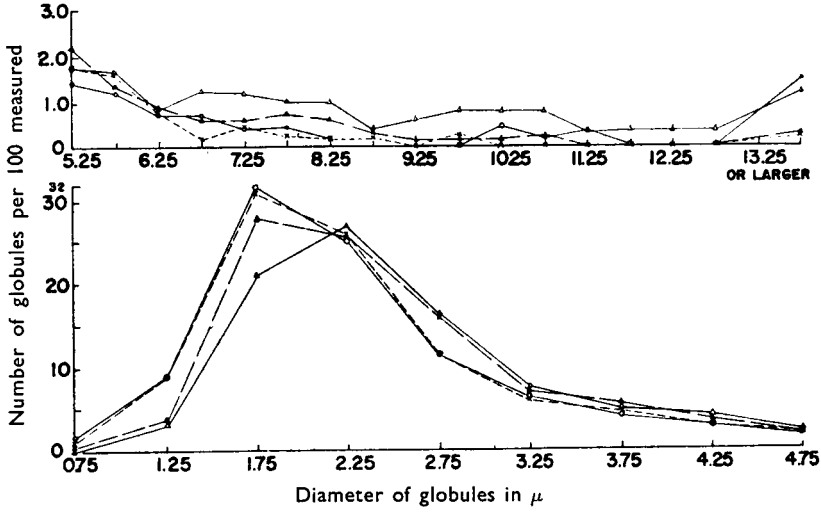

FIG. 4. Size frequency analyses. Liquid petrolatum emulsion with 0·5 per cent. w/v sodium lauryl sulphate, before storage and after 10 days.

---×--- Before storage
— — ▲ — — 4° C.
——○—— 30° C.
——△—— 75° C.

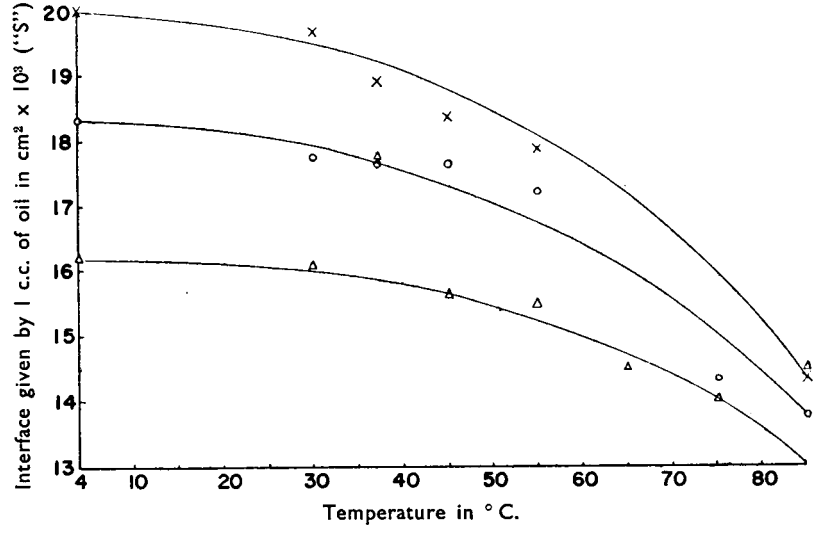

FIG. 5. Relationship of "S" to temperature of storage. Liquid petrolatum emulsion with 0·5 per cent. w/v castile soap N.F. as emulsifier, by method of globule counting.

× After 1 day's storage.
○ After 1·5 day's storage.
△ After 2 day's storage.

temperature of optimum stability varying with the emulsion examined. The emulsions containing castile soap and cetyltrimethylammonium bromide that were examined, have their optimum stability at about 37° C., while the remainder have their optimum stability at lower temperatures.

5. Previous workers have defined emulsion stability on the basis of the rate of decrease of specific interface. This work indicates that in doing so, a temperature should be defined. It is recommended that a temperature of 30° C. be selected, because the emulsions examined in this work show an optimum stability at about this temperature.

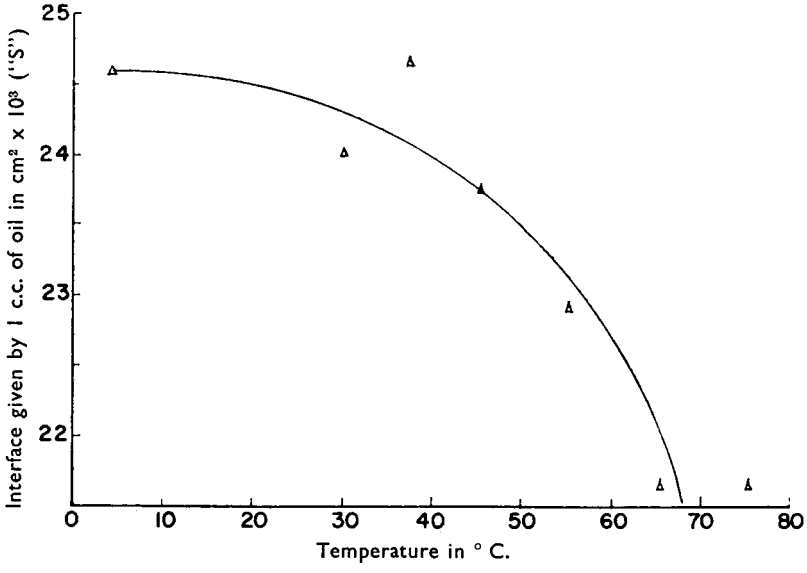

FIG. 6. Relationship of "S" to temperature of storage. Liquid petrolatum emulsion with 1·0 per cent. w/v castile soap N.F. as emulsifier. Calculated from size frequency analyses after 10 day's storage.

