

VOLATILE OILS IN PILLS.*

BY PROF. H. G. GREENISH AND MISS C. E. PEARSON.

Although prescriptions for pills containing volatile oils are not so common now as they formerly were, yet they occur sufficiently frequently to make the best method of dispensing them a matter of interest and importance to the pharmacist. Most authorities¹ recommend trituration of the oil with powdered curd soap and addition of powdered liquorice root to the paste so produced until the requisite firmness is obtained. Others² either do not specify the variety of soap to be used or include both hard and curd soap.

As no record could be found of a definite series of trials with these or other soaps with the object of determining their relative values for the purpose experiments in this direction were commenced in 1918 by Miss Williamson, Redwood Scholar, and, after an interruption of two years, resumed by Miss Pearson.

The first step was the collection or preparation of a series of soaps. The following were obtained from the usual commercial sources:

Powdered Hard Soap (Sapo Durus, B. P.),
Powdered Curd Soap (Sapo Animalis, B. P.),
Powdered Magnesium Oleate,
Powdered Calcium Stearate,
Powdered Sodium Stearate.

The following were prepared in the laboratory:

Sodium Oleate,
Sodium Palmitate,
Sodium Stearate,
Sodium Cerotate,
Sodium Abietate (Resin Soap),
Sodium Soap from Cocoanut Oil,
Sodium Soap from Hardened Cottonseed Oil.

Sodium oleate was made by neutralizing oleic acid (B. P.) with sodium hydroxide in the presence of alcohol, evaporating to dryness and powdering.

In making sodium palmitate and stearate commercial palmitic and stearic acids were recrystallized from alcohol and similarly combined with sodium.

Cerotic acid was prepared by boiling yellow beeswax with alcohol, filtering the solution while hot, and allowing the filtrate to cool; the cerotic acid that separated out was collected, washed with alcohol, and the operation twice repeated. The cerotic acid was then combined with sodium.

Sodium abietate was made by dissolving amber resin in alcohol, neutralizing with sodium hydroxide, and evaporating to dryness.

Cocoanut oil soap was made by saponifying cocoanut oil with alcoholic solution of sodium hydroxide, evaporating off the alcohol, dissolving the residual soap

* From the Research Laboratory. Read before an Evening Meeting of the Pharmaceutical Society of Great Britain. Reprinted from the *Pharmaceutical Journal and Pharmacist*, December 17, 1921.

¹ Squire, "Companion," 1916, p. 1025; "Art of Dispensing," 1908, pp. 86, 88, 110; Lucas and Stevens, "Practical Pharmacy," 3d Ed., p. 312.

² Barnard Proctor, "Lectures on Practical Pharmacy," 3d Ed., pp. 312, 335. British Pharmaceutical Codex, 1911, p. 1326.

in water, and liberating the fatty acids with hydrochloric acid. These were then washed with water and combined with sodium.

Hardened cottonseed oil was similarly treated, a very hard sample being used for the purpose.

Sodium cerotate was selected as it was thought that a soap made from a fat acid of very high molecular weight might differ in its action from a soap made from acids of lower molecular weight. Coconut oil soap was selected for the opposite reason, and soap made from hardened cottonseed oil was included because although doubtless the unsaturated fat acids with 18 carbon atoms are converted into stearic acid it is probable that other changes as well take place, giving rise possibly to isomeric acids.

The first series of experiments was made with 1 cc of volatile oil, 0.5 Gm. of soap, and from 1.5 to 2.0 Gm. of powdered liquorice root. The oil was triturated with the soap, and the powdered liquorice root gradually added. The volatile oil employed was dementholized peppermint oil. The following results were obtained:

	Oil.	Soap.	Liquorice Root.	Remarks.
Sodium oleate.....	1.0	0.5	2.0	Soft and oily
Sodium palmitate.....	1.0	0.5	2.0	Soft
Sodium stearate.....	1.0	0.5	1.5	Good mass
Sodium stearate.....	1.0	0.5	2.0	Inclined to crumble
Sodium cerotate.....	1.0	0.5	2.0	Very good
Sodium abietate.....	1.0	0.5	2.0	No absorption of oil
Hard soap.....	1.0	0.5	2.0	Soft
Curd soap.....	1.0	0.5	1.5	Good but not so good as stearate
Curd soap.....	1.0	0.5	2.0	Inclined to crumble
Cocoonut oil soap.....	1.0	0.5	1.8	Good
Hard-cotton-oil soap..	1.0	0.5	1.5	Very good
Magnesium oleate.....	1.0	0.5	1.5	Oily
Calcium stearate.....	1.0	0.5	1.5	Oily

