The samples analyzed lost (av.) 3.76 per cent in weight when heated at 200° C. to constant weight; and at a temperature of 1500° C. for two hours lost a further 1.83 per cent, apparently not due to hygroscopic moisture.

SUMMARY

From the analytical results obtained it appears that the formula for precipitated calcium phosphate, $Ca_3(PO_4)_2$, given in the National Formulary VI and in the French Codex are in error.

It also appears that the formula suggested $[Ca_3(PO_4)_2]_3.Ca(OH)_2$ more closely agrees with the true composition of the salt.

REFERENCES

(1) Bennett and Cocking, "Science and Practice of Pharmacy," Vol. 2 (1933), page 102, Churchill.

(2) Mellor, "Treatise on Inorganic Chemistry" (1925), page 725, Longmans-Green.

(3) *American Pharmaceutical Pamphlets*, 3 (1939), 319.

(4) Rogers, "Inorganic Pharmaceutical Chemistry" (1936), page 360, Lea and Febiger.

(5) Kolthoff and Santell, "Quantitative Inorganic Analysis" (1938), pages 324, 367, Macmillan.

(6) Lange, "Physical Constants," 2nd Edition, page 132, Hand Book Publications, Inc.

Pharmaceutical Emulsions. III. A Comparative Study of Various Mechanical Stirrers and the Hand Homogenizer*,†

*By William J. Husa‡ and Charles H. Becker***

INTRODUCTION

In earlier papers (1, 2) detailed studies were made of the Continental and English methods of emulsification. The present investigation is devoted to a study of the efficiency of these older methods of emulsification as compared with the use of mechanical stirrers and a homogenizer for making emulsions.

EXPERIMENTAL

Materials.—The stirrers used were: (*a*) motor stirrer, with a glass stirring rod, maximum speed about 3000 r. p. m., purchased from the Central Scientific Co., (*b*) Arnold automatic mixer, intended for use at the soda fountain, (*c*) hand egg beater. A portable hand homogenizer, purchased from the International Emulsifiers, Inc., was employed.

The fixed oils chosen for study were linseed oil, cod liver oil, heavy mineral oil and castor oil. All the oils were of U. S. P. grade Powdered acacia, U. S. P., was employed. One-tenth per cent sodium benzoate was added to the distilled water to prevent mold growth in the emulsions while standing for observation. *Methods.*—The general methods employed were the same as described in previous papers (1, 2).

Throughout, the parts of acacia were measured in Gm. and the parts of oil and water were measured in cc.

In the tables "oil sep." is used to indicate oil separation. The following abbreviations are used to indicate the average size of the oil globules:

A—Average diameter less than 2.5 microns.
B—Average diameter from 2.5 to 4 microns.
C—Average diameter from 4 to 6 microns.
D—Average diameter more than 6 microns.

Use of Motor Stirrer.—Four-ounce portions of $12^1/_2\%$ oil emulsions were prepared using the 4:2:1 proportion. In all cases the stirring was conducted at maximum speed. The emulsions were prepared in the following ways:

Method I: The 4 parts of oil and 1 part of acacia were first mixed well in a 150-cc. beaker with the motor stirrer, and then the 2 parts of water was added all at once. The primary emulsion was stirred for 5 minutes, and the remainder of the water was added gradually.

Method II: The primary emulsion was first made using a porcelain pestle, 15.0 cm. in length and 4.5 cm. in diameter at the base, and a No. 1 wedgwood mortar, and then this was transferred to a 150-cc. beaker and stirred for 5 minutes. The remainder of the water was added gradually.

Mineral oil did not yield an emulsion when made according to the procedure described in Method I. With cod liver oil and linseed oil, the motor stirrer appeared to be of little value, inasmuch as 5 minutes of stirring yielded emulsions which were equivalent, with respect to the average size of the oil globules, to products wherein the primary emulsion was triturated in a mortar for 1 minute. Castor oil yielded a Grade *A* emulsion.

---

* Presented before the Scientific Section, A. PH. A., Richmond meeting, 1940.

† This paper is based on part of a thesis presented to the Graduate Council of the University of Florida in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

‡ Head Professor of Pharmacy, University of Florida.

** Graduate Scholar, University of Florida, 1939–1940.

When making emulsions as described in Method II, similar results were obtained. Castor oil yielded a Grade *A* product, whereas the other oils yielded emulsions which were inferior to those made by longer trituration in a mortar.

