

## A COMPARATIVE STUDY OF THE STABILITY OF EMULSIONS WITH VARIATION IN THE PROPORTION OF INGREDIENTS.\*

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## DEFINITIONS OF TERMS.

An emulsion is a system containing two liquids that are immiscible, or practically so; one of which is dispersed in the form of globules in the other (1). The continuous or external medium is termed the dispersion phase (or dispersing phase), and the dispersed globules are called the internal or dispersed phase (or disperse phase) (2).

In general, there are two kinds of emulsions; namely, those that occur naturally and those that are produced artificially. Natural emulsions include animal emulsions and plant emulsions. Artificial emulsions may be produced by mixing two immiscible liquids. Theoretically, it should be possible to make two types of emulsions from any two given immiscible liquids. Assuming that oil and water are the two given liquids, one emulsion should correspond to the "oil-in-water" (o/w) type and the other should correspond to the "water-in-oil" (w/o) type. However, Clayton (3) states that if only *pure water* and *pure oil* are used only a single type of emulsion can be produced and that is a dilute oil-in-water (o/w) emulsion. A second class of emulsions exists which includes concentrated and more complex emulsions of both the oil-in-water and the water-in-oil type. The stability or permanence of this class depends upon the presence of a third substance called an emulsifying agent or emulsifier. These concentrated and complex emulsions possess considerable commercial and industrial importance, while the dilute, simple emulsions of oil-in-water have very little practical significance.

If two pure immiscible liquids are shaken together, both liquids are divided into globules and become intermixed. Upon standing, the globules of the respective liquids unite and separation into two distinct layers occurs. When a third substance, called an emulsifier, is included in a system consisting of oil and water it tends to stabilize the system, and to form a permanent emulsion. An emulsifying agent that is more readily wetted by water than by oil will form an oil-in-water emulsion; one that is more readily wetted by oil, a water-in-oil emulsion (4). Many substances have been used as emulsifiers. These include soaps, egg-yolk, acacia, tragacanth, Irish moss, proteins, carbon, clay and many other finely divided substances.

## THEORIES OF EMULSIFICATION.

The development of Colloidal Chemistry has given rise to several theories of emulsification. Ostwald (5) in 1910, formulated the "Phase-Volume Theory" which was based upon the theory of piled spherical balls. This theory is no longer generally accepted. A second theory is known as the "viscosity theory." Early investigators recognized the fact that the viscosity of the external phase probably had some influence on the stability of emulsions (6). Clayton states that "the majority of investigators to-day accept the conclusion that *viscosity aids emulsifi-*

\* An abstract of a thesis prepared under the direction of Professor J. B. Burt in partial fulfilment for the requirements of Master of Science. Scientific Section, A. PH. A., Toronto meeting, 1933.

*cation solely by virtue of the hindrance offered to coalescence of the dispersed globules, and is not the cause of emulsification."*

In 1917, Fischer (7) advocated the "hydration theory" of emulsions and emulsification. The "surface tension theory" was the forerunner of the "adsorption film theory" which is quite generally accepted to-day. Bancroft (8) formulated the "adsorption film theory" in 1913. He conceived the idea that the protective film surrounding the dispersed phase was a *separate phase*, which was wetted on one side by the oil phase and on the other side by the water phase and which had different surface tensions on the two sides. The type of emulsion produced depends upon the relative surface tension at the interfaces. The side of the intervening film which has the greater surface tension tends to become concave and enclose the liquid on that side, and the other liquid of lower surface tension tends to become the outer phase, since the tendency in any system is to assume the most stable condition, which is that which exists when the least surface energy is expended.

#### HISTORY OF PHARMACEUTICAL EMULSIONS.

Emulsions have been used medicinally for a very long period of time. H. Schelenz (9) says that Pliny described a drink made of almonds and honey that may have been the original almond emulsion. The earliest reference that he finds to the word emulsion is "de Emulsionibus" in Schroeder's Pharmacopœia of the seventeenth century. Oil emulsions were first described by Baumé.

The early pharmaceutical literature of the United States makes mention of emulsions. This early literature from about 1830 up until about 1865 was concerned largely with the publication of formulas for the production of emulsions.

During the forty-year period from about 1860 to 1900 investigations were made relative to methods of emulsification, to the kind of emulsifier, and to the proportions of ingredients which should be used in emulsions. The "bottle method," the "English method" and the "Continental method" of emulsification were advocated. Many different emulsifying agents were proposed. There appears to have been a great diversity of opinion regarding the proportion of ingredients to be used in emulsions.

