HYDROGENATED OIL AS AN OINTMENT BASE.*

BY GEORGE W. FIERO.**

There is a long-felt need for a satisfactory ointment base. None of the bases employed by the U. S. P. is entirely satisfactory for all purposes. Lard has been used for a large number of ointments but has the disadvantage of the tendency to develop rancidity. Attempts to preserve lard by the addition of other substances has not been satisfactory; benzoin is used as a preservative for lard in many ointments and has been found to retard, but does not entirely prevent the development of rancidity. This is indicated by the fact that only fifteen of seventy-five samples of sulphur ointment (prepared with benzoinated lard) purchased at retail pharmacies were free from rancidity. Over four hundred samples of lard containing various quantities of a number of substances as preservatives were allowed to stand unstoppered for a period of 25 weeks; rancidity developed rapidly in all samples except those containing guaiacol, creosote, oil of clove and resorcinol.[1] Husa[2] reports that most attempts at preserving lard have been unsatisfactory.

Other substances frequently employed in ointments are wool fat and petrolatum. Neither of these substances is a true fat (wool fat being a cholesterol and petrolatum a hydrocarbon) and hence are not readily susceptible to rancidity. Wool fat has been found by many experimenters to be a very absorbent base and hence is valuable for many ointments. However, it possesses certain disagreeable properties, such as its very tenacious consistency and characteristic odor. Petrolatum has been used for a large number of ointments but has been found to be practically non-absorbent.[3] In most cases it is desirable to use an ointment base which will penetrate the skin, carrying the medicaments with it or acting as a medium through which they can pass.

Rancidity.—The rancidity question is definitely related to ointments, since rancid fats not only have a disagreeable odor but also develop irritating properties which render them unfit for application to the skin. The exact nature of rancidity is not definitely known, as is indicated by a search of the literature. Certain factors seem to be necessary for the development of rancidity. Kerr and Sorber[4] and many others found that oxygen is necessary for rancidity and that the products of rancidity are, to a larger extent, oxidation products such as aldehydes, ketones and peroxides. Light has also been pointed out as a factor in the problem by Salkowski[5] and others. In the development of rancidity, it has been demonstrated[6] that fats develop acidity and that rancidity does not develop rapidly in absolutely dry fats, which indicates that moisture is a factor, and the acidity is a result of hydrolysis. Heat also seems to be a factor, and it has been pointed out that

* Department of Pharmaceutical Research, University of Southern California, Los Angeles. Part of a thesis presented to the Department of Pharmacy in partial fulfilment of the requirements of the degree of Master of Science.

** Assistant Professor of Materia Medica, University of Buffalo, Buffalo, N. Y.

[1] *Amer. Jour. Phar.*, 102 (1930), 146.

[2] Jour. A. Ph. A., 15 (1926), 1071; *Ibid.*, 18 (1928), 243.

[3] *Brit. Med. Jour.*, 2 (1911), 161; *Ibid.*, 1 (1908), 1225.

[4] *Ind. Eng. Chem.*, 15 (1923), 383.

[5] *Z. Nohu. Genussm.*, 34 (1919), 305.

[6] *J. Soc. Chem. Ind.*, 10 (1891), 29.

bacteria are the cause of rancidity, although it has been found that rancidity will develop in fat which is free from micro-organisms.[1] Metals also seem to increase the rate of development of rancidity.[2] This would indicate that fats susceptible to rancidity should be stored in non-metallic containers, air-tight, free from light, in a cool, dry place.

All fats do not develop rancidity at the same rate. The susceptibility of a fat to rancidity seems to be relative to the iodine number; fats with a high iodine number usually develop rancidity rapidly, those with a lower number being much less susceptible. Since halogens combine with the "double bonds" of the fatty acid radical, the iodine number is a measure of the extent of unsaturation of a fat. This would indicate that in rancidity the oxygen attacks the unsaturated carbon atoms, and rancidity is definitely related to unsaturation.