Stirring the primary emulsions in a 4-ounce-square powder jar was of no advantage.

Use of Hand Egg Beater.—Six-ounce portions of 12½% oil emulsions were prepared using the 4:2:1 proportion and employing a No. 3 wedgwood pestle and a No. 3 wedgwood mortar. The 4 parts of oil and 1 part of acacia were first triturated well, and then the 2 parts of water was added all at once. The resulting primary emulsion was triturated with the pestle for about a half minute, after which the hand egg beater was used to stir the primary emulsion for 5 minutes. The remainder of the water was added gradually, triturating constantly with the pestle.

With respect to stability and the average size of the oil globules, stirring of the primary emulsion with a hand egg beater produced emulsions equal to those in which the primary emulsion was triturated with a pestle for 5 minutes.

Use of Arnold Automatic Mixer.—Sixteen-ounce portions of 25% oil emulsions were prepared using the 4:2:1 proportion. When using the Continental method of emulsification, the 4 parts of oil and 1 part of acacia were stirred well in the Arnold automatic mixer, and then the 2 parts of water was added all at once. The resulting mixture was stirred for 5 minutes and then the remainder of the water was added slowly. When employing the English method, the acacia and water were first made into a mucilage and placed in the mixer. The oil was added gradually, allowing the oil to be well emulsified before the next portion was added. After adding the total amount of oil, the mixture was stirred for 5 minutes and then the remainder of the water was added gradually. The results of use of the Arnold automatic mixer are given in Table I.

Table I.—Use of Arnold Automatic Mixer

Oil	Appearance of Emulsion, 3 Hours	Average Size of Oil Globules
	Continental Method	
Cod liver oil	No emulsion formed	
Linseed oil	No emulsion formed	
Mineral oil	Stable	*A*
Castor oil	Stable	*A*
	English Method	
Cod liver oil	Stable	*A*
Linseed oil	Oil sep.	*A*
Mineral oil	Stable	*A*
Castor oil	Stable	*A*

Results of Table I show that in the case of the Continental method, an emulsion could not be formed with cod liver oil and linseed oil; mineral oil and castor oil yielded Grade *A* emulsions. When using the English method, only linseed oil yielded a poor emulsion which showed oil separation within a period of 3 hours of standing.

When making 8-ounce portions of 50% oil emulsions using the Continental method in the Arnold automatic mixer, it was also found that mineral oil and castor oil yielded Grade *A* products, whereas no emulsions could be formed with linseed oil and cod liver oil.

Use of Hand Homogenizer.—Although it is generally accepted that a homogenizer will reduce the size of the oil globules in an emulsion prepared with a mortar and pestle, yet, little comparative study has been made on this phase with respect to emulsions prepared with various fixed oils. Sixty cc. portions of 12½% oil emulsions were prepared using various proportions of acacia and employing a No. 1 wedgwood pestle and a No. 1 wedgwood mortar. The 4 parts of oil and acacia were triturated well and the 2 parts of water was added all at once. Where a primary emulsion resulted, it was triturated for about a half minute, and then the remainder of the water was added gradually. In cases where a primary emulsion did not form, the remainder of the water was added, nevertheless, to make up to volume. In all cases, the final product was passed three times through a hand homogenizer. The results of the use of a hand homogenizer are given in Table II.

Results on homogenization of the various fixed oils show that in the case of linseed oil and cod liver oil Grade *A* preparations were formed when using from 4 parts to 0.013 part of acacia. The linseed oil emulsions showed creaming within a period of 3 hours. In the case of castor oil and mineral oil the hand homogenizer did not seem to have much advantage over the mortar and pestle method of making emulsions. Although the homogenizer permitted emulsification with lower proportions of acacia, more stable emulsions were produced with the mortar and pestle method when using one or more parts of acacia for 4 parts of oil.

It was noticed that passing an emulsion more than 3 times through the homogenizer did not seem to cause further reduction in the size of the oil globules.

When making 50% oil emulsions with the use of the hand homogenizer, similar results were obtained except that the finished products were found to show less creaming within a 3-hour period of standing.