From these experiments it appears that sodium abietate has no appreciable action in absorbing the oil. Magnesium oleate and calcium stearate are unsatisfactory under the conditions given. Sodium stearate is rather more efficacious than ordinary curd soap, considerably better than sodium palmitate and than ordinary hard soap, and far better than sodium oleate. Sodium cerotate seemed to give a rather better mass than sodium stearate, but the difference was not marked. Cocoonut oil soap was distinctly better than sodium stearate, while the soap made from hardened cottonseed oil was the best of all; indeed, further experiments showed that even in the proportion of 1 cc of the oil, 0.3 Gm. of the soap, and 1.5 Gm of powdered liquorice root a good mass was obtained.

With magnesium oleate a fairly good, stiff mass was obtained with 1 cc of the oil and 2.2 Gm. of the oleate, and calcium stearate in the proportion of 5.0 Gm. to 1 cc of the oil also gave a good mass. Neither of these substances, however, has any appreciable advantage over the sodium soaps.

A further comparison was made with sodium stearate, curd soap and hard soap, the proportion of soap being increased and that of the liquorice powder diminished.

	Oil.	Soap.	Liquorice Root.	Remarks.
Sodium stearate.	1.0	1.0	1.5	Very good mass
Curd soap	1.0	1.0	1.5	Not so good
Hard soap.	1.0	1.0	1.5	Distinctly soft

Again, curd soap is better than hard soap, and sodium stearate is better than either.

In the next series of experiments sodium stearate was used in varying quantities and sufficient liquorice powder added to produce a good mass:

	Oil.	Soap.	Liquorice Root.	Remarks.
Sodium stearate.	1.0	0.4	2.0	Good mass
Sodium stearate.	1.0	0.5	2.0	Good mass
Sodium stearate.	1.0	1.0	1.5	Good mass
Sodium stearate.	1.0	1.5	1.0	Good mass
Sodium stearate.	1.0	2.0	0.5	Good mass

In all the foregoing experiments the oil was mixed with the soap and the powdered liquorice added. No difference could be detected when the oil was mixed with the liquorice powder and the soap added.

As the powdered liquorice root used to stiffen the soft mass of soap and oil consists mainly of water-soluble substances, starch, and the more or less broken parenchymatous cells, vessels and fibers, it was thought desirable to ascertain whether any one of those constituents had any special advantage over the others for this purpose. Accordingly, some of the powdered liquorice root used in the foregoing experiments was exhausted by repeated maceration with chloroform water and decantation, the insoluble matter being collected, washed, dried, and powdered. From a portion of this the starch was removed by kneading under water in a linen bag, collected, washed and dried. Another portion was entirely freed from starch by boiling with dilute hydrochloric acid, the residue collected, washed, and dried. Using 1 cc of the oil and 1 Gm. of sodium stearate, the following quantities were required:

Water-insoluble residue.	1.5 Gm.
Starch.	1.0 Gm.
Fibrous material.	1.0 Gm.

Of these three masses, that made with the fibrous material was the best.

Barnard Proctor¹ found that exhausted quassia wood was better than disintegrated blotting paper, sarsaparilla root, or liquorice root for imparting retentiveness of shape to a soft pill.

Harold Wyatt² recommended powdered chamomile flowers for the same purpose. Experiments were accordingly made with powdered quassia wood, and powdered chamomile flowers, and also with kaolin and calcium phosphate. Of these powdered quassia proved to be the most efficacious, 0.6 to 0.7 Gm. being sufficient to stiffen a mass made with 1 cc of oil and 1 Gm. of sodium stearate.

As it was thought that possibly oils of varying composition might require varying amounts of soap for their absorption, comparative experiments were undertaken with dementholized oil of peppermint, clove oil, cajuput oil, caraway oil,

¹ *Loc. cit.*

² *Pharm. Journ.*, [4], 38, 518.

and cassia oil. In each case 1 cc of the oil was used with 0.5 Gm. of soap made from hardened cottonseed oil and 1.5 Gm. of powdered liquorice root. No appreciable difference could be detected.