Hydrogenated Oils.—Fats with a high iodine number are often liquids, while fats with a low iodine number are usually solids. It has been found that a liquid fat with a high iodine number (such as olein) can be converted into a solid fat with a low iodine number (such as stearin) by passing a stream of hydrogen through the fat in the presence of a catalyst. Any desired consistency can be obtained by increasing or decreasing the amount of hydrogen. Chemically, the hydrogenated fat is more saturated than the original fat and hence should be less susceptible to rancidity. The physical characters of the product, such as is illustrated in household hydrogenated oil lard substitutes such as *Crisco*, *Velvet Shortening*, etc., indicates the possibility as an ointment base.

Experimental Procedure.—In order to ascertain the stability of hydrogenated oil to rancidity, samples were placed unstoppered in a warm, light place for twenty-five weeks. Lard under the same condition developed rancidity in about three weeks as indicated by the Kreis Test[3] and at the end of twenty-five weeks developed a very strong, disagreeable odor. The hydrogenated oil, however, did not develop rancidity as indicated by the Kreis Test after twenty-five weeks.

Hydrogenated oil with an iodine number of 75 prepared from cottonseed oil was used in these experiments. Physically, it was a soft, white, odorless fat of satisfactory consistency and melting near body temperature. Chemically, it was not susceptible to rancidity. Therapeutically, it was practically inert since cottonseed oil is used as a base for pharmaceutical liniments.

CONSTANTS OF HYDROGENATED OIL USED.

Specific gravity at 40° C./25° C.	0.901
Refractive index at 20° C.	1.4633
Iodine number	75.85
Saponification number	191.8
Halphen test	Negative
Melting point	36.5° C.

In order to determine the pharmaceutical application of hydrogenated oil, it was necessary to ascertain whether it is absorbed by the skin as compared with

[1] *Cotton Oil Press*, 5 (1921), No. 3, 45.

[2] *Ind. Eng. Chem.*, 14 (1922), 937.

[3] The U. S. Government test for rancidity: Equal volumes of melted fat and concentrated hydrochloric acid are shaken together; ethereal solution of phloroglucinol is added. A pink to red color indicates rancidity.

other ointment bases. This was done by a direct application method and compared with lard as a standard.[1] Lard was chosen as a standard because it has been shown to be an absorbent base and can be spread without difficulty. Wool fat cannot be spread easily because of its tenacity; petrolatum is practically non-absorbent.

Determination of Relative Absorption of Hydrogenated Oil.—A definitely weighed quantity (approximately one Gm.) of hydrogenated oil was applied to a definite area (16 sq. in.) of the human chest, which had been previously cleaned with ether. The weighed fat was then rubbed over the surface for a period of 150 seconds, the residue carefully scraped off and weighed. The difference in weights indicated the amount of fat absorbed. Simultaneously a similar quantity of lard was applied to the other side of the chest in the same manner. By comparing the quantities of each fat absorbed, a ratio was established which indicated the relative absorption of the two fats.

The value of this experiment depends, to a large extent, upon the care in treating each fat identically, using the same speed of rubbing, the same pressure, etc. It was found that the absorption ratio of the two fats was fairly constant even though the actual quantities of fats absorbed differed with each subject. The results are shown in Table I from which it can be seen that hydrogenated oil is approximately 73% as absorptive as lard under the conditions of the experiment.

TABLE I.—COMPARATIVE ABSORPTION OF HYDROGENATED OIL AND LARD APPLIED TO THE SKIN BY INUNCTION.

Subject.	Hydrogenated oil absorbed.	Lard absorbed.	H/L constant.*
A	0.2250 Gm.	0.2900 Gm.	0.722
B	0.2300 Gm.	0.3000 Gm.	0.767
C	0.1830 Gm.	0.2502 Gm.	0.731
D	0.1300 Gm.	0.1800 Gm.	0.722
E	0.1100 Gm.	0.2100 Gm.	0.505
F	0.1270 Gm.	0.1600 Gm.	0.793
G	0.2070 Gm.	0.2248 Gm.	0.833
H	0.1660 Gm.	0.2250 Gm.	0.737
I	0.2005 Gm.	0.2630 Gm.	0.762
Average absorption constant H/L.....			0.730

* The absorption constant (H/L) for hydrogenated oil as compared with lard is shown by the quotient of the amount of hydrogenated oil absorbed divided by the amount of lard absorbed.

