of foreign substance. You may call them droplets if you choose, but as units of measure they have ceased to have value.

It is not necessary to go into detail, showing precisely how much variation is occasioned by this or that particular vapor. Little or no practical use could be made of such data. The important thing is to keep in mind the possibility of such disturbing influences in any use made of the dropper for exact measurements.

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## HYDROGENATED OILS AS FUTURE OINTMENT VEHICLES.*

BY ERNEST R. JONES.

### INTRODUCTION.

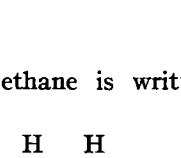
For many years oil chemists had been searching for a simple means of changing oleic acid into stearic acid in order to convert relatively cheap raw material into more valuable fats.

While the matter would seem very simple because of the closeness of their empirical formulae, *i. e.*, $C_{18}H_{34}O_2$ or oleic acid and $C_{18}H_{36}O_2$ or stearic acid, a difference of only two hydrogen atoms, it was not until a suitable hydrogen carrier or catalyzer was found at the very close of the nineteenth century that the changing of oleic acid into the harder stearic acid was commercially accomplished. A German patent in 1901 is probably the first one recorded having to do with the reduction of organic bodies by hydrogen in the presence of nickel catalyzers. Since that time many improvements and patents have followed rapidly.

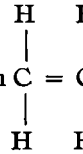
It is not the intention of this paper to go into the technique and processes used for the hydrogenation of oils and fats, but briefly, the process consists of converting a soft fat or oil into a harder one by causing the unsaturated acids or glycerides to take on more hydrogen. To do this the fat is heated in a suitable container to about 160° C. (temperature varies in different processes) a suitable catalyzer is added, usually a salt of nickel or palladium, or the finely divided metals themselves, and hydrogen is run in under pressure, the process being continued for several hours or until the desired degree of hardness is obtained. The catalyzer is then filtered out, the product cooled and is ready for use unless further bleaching or deodorizing is desirable.[1]

### CHEMISTRY OF PROCESS.

Although the hydrogenation process is essentially one of reduction it will be easier understood if we consider the new product as obtained by "addition." To explain—the graphic formula for ethane is written



The graphic formula for ethylene is written



It will be noticed that in the latter

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* Read before Detroit Branch A. Ph. A., April meeting, 1918.

[1] For a more extended discourse on these processes see "Hydrogenation of Oils," by Ellis.

compound the linkage between the two carbon atoms is double whereas in the former compound the linkage is single. Compounds in which the linkage between the carbon atoms is single are called "saturated" compounds and can only form new compounds by "substitution," that is by substituting a different atom or group of atoms for one of the H atoms which is present.

A double bond or linkage in the structural formula of any compound, as in ethylene, is merely a convenient expression of certain facts which have been established experimentally, namely, that the compound is "unsaturated" and has the power of combining directly with certain other atoms or groups. In such cases the double linkage between the carbon atoms is changed to single and the new compound is said to have been formed by "addition."

Compounds which are unsaturated are the only ones then which are susceptible to hydrogenation. Thus its application to fats, now that suitable catalyzers have been found, is limited to those which contain unsaturated acids or glycerides.

Oleic acid, formula $CH_3.(CH_2)_{14}.CH : CH.COOH$, is a familiar example of an unsaturated acid. (Note the double linkage indicated by the two dots.) Therefore it is capable of being hydrogenated or converted into stearic acid, which is a saturated acid. The following equation represents the change which takes place:

$$\underset{\text{oleic acid}}{C_{18}H_{34}O_2} + H_2 = \underset{\text{stearic acid}}{C_{18}H_{36}O_2}$$

$$282 + 2 = 284$$

From the molecular weights you will see that 282 pounds of oleic acid will yield 284 pounds of stearic acid by the addition of two pounds of hydrogen.

As the individual molecules of oleic acid are changed to stearic acid they of course exhibit the properties of that acid. The chief physical difference between oleic and stearic acids is that the former is a liquid and the latter a solid. If the process of hydrogenation is carried to completion, a hard, solid stearic acid would result on cooling, but as the process is entirely within our control we may stop it when any desired consistency has been obtained. This brings the possibility of using these fats for pharmaceuticals close to our own doors and one which we are not yet alive to the advantages obtainable. In pharmacy we have little use for either oleic or stearic acids, but the glycerides of the acids, namely, olein and stearin, are natural constituents of every fat or fixed oil we use in ointments, and this is where they seem destined for a great future use, in my opinion, as the glycerides can also be hydrogenated and thus yield us an entirely new set of ointment vehicles devoid of some of the objections of the present ones.

### AN APPLICATION TO PHARMACY.

The most unsatisfactory ointment which pharmacists have to dispense is Zinc Oxide Ointment, U. S. P. In a paper, which I read before the A. Ph. A. convention in Detroit in 1914, it was plainly shown that the granulation and unsightly appearance of this ointment was due to the physical characteristics of the lard and could not be corrected. A hardened petrolatum vehicle was suggested and the Section on Pharmacopoeias and Formularies passed a motion suggesting that such a change be made in the U. S. P. IX formula for this ointment. The

sub-committee on ointments rejected the suggestion saying that "leading dermatologists favored the retention of the old formula." The reason was because benzoinated lard is absorbed by the skin, whereas petrolatum is not or only very slow. I doubt whether this ointment is intended to be absorbed when used, but that is a question of therapeutics which we will not consider at this time. If we can supply a substitute for lard, which will satisfy dermatologists from the standpoint of absorption and satisfy pharmacists at the same time, such a move would seem desirable to every fair-minded person. Such a thing can be accomplished with a hydrogenated cottonseed oil vehicle stiffened with wax as I have samples here to prove. These samples are all from two to four years old, have been kept at room temperature and are as perfect as when made.