Pharmaceutical literature indicates that emulsions were first produced upon a large scale for commercial distribution about 1900.

#### EXPERIMENTAL STUDY AND RESULTS.

The object of this experiment was twofold; *first*, to determine the effect of dilution upon the stability of emulsions of oils of animal and vegetable origin which are used pharmaceutically; and, *second*, to determine the limits of emulsification or emulsibility of these oils when variation in proportion of ingredients occurred, and incidentally, to determine whether or not the proportions of ingredients, which are recommended by the present United States Pharmacopœia and National Formulary for the preparation of emulsions of fixed oils, are optimum.

It should be said, in the beginning, that this problem was approached from the practical standpoint. An attempt was made to simulate the conditions which occur in the average drug store. The materials and apparatus used were, for the most part, similar to those found in drug stores; and, the manipulation was as

uniform as possible. The acacia was weighed on a torsion balance and the water and oils were measured in cylindrical or conical graduates. These measurements were made in this manner so that the conditions of the experiment might be duplicated in the average drug store where, it is hoped, this work may prove to be of some practical value.

The materials used were purchased on the open market in quantities sufficient to run the entire series of experiments so as to insure uniformity of ingredients. The oils included expressed oil of almond, castor oil, cod liver oil, cottonseed oil, raw linseed oil, olive oil and sesame oil. Acacia was chosen as the emulsifying agent since it is most commonly used. The specific gravities of the oils were checked using both the pycnometer and the Mohr-Westphal balance. Relative or specific viscosity was determined, the Saybolt viscosimeter being used. These physical constants appear in Table I.

In studying the effect of dilution upon pharmaceutical emulsions, large quantities of primary emulsions were prepared. Enough primary emulsion was made to supply the base for a single series of dilutions, separate primary emulsions were prepared for each series. Duplicate series of each oil were run, the Continental or 1:2:4 (A:W:O) method of emulsification was used. Twelve hundred cc. of a given oil which contained 0.5% of dissolved thymol (this was used as a preservative) were thoroughly mixed with 300 Gm. of acacia in a large wedgewood mortar, then 600 cc. of water were dashed in at once, and the mixture triturated until a thick, viscous, homogeneous, creamy emulsion resulted.

Dilutions of these primary emulsions were made. In order to not lose any of the primary emulsion by pouring from one container to another, the required amount of primary emulsion was measured directly into graduated 8-ounce prescription bottles. The required amount of emulsion was determined in the following manner. For example, it was necessary to make a dilution of primary emulsion of cod liver oil, which when finished would contain 10 per cent of oil. The factor used in determining the quantity of primary emulsion necessary in any given dilution was determined in the following way. One hundred cc. of oil were thoroughly mixed with 25 Gm. of acacia in a graduated 240-cc. bottle. Then 50 cc. of water were added and the mixture was shaken until emulsification or at least uniform mixing occurred. The mixture was allowed to settle until air bubbles had escaped and then the quantity of emulsion measured. In the case of cod liver oil, 100 cc. of oil produced 168.75 cc. of emulsion. The resulting factor was  $168.75/100$  or 1.6875 in this case. Then if a 10 per cent emulsion of cod liver oil was required, 24 cc. of oil would be required. The amount of primary emulsion corresponding to this would be 24 times the factor 1.6875 or 40.50 cc. The primary emulsion was poured into the graduated bottle up to the indicated mark. Dilution was made by adding the required water in 5-cc. portions; thorough mixing occurred after each addition. The finished emulsions were stored at room temperature.

These dilute emulsions were examined daily over a period of 30 days for signs of cracking, decomposition and other changes that might occur. (By cracking is meant the complete separation of the mixture into two distinct layers, an oil layer and a water layer.) There were no cases of cracked emulsions. However, emulsions which contained 30 per cent or less of oil, usually showed a separation in the form of a supernatant, creamy layer which was readily reincorporated by

shaking. The number of cubic centimeters in this creamy layer was measured daily. This was done by measuring the liquid upon the side of the graduated bottle. Then, the emulsions were thoroughly shaken up and allowed to stand until the following day. At the end of the 30-day period, the average number of cubic centimeters of separation was calculated and converted into percentage.

Decomposition occurred in the castor oil emulsions which developed rancidity after about the fourth day. Considerable gas was evolved and in several cases sufficient pressure was developed to force the corks from the bottles. A decided odor of butyric acid was present. In emulsions ranging from 25 to 40 per cent a dark lumpy-looking layer formed at the bottom of the bottle. This was probably due to decomposition products.