However, since most ointments are used therapeutically by applying them to the skin and allowing them to remain there without prolonged rubbing, the above method was modified. The fats were rubbed for 20 seconds evenly covering the surface and allowed to remain without additional rubbing for 130 seconds. The fats were then carefully scraped off, weighed and the absorption constant calculated. The results are shown in Table II. It was found that the absorption constant for hydrogenated oil was greater than that of lard, being 1.112 times more absorptive.

[1] Other methods for comparative absorption of hydrogenated oil determination being carried on at present time.

TABLE II.—COMPARATIVE ABSORPTION OF HYDROGENATED OIL AND LARD APPLIED TO THE SKIN WITHOUT RUBBING.

Subject.	Hydrogenated oil absorbed.	Lard absorbed.	H/L constant.
A	0.1130 Gm.	0.1100 Gm.	1.027
B	0.1050 Gm.	0.0840 Gm.	1.250
C	0.1030 Gm.	0.1005 Gm.	1.024
D	0.1500 Gm.	0.1500 Gm.	1.000
E	0.1421 Gm.	0.1177 Gm.	1.207
F	0.1150 Gm.	0.1100 Gm.	1.045
G	0.1220 Gm.	0.1030 Gm.	1.184
H	0.1366 Gm.	0.1280 Gm.	1.067
I	0.1080 Gm.	0.1020 Gm.	1.059
J	0.1300 Gm.	0.1110 Gm.	1.261
Average absorption constant H/L.....			1.112

Table III shows the results using the modified method, employing a simple ointment consisting of hydrogenated oil 80%, white wax 10% and wool fat 10%. It was found that this ointment was slightly more absorptive than the pure hydrogenated oil, probably due to the wool-fat content.

TABLE III.—COMPARATIVE ABSORPTION OF A SIMPLE OINTMENT AND LARD BY APPLICATION TO THE SKIN.

Subject.	Ointment absorbed.	Lard absorbed.	O/L constant.
A	0.0700 Gm.	0.0600 Gm.	1.167
B	0.1280 Gm	0.1080 Gm.	1.157
C	0.0750 Gm.	0.0700 Gm.	1.071
D	0.1100 Gm.	0.0960 Gm.	1.145
E	0.0800 Gm.	0.0680 Gm.	1.176
F	0.1260 Gm.	0.1160 Gm.	1.086
G	0.2600 Gm.	0.2200 Gm.	1.182
H	0.1700 Gm.	0.1530 Gm.	1.100
I	0.1350 Gm.	0.1190 Gm.	1.134
J	0.2000 Gm.	0.1800 Gm.	1.111
K	0.1800 Gm.	0.1700 Gm.	1.159
Average absorption constant O/L.....			1.149

Hydrogenated Oil as an Ointment Base in Official Ointments.—Ointments prepared with hydrogenated oil were found to have all of the attributes essential to good ointments. They were found to be more solid than ointments with a lard base, but melted more readily when applied to the skin. Ointments of hydrogenated oil did not develop rancidity or become granular like those with lard. Ointments prepared with a benzoinated lard base became rancid, but this deterioration was not as rapid as with untreated lard. Hydrogenated oil was found satisfactory for all U. S. P. ointments, the following being suggested particularly since the hydrogenated oil ointment was found superior to the official product.

Unguentum Belladonnæ.—In the last revision of the U. S. P. the base was changed from lard and wool fat to petrolatum and wool fat; the formula of the "British Pharmacopœia" is similar to that of the U. S. P. IX. This ointment is usually used therapeutically where absorption of the belladonna is desired and hence should have an absorptive base. Lard of the U. S. P. IX formula was replaced with petrolatum, a non-absorbent base. A very satisfactory ointment was prepared substituting hydrogenated oil for petrolatum in the official formula.