It is not the intention of this paper to recommend any particular manufacturer's hydrogenated products, but as Crisco, a hydrogenated cottonseed oil, is quite a popular article particularly in the home, the experiments were conducted with that product. If such a product were marketed under a scientific name indicating its composition, it would, of course, be more desirable for our work. Also Crisco is a little too soft to replace lard entirely in our ointments and is open to the further objection that when melted alone it cannot be cooled to a smooth product by any practicable means. If the hydrogenation process were carried further these deficiencies could probably be eliminated. For this reason, I found it necessary to use wax to stiffen the ointments, which at the same time gives a smooth product.

The following formula is proposed:

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|---|---|
| Zinc oxide | 200 Gm. |
| White wax | 125 Gm. |
| Hydrogenated cottonseed oil (Crisco) | 675 Gm. |

Melt the wax and hydrogenated cottonseed oil, add a small portion of the melted mixture and triturate with the zinc oxide till a smooth paste is obtained, then add the balance of the melted mixture and triturate till cool.

It may be found desirable to increase or decrease slightly the amount of wax, but this will be found out in time. Also it may be desirable to benzoinate the fat before making the ointment.

While I do not intend that such an ointment should be kept that long, I know from my experiments that it will keep perfectly for two years at least.

### AS TO THE FUTURE.

Of course, at present such an ointment could not be dispensed as U. S. P. without the consent of the physicians. Most physicians will be open to such a suggestion when you tell them it is as quickly absorbed as lard, is cleaner, less liable to become rancid and is a more stable product in every way. I hope the demand will be such that it will eventually displace the present U. S. P. formula. Perhaps the demand for a hydrogenated fat suitable for pharmacy will cause manufacturers of such products to take notice of our wants and make one suitable to our needs. When they do, I predict an extensive future for such a product. We can use it to replace lard in all our ointments and thus eliminate some of our troubles.

Although I started to experiment with hydrogenated oils on an extensive scale two years ago, a change in positions has kept me so busy that I have not had time to continue the work since, consequently my experiments have been confined to only Zinc Oxide Ointment.

Acknowledgment is made to Parke, Davis & Company, in whose laboratories this work was conducted.

DETROIT COLLEGE OF PHARMACY,
April 19, 1918.

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## WHAT THE DRUG TRADE HAS DONE TO WIN THE WAR.*

The first paper of the symposium under above title and presented at the April meeting of the New York Branch, A. Ph. A. was by Mr. R. C. Stofer, who in his preliminary remarks referred to some of the orders that their firm had completed. He also stated that, in his opinion, pharmacy should disregard its characteristic modesty and take due credit for its achievements, many of which are the result of the marked degree of coöperation at present existing, by reason of the fluxing process which is going on between educators in pharmacy, retail pharmacists, and the excellently equipped scientific and research laboratories of progressive pharmaceutical manufacturers. Parts of his paper follow:

**Digitalis:** Through the intelligent direction of its collection and preparation for the market, American growers have succeeded in supplying digitalis much superior to the European article. We have received American-grown digitalis, which tested nearly two and a half times the U. S. P. standard. Experiments have been conducted in the scientific department with a view of determining the best physiological method for the estimation of the strength of digitalis preparations. Comparative tests are now being made by the one-hour frog method, the twelve-hour frog method, the cat method of Dr. Hatcher, and also the guineapig method. It is hoped from the results of these experiments a definite, scientific conclusion may be drawn as to which is the best method for testing digitalis and its preparations.

**Mexican Scammony:** Owing to the world war, true scammony became unobtainable in commercial quantities. Experiments, both chemical and physiological, have been made with the resin obtained from true scammony and that from the Mexican scammony. From the results of experimental work, data is now in the hands of the U. S. P. Revision Committee and they have been requested to permit the use of Mexican scammony as a source of resin scammony, as is done at the present time by the British Pharmacopoeia.

**Aconite:** It has been definitely shown by many investigators, that the present chemical method for the assay of aconite and its preparations is entirely unsatisfactory, as the results obtained do not indicate the therapeutic activity of the drug and its preparations. Experiments are being made, looking to the isolation of aconitine from benz-aconine and aconine, as it is claimed that these two alkaloids are not therapeutically active, to any great extent. Much research work is being performed upon the physiological method, in an endeavor to improve the new semi-official guineapig method of the Pharmacopoeia.

**Belladonna Leaves:** The leaves of Hungarian and German growth which we formerly received were oftentimes brown, of low assay, probably due to improper collection and preparation for the market. Much attention has been given in various sections of the United States to the cultivation, upon a commercial scale, of belladonna, and the American growers have been quick to grasp the advantage of high assay. By efficient methods, proper selection of seeds

* A symposium of the New York Branch, American Pharmaceutical Association, April meeting, 1918. Abstracts from papers by R. C. Stofer of Norwich Pharmacal Company; Saunders Norvell of McKesson & Robbins; H. C. Lovis of Seabury and Johnson, and S. B. Penick of S. B. Penick & Co.