In none of the works to which reference was made could any explanation be found of the action of the soap in absorbing the oil, and the foregoing experiments fail to throw any light on the matter. While it is true that the sodium soaps of oleic, palmitic and stearic acids show increase in the absorptive power with increase in the molecular weight of the fat acid, the opposite is the case with soap made from cocoanut oil and sodium cerotate failed to show the advantage expected of it. It occurred to us that possibly part of the soap, with the aid of the moisture still present in it, and also in the powdered liquorice root, might emulsify the oil and so allow of its incorporation into a pill mass. A mass was accordingly made with sodium stearate and powdered liquorice root, both previously dried at 100°. No difference was perceptible. The addition of 0.2 cc of water to 3.5 Gm. of mass was not followed by any material alteration, but the addition of larger quantities led to unsatisfactory results. If emulsification of the oil had taken place, microscopical examination might be expected to show the oil in minute globules. To render it more easily visible the oil was deeply stained with Sudan-red. In no instance could globules of oil be detected; it appeared rather to be distributed throughout the mass in the form of a more or less uniform film.

M. E. Laing and J. McBain,¹ in their researches on soap, have shown that an aqueous solution of soap can be brought at will into any one of three typical states—*viz.*, a clear, oily, liquid sol, a transparent, elastic gel, or a white, opaque solid curd. A soap curd is a sol or gel from which a part or nearly all of the soap has been abstracted through the formation of white curd fibers. The distinctive structural feature of soap curd is the separation of hydrated soap as a felt of long, white fibers of barely microscopic diameter. This formation of curd is analogous to a process of crystallization. A transparent soap is a gel, but hard commercial soaps are gels, containing a felt of curd fibers.

It would appear possible, then, that if the oil could penetrate the particles of the dry powdered soap with which it is triturated it might form a very thin film, covering the curd fibers and becoming enmeshed in them. The total area of the curd fibers must be exceedingly large on account of their very small diameter, and the film of oil covering them, or possibly adsorbed by them, would be exceedingly thin. To ascertain whether a volatile oil can readily penetrate dry soap, the following experiment was made: A piece of hard, dry soap, many years old, was immersed in peppermint oil deeply stained with Sudan-red. In the course of a week the color had penetrated into the soap to the depth of about 1 to 1.5 mm. At the same time, the weight of the soap had increased by about 15 percent, showing that infiltration of the oil had accompanied infiltration of the color; the outer layers of the soap became simultaneously softened, and a small portion passed into solution. Infiltration of the oil into the particles of the soap and adsorption by the curd fibers of which the soap largely consists must, therefore, be admitted as a possible explanation of the action of the soap in absorbing the oil.

The chief results of the foregoing experiments are:

¹ *Journ. Chem. Soc.*, Dec. 1920, p. 1506.

1. Of the soaps that are at present commercially available sodium stearate is the best for absorbing volatile oils.
2. Soap made from a strongly hardened cottonseed oil, if procurable, would be still better.
3. The best material for stiffening the soft soap and oil mass is a fibrous material, such as powdered quassia wood.
4. The peculiar property possessed by soap of absorbing the oil is probably infiltration of the oil into the particles of the soap and its adsorption by the curd fibers of which the soap largely consists.

ABSORPTION OF VOLATILE OILS BY FATTY ACIDS.

Induced by the foregoing paper, Mr. Cofman-Nicoresi reports on his work on the absorption of volatile oils and other liquids by salts of higher fatty acids, in the *Chemist and Druggist* of December 31, 1921. The article follows:

"In 1915, while making solidified alcohol for use in the Army, I came to the conclusion that salts of higher fatty acids crystallize in the shape of a spongy compound, which retains the whole of the liquid in which they were dissolved, forming what is, for all practical purposes, a solid body. In order to confirm my assumption I conducted various experiments, starting with turpentine, rectified oil of amber, and almost every volatile oil in turn. After a little while I succeeded in making solid shapes containing as little as 5 percent of salts of fatty acids. In the case of turpentine, though the experiments were dangerous and troublesome, the result proved to be an ideal liniment, containing no water, and which is completely absorbed by the skin. (Pat. 18,060/1915.)