Some of the cottonseed oil emulsions, while apparently not rancid, developed a "slimy," "buttery" appearance in the supernatant layer and toward the end of the period it was impossible to mix this layer with the rest of the mixture.

The more dilute emulsions of expressed oil of almond showed a double layer, the upper one having a very oily appearance.

Several emulsions in the various series showed a tendency to form lumps which could be shaken out easily.

After the 30-day period, the specific viscosity of these emulsions was determined so far as it was possible to run them through the viscosimeter. These values may be found in Table II.

Table III indicates the percentage of separation of these emulsions.

An effort was made to determine the limits of emulsibility of these seven oils when varying proportions of ingredients were used. The order of mixing used was that of the Continental method. Starting with the 1:2:4 proportion, three series of emulsions were made, varying acacia, water and oil, respectively. In each case, the variation amounted to a progressive increase or decrease equal to 20 per cent of the original proportion of the variable ingredient. For example, in a series in which water was varied, the proportions were 1:4:4, 1:(3.6):4, 1:(3.2):4, 1:(2.8):4, 1:(2.4):4, 1:2:4, 1:(1.6):4, 1:(1.2):4, 1:(0.8):4, 1:(0.4):4. Small portions of these emulsions were prepared, averaging about 20 cc.-25 cc. of finished emulsion. The smallest amount of liquid used was never less than 5 cc. When an emulsion resulted at the first trial it was not repeated. When emulsions failed at the first attempt, three or more trials were made, unless it was obvious that an emulsion could not be formed, as for example, when so great a bulk of acacia was present that the system could not be manipulated.

It was found that emulsibility was not limited to any given proportion of ingredients, but rather that it was possible to produce an excellent grade of emulsions over a small range, and emulsions of decreasing quality with increasing variation in proportions of ingredients beyond that range.

Since emulsions were produced over a considerable range and the limit of emulsibility was not sharp, the diameter of the oil globules in the various emulsions was determined microscopically, in the effort to see if they might give a numerical criterion of quality.

The procedure was as follows. A graduated eyepiece was calibrated to read in microns. High power was used for the determinations. Three slides were made from each emulsion, similar to the way in which smears are made in bac-

teriology. The diameters of ten oil globules from each slide were recorded, those globules which touched the 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5 and 5.0 marks on the scale were arbitrarily selected. The average diameters are listed in Tables IV, V and VI.

Table IV which shows the changes in proportion of acacia tends to show that an increase in acacia is accompanied by a reduction in the size of oil globules. An increase in the proportion of acacia is limited by the thickness developed in the mixtures containing high proportions of acacia, rendering the manipulation of the system impossible. A decrease in acacia beyond about 1.0 part or 0.8 part tends to cause a rapid increase in globule size and lack of emulsibility.

When the proportion of water was varied an increase in water resulted in an increase in the size of the oil globules. If less than 1.6 parts of water were used the mixture was a thick gummy mass, in most cases almost doughy. Upon the addition of more water, a fairly good emulsion generally resulted. Greater quantities than about 2.5 parts of water resulted in emulsions which creamed rapidly (Table V).

Emulsions made with variations in the proportions of oil showed that the most stable emulsions resulted when from 2.0 to 4.0 parts of oil were used (Table VI)

TABLE I.—SHOWING SPECIFIC GRAVITY AND RELATIVE VISCOSITY OF THE OILS USED IN PREPARING EMULSIONS.

Oil.	Sp. Gr. (25° C.).	Relative Viscosity (25° C.).
Expressed oil of almond	0.9131	16.84
Castor oil	0.9592	104.04
Cod liver oil	0.9210	8.35
Cottonseed oil	0.9199	16.89
Raw linseed oil	0.9266	12.21
Olive oil	0.9115	11.37
Sesame oil	0.9196	10.53

TABLE II.—SHOWING SPECIFIC VISCOSITY OF EMULSIONS AT THE END OF THE 30-DAY PERIOD.