Castor oil has an unusually high viscosity. Heat tends to lower surface tension. A 60 cc. portion of a 12½% castor oil emulsion was prepared using the 4:2:1 proportion and triturating the primary emulsion for 1 minute. The finished product was heated to 35° C. and then passed three times through the hand homogenizer. Heating the emulsion to 35° C. was of no advantage since it did not cause further reduction of the oil globules when passed through the homogenizer.

Four ounces each of homogenized cod liver and linseed oil emulsions containing 0.05 part of acacia

Table II.—Use of Homogenizer

Parts of Acacia[a]	*Linseed Oil* Appearance of Emulsion, 3 Hours	*Linseed Oil* Average Size of Oil Globules	*Cod Liver Oil* Appearance of Emulsion, 3 Hours	*Cod Liver Oil* Average Size of Oil Globules	*Castor Oil* Appearance of Emulsion, 3 Hours	*Castor Oil* Average Size of Oil Globules	*Mineral Oil* Appearance of Emulsion, 3 Hours	*Mineral Oil* Average Size of Oil Globules
4.0	Creaming	*A*	Stable	*A*	Stable	*B*	Stable	*B*
2.0	Creaming	*A*	Stable	*A*	Stable	*B*	Stable	*B*
1.0	Creaming	*A*	Stable	*A*	Creaming	*B*	Stable	*B*
0.6	Creaming	*A*	Stable	*A*	Creaming	*B*	.....	.....
0.4	Creaming	*A*	Creaming	*A*	Creaming	*B*	.....	.....
0.2	Creaming	*A*	Creaming	*A*	Oil sep.	*D*	Creaming	*B*
0.1	Creaming	*A*	Creaming	*A*	.....	.....	Creaming	*C*
0.05	Creaming	*A*	Creaming	*A*	Oil sep.	*D*	Creaming	*D*
0.025	Oil sep.	*A*	Oil sep.	*A*	.....	.....	Oil sep.	*D*
0.013	Oil sep.	*A*	Oil sep.	*A*	.....	.....	Oil sep.	*D*

[a] Number of parts used for 4 parts of oil and 2 parts of water.

for 4 parts of oil were allowed to stand for two weeks to observe their stability. There was creaming but no oil separation during two weeks of standing. Likewise, 4 ounces each of cod liver and linseed oil emulsions containing the same proportion of acacia were allowed to stand for two weeks, but during the 2-week period a teaspoonful of each emulsion, morning and night, was taken out after shaking. It was noticed that after 3 days of standing there was surface demulsification in both products, but the oil was readily emulsified on agitation. In the case of cod liver oil and linseed oil, the use of 0.05 part of acacia gave emulsions which would be acceptable for dispensing.

DISCUSSION OF RESULTS

Motor Stirrer.—The motor stirrer appeared to be of little value with cod liver oil, linseed oil and mineral oil. With respect to the average size of the oil globules, better emulsions were prepared by the mortar and pestle method. Only castor oil yielded a Grade *A* emulsion when using the motor stirrer.

Hand Egg Beater.—When using a hand egg beater to stir the primary emulsion, it was found that it produced just as good emulsions as triturating with a pestle with respect to stability of the preparation and the average size of the oil globules. It is more convenient to make emulsions with a mortar and pestle alone, since it takes less time to make these by avoiding washing of extra utensils.

Arnold Automatic Mixer.—When making emulsions in the Arnold automatic mixer using the Continental method, castor oil and mineral oil yielded Grade *A* products. No emulsions could be made with linseed oil and cod liver oil. Rees (3), likewise, could not make an emulsion of cod liver oil when using a malted-milk mixer even after 16 minutes of agitation. When using the English method, all the oils used yielded Grade *A* products. However, the linseed oil emulsion showed oil separation within a 3-hour period of standing; the cod liver, mineral and castor oil emulsions were stable over that period of time.

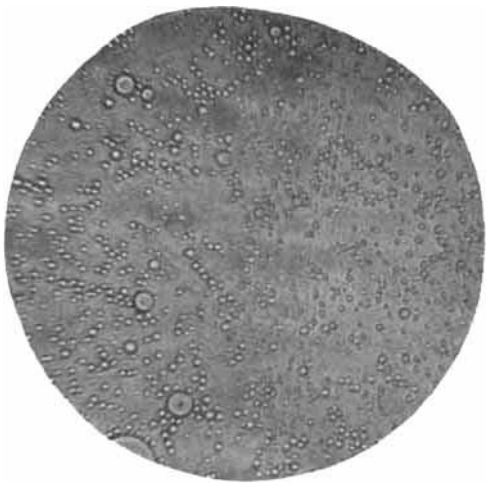

Fig. 1.—Mineral Oil Emulsions—Arnold Automatic Mixer (×430).