"My next step was to dissolve various drugs like phenol, iodine, etc., in liquid paraffin, glycerin, and in other liquids, and the results proved satisfactory in so far as they did not affect the spongy compound and the solutions did not undergo any changes. (Pat. 6,198/1916.) It seemed clear to me that this process would prove very useful in the manufacture of suppositories, and also of ampuls, where the glass tubing could be conveniently replaced by the soap enclosure. Then I proceeded to subject the various liquids to currents of gases like ammonia, formaldehyde, etc., and found that these gases were retained in the resulting solids and could be recovered on warming. (Pat. 1,415/1917.) Chloroform, amongst other liquids, gave good results, but cresol proved a dangerous element. After many experiments, and after having succeeded in incorporating a large number of different liquids and solutions into salts of higher fatty acids, I believe I have established the following facts, which may prove of use to soap analysts and those interested in the chemistry of higher fatty acids:

"That salts of higher fatty acids, when in solution, crystallize in the shape of a spongy mass, which retains the whole of the liquid in which they were dissolved.

"The liquids from which the salts of higher fatty acids crystallize in a spongy shape are usually of the nature of an alcohol.

"The formation of this spongy compound takes place at a given concentration, usually above 5 percent."

By means of heat a much larger percentage of salts of fatty acids can be incorporated, without apparently interfering with the absorption of liquids, but naturally diminishing the amount absorbed.

The spongy compound formed is what I presumed to be a definite salt of stearic and palmitic acid, which I called stearo-palmitate of soda. (Pat. 18,060/-1915.)

This stearo-palmitate compound is always formed, apparently, at the boiling point of the liquid in which it is dissolved, and not at a fixed temperature.

The amount of liquid retained does not vary with the nature of the different liquids, but seems to be the same for all liquids under the same conditions.

Many chemists, and even expert analysts, look upon these solidified preparations as being soaps or, more precisely, medicated soaps. The facts do not confirm this view. While medicated soaps contain the various ingredients, in the shape of a salt like sodium phenate or sodium stearo-cresolate, etc., these ingredients cannot be extracted, except by a breaking-down of their salts. In the solidified preparations the liquids can be obtained in their normal state by simple pressure, without any physical or chemical change. The whole of the liquid solution, chemically and physically unchanged, can be recovered by evaporation, leaving the spongy case behind. I tried to submit various slides of these preparations to microscopical examination, but the difficulty of staining without dissolving them could not be overcome. I then tried polarized light, with splendid results, clearly revealing the structure of the spongy compound, with its series of sparkling crystals, in symmetrical rows, and intervening liquid, looking like a diamond studded map. I hope on a future occasion to show the importance of polarized light in the analysis of soaps.

ACETYSALICYLIC ACID IN SODIUM CITRATE SOLUTION.*

BY PAUL NICHOLAS LEECH, PH.D.

Acetylsalicylic acid ("aspirin") is dispensed in dry condition because it is easily decomposed in the presence of moisture; also it is insoluble in water. However, articles have appeared recently in both medical and pharmaceutical literature claiming that acetylsalicylic acid may be dispensed *in solution* by aid of sodium citrate; also that the acetylsalicylic acid would not be decomposed. For instance, the following, which was probably abstracted from some American pharmaceutical publication, appeared in the *Prescriber*.¹

Acetylsalicylic acid (aspirin) is practically insoluble in water, and though soluble in alcohol such a solution is not generally suitable for administration. It is therefore usually given in tablets or cachets. Solution may be effected by addition of sodium bicarbonate, but as the resulting solution is merely a mixture of sodium acetate and sodium salicylate, this method is not admissible. It is said that sodium citrate will dissolve acetylsalicylic acid without dissociation: for each grain of aspirin 4 grains of sodium citrate should be added. Such a solution, flavored with syrup of lemon, is suitable for administration to children.

The usual test for decomposition of acetylsalicylic acid is the detection of the freed salicylic acid by means of ferric chloride solution. It occurred to me, therefore, that possibly such a test was used as a basis of the contention of the non-decomposition of acetylsalicylic acid in sodium citrate solution. If so, the seem-

* From the Chemical Laboratory of the American Medical Association, and reprinted from the *Journal A. M. A.*, January 28, page 275.

¹ "Solvent for Acetyl-Salicylic Acid," *The Prescriber*, June 1921, p. 247.