% of Oil.	Expressed Oil of Almond.	Castor Oil.	Cod Liver Oil.	Cottonseed Oil.
5	1.11	1.14	1.30	<i>d</i>
10	1.22	1.17	1.40	<i>d</i>
15	1.34	<i>d</i>	1.67	1.46
20	1.61	1.49	2.03	1.92
25	1.93	2.16	3.02	2.65
30	2.90	3.37	4.81	4.28
35	5.98	5.54	..	..
% of Oil.	Raw Linseed Oil.	Olive Oil.	Sesame Oil.	
5	1.07	1.25	1.15	
10	1.17	1.40	1.28	
15	1.38	1.57	1.51	
20	1.82	2.14	1.92	
25	2.53	3.21	2.91	
30	4.23	5.05	4.27	
35	..	..	..	

*d* signifies decomposition or rancidity.

TABLE III.—SHOWING THE AVERAGE PERCENTAGE OF SEPARATION IN EMULSIONS OF VARYING OIL PERCENTAGE.

Oil.	Series.	% of Oil in the Finished Emulsion.				
		5%.	10%.	15%.	20%.	25%.
Expressed oil of almond	A	10.46	15.46	21.29	26.50	31.83
	B	10.71	15.96	21.14	27.31	30.54
Castor oil	A	10.86	15.33	21.54	26.92	31.38
	B	10.68	15.44	20.92	23.35	*
Cod liver oil	A	12.42	15.46	20.04	18.13	*
	B	11.63	14.48	16.79	16.54	*
Cottonseed oil	A	10.72	17.46	22.51	26.21	25.54
	B	12.03	17.63	22.53	24.13	*
Linseed oil	A	10.33	13.38	16.79	17.42	15.95
	B	12.63	14.01	17.04	17.46	17.04
Olive oil	A	10.82	17.23	20.63	23.88	*
	B	10.83	17.43	20.75	24.89	*
Sesame oil	A	10.92	16.83	22.99	30.43	35.54
	B	10.71	16.58	22.67	28.71	*

Oil.	Series.	% of Oil in the Finished Emulsion.				
		30%.	35%.	40%.	45%.	50%.
Expressed oil of almond	A	36.77	43.46	59.04	81.00	*
	B	37.88	47.42	59.13	87.46	*
Castor oil	A	*	*	*	*	*
	B	*	*	*	*	*
Cod liver oil	A	*	*	*	*	*
	B	*	*	*	*	*
Cottonseed oil	A	*	*	*	*	*
	B	*	*	*	*	*
Linseed oil	A	18.29	*	*	*	*
	B	31.21	*	*	*	*
Olive oil	A	*	*	*	*	*
	B	*	*	*	*	*
Sesame oil	A	*	*	*	*	*
	B	*	*	*	*	*

\* No separation occurred within the 30-day period.

TABLE IV.—SHOWING THE AVERAGE DIAMETER IN MICRONS OF OIL GLOBULES IN EMULSIONS, WHICH HAVE VARYING PROPORTIONS OF ACACIA.

Prop. of Acacia.	Expressed Oil of Almond.	Castor Oil.	Cod Liver Oil.	Cottonseed Oil.
2.0	**	3.0	2.4	4.2
1.8	3.8	2.6	4.1	3.3
1.6	3.5	2.5	3.2	3.4
1.4	4.7	3.7	4.6	3.5
1.2	4.1	2.6	5.8	4.3
1.0	5.0	4.2	4.4	3.4
0.8	5.5	5.2	6.0	5.7
0.6	8.1	6.5	10.3	7.9
0.4	10.6	**	**	8.0

  

Prop. of Acacia.	Raw Linseed Oil.	Olive Oil.	Sesame Oil.
2.0	4.8	4.4	**
1.8	5.6	3.8	4.6
1.6	5.4	3.9	5.2
1.4	4.7	4.9	5.2

1.2	6.3	4.1	5.4
1.0	6.2	3.6	2.9
0.8	5.5	5.7	5.8
0.6	11.6	14.8	7.9
0.4	14.8	14.7	22.7

\*\* No emulsification obtained.

TABLE V.—SHOWING THE AVERAGE DIAMETER IN MICRONS OF OIL GLOBULES IN EMULSIONS WHICH HAVE VARYING PROPORTIONS OF WATER.

Prop. of Water.	Expressed Oil of Almond.	Castor Oil.	Cod Liver Oil.	Cottonseed Oil.
4.0	**	**	17.9	16.6
3.6	10.0	15.2	17.3	12.0
3.2	9.5	14.9	12.3	8.6
2.8	10.4	8.3	8.6	6.0
2.4	6.3	4.8	6.5	4.6
2.0	5.0	4.2	4.4	3.4
1.6	5.4	3.5	4.2	3.8
1.2	**	**	**	**

  

Prop. of Water.	Raw Linseed Oil.	Olive Oil.	Sesame Oil.
4.0	**	**	**
3.6	8.8	19.2	18.1
3.2	8.7	11.8	9.2
2.8	7.2	7.4	5.4
2.4	5.7	4.5	6.5
2.0	6.2	3.6	2.9
1.6	7.9	3.0	3.9
1.2	**	**	**

\*\* No emulsification obtained.