6. The size frequency analyses gave normal frequency distribution curves. These curves possess a "skewness" which becomes more pronounced as the emulsion breaks down. The peak of these curves is at a globule size of about 1·75μ. There is a shift of the peak to a larger globule size as the temperature becomes further removed from the optimum. The percentage of large size globules was small, but this figure increased with a rise in temperature. At the same time there was a reduction in the smaller size globules. It should be noted that the average globule size does not correspond to the peak of the curve.

7. "S" was selected as the function related to breakdown on which to base the curves, because this value was shown by King and Mukherjee to be linearly related to time of storage. The curves obtained in the present work relating "S" to temperature, were sensibly similar in each case. This fact indicates that short-term stability tests performed at elevated temperatures will give some reliable information as to the comparative behaviour of emulsions under normal storage conditions.

Discussion

The problem of assessing emulsion stability is complex. Storage tests, in general, are unsatisfactory because many months may be required to elapse before their results may be evaluated, and then only approximately, if examined visually. The experimental methods described in this paper have yielded some information about the behaviour of emulsions under different conditions of storage. The results obtained by the two methods are similar, although it is believed that the results given by the size frequency analyses method are more reliable than those given by simple globule counts. The rate of decrease of the interfacial area gives a measure of emulsion stability, i.e., the greater the rate of decrease, the lower the stability. Elevated temperature may be used to accelerate the rate of decrease, and stabilities of individual emulsions may be compared at various temperatures. The results obtained in this work in no way offer a complete assessment of the problem. It is hoped that modifications of these techniques will prove of value to workers formulating or testing emulsions.

Summary

1. The breakdown of emulsions was studied at different temperatures varying from 4° to 85° C.

2. Two methods were employed: size frequency analyses and a method of globule counting.

3. It is considered that size frequency analyses yield a more complete and reliable picture of the internal state of the emulsion.

4. Elevated temperature is proposed as an artificial breakdown stress for the evaluation of emulsion stability.

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DISCUSSION

The paper was presented by MR. H. P. LEVIUS.

MR. E. ADAMS (Plymouth) expressed the view that while the idea was a good one, the results were rather disappointing. It was apparent from the graphs in Figure 1 that the increase in globule size was not really very much, and he asked whether it could be increased by yet further prolonging the period of heat treatment. At the same time, the authors might consider whether the separation of oil (shown in Table IV) would not be a better end-point. A warning should also be issued that certain emulsifying agents—some of those prepared by the condensation of ethylene oxide—were liable to a change in type, that is to say, to change from oil-in-water to water-in-oil emulsifiers on a rise in temperature.

MR. J. H. OAKLEY (London) said that he had been under the impression that evenness of particle size with as small a diameter as possible was a criterion of stability, in fact, the ultimate aim; but he was not now convinced that it was always true. It might be that evenness of particle size and close packing produced a strain in the emulsion causing a tendency to instability and increased viscosity, whereas variation in the particle size, by allowing the globules to fit better into the inter-globular spaces, lessened the strain thus increasing the stability. He asked whether the authors had noticed any evidence that evenness of size decreased stability.

MR. VAN ABBE (Loughborough) said that the method involved confusion between the effects of temperature on viscosity and on actual emulsification. In practice, a test must take account of viscosity effects in emulsions, and from that point of view the centrifugal method carried out at the temperature of storage might be expected to be more reliable. A storage test at elevated temperature might be an accelerated test for storage under temperate conditions; but it was not an accelerated test for tropical conditions.

MR. J. ARMSTRONG (Nottingham) asked the authors whether any correlation between stability and viscosity existed. He had found that emulsions stored at 20° C. were far more stable than those stored at 37° C. It would be of interest to know whether creaming had occurred in the authors' emulsions. While that was not quite so important as breakdown, it was, nevertheless, an important feature of pharmaceutical emulsions that they should not cream on storage. Was any correlation noted between creaming and general stability of the emulsions?

MR. H. P. LEVIUS, in reply, said that separation of oil had been tried as a criterion but had been found impracticable because the deterioration was gradual and it was impossible to fix a definite end-point. He agreed that small globule size was not invariably indicative of emulsion stability, although in general, small size increased stability. It was, however, something to be sought after because it enhanced the appearance of the emulsion. The work had not been concerned with the causes of instability. In fact, some of the emulsions were purposely made rather unstable in order that deterioration might be studied without studying its causes. In general, however, increase in viscosity increased stability, but no definite rule could be laid down. He agreed that variation in particle size might increase stability. He also agreed that the fact that emulsions showed up well at elevated temperatures did not mean that they would also show up well under normal conditions and vice versa. The temperature at which maximum stability was obtained varied a great deal for different emulsions. Creaming had been experienced, but their emulsions had been agitated carefully. He could not say whether there was any correlation between tendency to cream and tendency to crack.