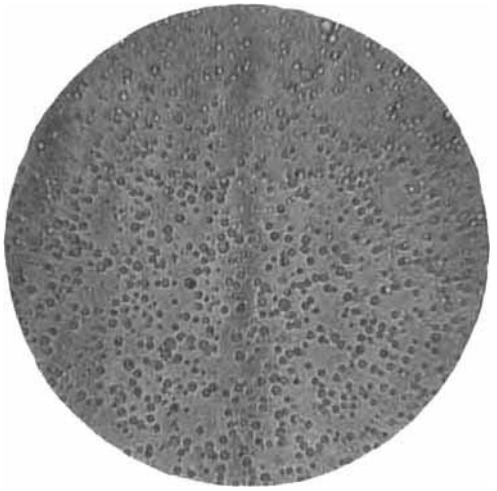

Fig. 2.—Castor Oil Emulsions—Arnold Automatic Mixer (×430).

Homogenizer.—Results on homogenization of the various oils showed that in the case of linseed oil and cod liver oil Grade *A* preparations were formed when using from 4 parts to 0.013 part of acacia for 4 parts of oil. The linseed oil emulsions showed creaming within a 3-hour period of standing. It was felt that 0.05 part of acacia in the case of these oils gave emulsions which would be acceptable for dispensing. Tice (4) showed that the hand homogenizer permitted cutting down the amount of acacia from 12.5% as used in a 50% oil-in-water emulsion prepared by the Continental method to 5 per cent. Rees (3) prepared cod liver oil emulsions by four different methods and found that the hand homogenizer produced the best emulsion.

Fig. 3.—Castor Oil Emulsions—Homogenizer (×430).

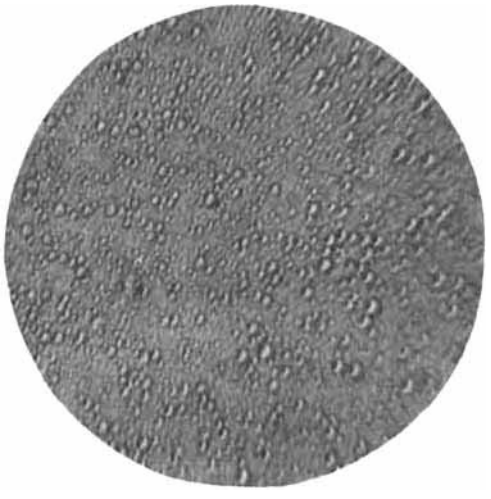

Fig. 4.—Linseed Oil Emulsions—Homogenizer (×430).

Very little work has been done on homogenization of castor oil and mineral oil. Brown (5) studied the effect of homogenization on a mineral oil emulsion and an emulsion consisting of a mixture of magnesium hydroxide and liquid paraffin. The average diameter of the oil globules in unhomogenized samples was about 15 to 20 microns. Homogenization gave an average globule size from 2 to 5 microns. In the present investigation, homogenization of castor oil and mineral oil gave an average globule size of about 3.5 microns when larger proportions of acacia were used. However, for these oils the hand homogenizer did not seem to have much advantage over the mortar and pestle method of making emulsions. Although the homogenizer permitted emulsification with lower proportions of acacia, better emulsions, with respect to the average size of the oil globules, were produced with the mortar and pestle method when using one or more parts of acacia for 4 parts of oil. The fact that castor oil and mineral oil have a high viscosity may be one of the reasons why the homogenizer did not give as good emulsions in the case of these oils.

SUMMARY

A study was made of the efficiency of the Continental and English methods of emulsification as compared with the use of mechanical stirrers and a hand homogenizer for making emulsions.

The motor stirrer was inferior to the mortar and pestle method of making emulsions when using cod liver oil, linseed oil and mineral oil. Only castor oil yielded a Grade *A* product.

Stirring the primary emulsion with a hand egg beater produced just as good emulsions as the mortar and pestle method.