TABLE VI.—SHOWING THE AVERAGE DIAMETER IN MICRONS OF OIL GLOBULES IN EMULSIONS WHICH HAVE VARYING PROPORTIONS OF OIL.

Prop. of Oil.	Expressed Oil of Almond.	Castor Oil.	Cod Liver Oil.	Cottonseed Oil.
6.4	**	5.0	**	**
5.6	5.8	4.6	**	4.5
4.8	5.5	4.2	4.8	4.9
4.0	5.0	4.2	4.4	3.4
3.2	4.1	3.1	3.2	4.0
2.4	5.0	3.9	3.7	4.2
1.6	6.4	4.5	4.6	4.9
0.8	11.3	6.6	10.0	9.9

  

Prop. of Oil.	Raw Linseed Oil.	Olive Oil.	Sesame Oil.
6.4	**	**	**
5.6	7.4	5.0	**
4.8	5.5	5.9	7.1
4.0	6.2	3.6	2.9
3.2	4.6	4.1	4.7
2.4	4.8	4.3	4.6
1.6	4.4	5.9	7.4
0.8	6.0	8.1	10.0

\*\* No emulsification obtained.

## SUMMARY AND CONCLUSIONS.

1. Dilutions of primary emulsions of expressed oil of almond, castor oil, cod liver oil, cottonseed oil, raw linseed oil, olive oil and sesame oil were prepared so that the finished emulsions contained oil percentages varying from 5 to 55 per cent. In no case, did cracking or breaking of the emulsion occur. "Creaming" occurred in emulsions containing 30 per cent or more of oil, but this cream layer was readily reincorporated by agitation.

2. A change in the variation of proportion of ingredients in emulsions of the oils named above resulted in the following conclusions:

(a) An increase in the proportion of acacia is accompanied by a decrease in the size of the oil globules and vice versa.

(b) An increase in the proportion of water results in an increase in the size of dispersed oil globules.

(c) Emulsions containing from 2.0 to 4.0 parts of oil had the smallest oil globules.

(d) It appears probable that the smaller the range in variation of size of oil globules the more stable the emulsion.

(e) Emulsions of fixed oils may be prepared with a much wider range in variation in proportion of ingredients than the 1:2:4 rule would indicate. The results of this experiment showed that emulsions made according to the 1:2:4 rule were not always optimum; however, satisfactory emulsions of fixed oils should result when these proportions of ingredients are used.

## BIBLIOGRAPHY.

- (1) W. Clayton, "Theory of Emulsions," 2nd Edition (1928), page 1.
- (2) Kruyt and von Klooster, "Colloids," 2nd Edition (1930), page 7.
- (3) W. Clayton, "Theory," page 2.
- (4) *Ibid.*, page 25.
- (5) *Kolloid-Z.*, 6 (1910), 103; 7 (1910), 64; through Clayton, "Theory," page 45.
- (6) W. Clayton, "Colloidal Aspects of Food Chemistry and Technology" (1932), page 165.
- (7) Fischer and Hooker, "Fats and Fatty Degeneration" (N. Y., 1917), page 5; through Clayton, "Theory," page 60.
- (8) *J. Phys. Chem.*, 17 (1913), 514-518; through Clayton, "Theory," page 120.
- (9) YEAR BOOK, A. PH. A., Vol. 10 (1921), 81; *Schweiz. Apoth.-Ztg.*, 59 (1921), 657.

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## DECEPTIVE LITERATURE OF 50 YEARS AGO.

*The Chemist and Druggist*, of April 14, 1883, contains this paragraph—"Seldom has a richer specimen of our omniscient journalism been printed than this choice sentence: 'It has been stated recently that in the manufacture of soda water, marble dust and oil of vitriol are largely used; and although there may be exaggeration in this, as there generally is in assertions of a wholesale character, still the imputation is one which the great brewers should be anxious to refute, as indeed they did successfully refute the charge of using aconite instead of hops in the manufacture of bitter beer.'" This is not so very different from recent literature. "Let it be the ardent desire of every pharmacist that pharmacy and pharmacists will maintain their dignity and professional standards."