When making emulsions in the Arnold automatic mixer, using the Continental method, castor oil and mineral oil yielded Grade *A* products; no emulsions could be made with linseed oil and cod liver oil. When using the English method in the Arnold automatic mixer, all the oils studied yielded Grade *A* products; the linseed oil emulsion was the only one showing oil separation within a 3-hour period of standing.

Hand homogenization of cod liver oil and linseed oil emulsions produced Grade *A* products when using from 4 parts to 0.013 part of acacia for 4 parts of oil. The linseed oil emulsions showed creaming within a 3-hour period of standing. When using castor oil and mineral oil, the homogenizer permitted emulsification with lower proportions of acacia; however, better emulsions with respect to the average size of the oil

globules were produced by the mortar and pestle method when using one or more parts of acacia for 4 parts of these oils.

REFERENCES

(1) Husa, William J., and Becker, Charles H., "Pharmaceutical Emulsions. I. A Study of the Continental Method," JOUR. A. PH. A., 30 (1941), 83.

(2) Husa, William J., and Becker, Charles, H., "Pharmaceutical Emulsions. II. A Study of the English Method," *Ibid.*, 30 (1941), 83.

(3) Rees, P. T., *Ibid.*, 27 (1938), 607.

(4) Tice, L. F., *Am. J. Pharm.*, 107 (1935), 160.

(5) Brown, H. T., *Pharm. J.*, 132 (1934), 307.

(To be concluded.)

Hydrogenated Castor Oil in Ointments

VI. Sulfated Product in Official Ointments

*By George W. Fiero**

The first ointments were prepared from animal fats such as lard, horse fat, goose grease, etc. These fats were unsatisfactory from a pharmaceutical standpoint because they readily developed rancidity. Addition of preservatives such as benzoin retarded but did not prevent rancidity. The use of lard as an ointment base in the official ointments continued until the U. S. P. IX (1916) when petrolatum replaced it in most ointments.

The most widely employed base to-day is petrolatum, both for official ointments and individual prescriptions. This base is used largely because of the fact that it is stable and that it is compatible with most medicaments. Being a hydrocarbon, however, it definitely has no tendency to absorb water—not even as much as the natural fats. Because of this property, it is often used in conditions where it is contra-indicated. Certain types of dermatitis of the hands should not, as is often the case, be covered with a greasy ointment because this prevents evaporation of perspiration and may cause secondary infection.

Where there is perspiration or a serous discharge, it seems that they act as a barrier between the skin and the medicament in a petrolatum base. For such cases a hydrophilic ointment base is essential so that perspiration acts as a medium and not a barrier. Such a base should consist entirely, or in large part, of water-soluble material.

Mumford (1) states: "An ideal base would be one which acted with equal efficiency on dry and oily skins, which could be removed with water instead of olive oil or liquid paraffin, and which could suspend within itself water-soluble and fat-soluble chemicals and transfer them to the skin in a manner which vaseline cannot." He also pointed out that a base should be able to utilize perspiration and serous discharge instead of acting as a barrier to them as in the case of vaseline. Of course, there is doubt about the term "ideal ointment base" as in certain cases a non-hydrophilic occlusive base might be desired. Usually, however, a hydrophilic base is desirable.

There have been several suggestions made for hydrophilic ointment bases (2). The addition of cholesterin to petrolatum renders it capable of absorbing water. This type of base has been quite widely employed. Emulsions have likewise been employed. Many of these are satisfactory for certain medicaments but definitely unsatisfactory for substances such as salicylic acid, mercurials, etc., due to their alkalinity.

Unlike other vegetable oils, when castor oil is catalytically hydrogenated to an iodine number of less than 10, it is still capable of sulfation because of the presence of the hydroxyl radical. This product, sulfated (or sulfonated) hydrogenated castor oil (abbreviated "SHCO") is now being manufactured in commercial quantities.[1] It appears from clinical data to meet Mumford's specifications for an ideal ointment base. It has the consistency of an ointment, unlike other sulfated oils which are liquid. Unlike petrolatum, it is soluble in water and has a body and color similar to that of wool fat. The consistency varies, of course, with the extent of sulfation; the material used in these experiments possessed the following characteristics:

* University of Buffalo, School of Pharmacy.

[1] Manufactured by National Oil Products Co., Harrison, N. J.