Unguentum Chrysarobini.—The base was changed from benzoinated lard to wool fat in the last revision of the U. S. P. It was found, however, that the official product soon developed a dark color which did not develop when prepared with hydrogenated oil substituted for the wool fat.

Unguentum Hydrargyri Ammoniati.—The U. S. P. and the German Pharmacopœia employ petrolatum and wool fat, the French Codex petrolatum and the B. P. benzoinated lard. An ointment prepared with hydrogenated oil substituted for the petrolatum in the U. S. P. formula resulted in a very satisfactory ointment which was more absorbent and slightly less tenacious than the official product. However, if the ointment is prepared using hydrogenated oil and five per cent of white wax as a base, the resulting product has a beautiful white color, is odorless and has a smooth consistency, while that of the U. S. P. is very tenacious and has a decided wool-fat odor.

Unguentum Iodi.—The base of this ointment was changed in the U. S. P. X from benzoinated lard to wool fat. One of the reasons for this change was that lard has a high iodine number and tends to absorb the iodine of the ointment, while wool fat, not being a true fat, has a very low iodine number. This appears to be an unhappy change from a therapeutic standpoint since it has been found[1] that iodine is readily absorbed from lard but scarcely at all from wool fat. Hydrogenated oil, since the iodine number has been reduced by hydrogenation, would be a very satisfactory base, as lard and hydrogenated oil are somewhat similar in chemical constitution while wool fat is entirely different. A very satisfactory ointment was prepared using 75 Gm. of hydrogenated oil and 5 Gm. of wax in place of the 80 Gm. of wool fat in the U. S. P. formula. This ointment was possessed with a much smoother consistency than the official ointment.

Unguentum Iodoformi.—In the U. S. P. X the base was changed from benzoinated lard to petrolatum and wool fat. The B. P. employs benzoinated lard and the French Codex petrolatum. A very satisfactory ointment was prepared from a base consisting of 5 per cent of white wax with hydrogenated oil.

Unguentum Sulphuris.—This ointment, which is prepared with benzoinated lard according to the formulas of the U. S. P. X, the B. P. and the French Codex, is very unsatisfactory. As mentioned above, samples purchased in retail pharmacies were found to be rancid in most cases. This difficulty is overcome by some pharmacists who employ "benzoinated petrolatum" in their product. Such an ointment is not official, of course, and cannot be labeled as such; it is an obvious attempt at substitution since there is no reason for the use of benzoin other than to give the product the odor of the official ointment. Often a "compound sulphur ointment" is dispensed which is prepared from petrolatum rather than lard. The most satisfactory method of preparing the U. S. P. sulphur ointment is to manufacture it fresh when needed or to store it in the refrigerator in tightly stoppered, non-metallic containers. Sulphur ointment prepared with a base consisting of five per cent of white wax and hydrogenated oil was found to have satisfactory physical properties and, as could be determined by using in place of the U. S. P. product in several cases, to have satisfactory therapeutic properties.

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[1] *Arch. Dermatol. Syphilis*, 62 (1904), 163; also *Z. klin. Med.*, 12 (1887), 276.

Unguentum Picis Pini.—The U. S. P. X changed the base from benzoinated lard to petrolatum, but the B. P. and French Codex employ benzoinated lard. The use of hydrogenated oil in this ointment was very satisfactory.

Unguentum Zinci Oxidi.—The U. S. P. X and the French Codex employ petrolatum as a base for this ointment, but the B. P., German Pharmacopœia, and the U. S. P. IX employ benzoinated lard. According to the "U. S. Dispensatory,"[1] if this ointment is prepared with an absorbent base, the base is absorbed which leaves a protective coating of zinc oxide, but with a non-absorbent base such as petrolatum, the skin remains greasy. Sollman[2] pointed out that dermatologists were divided in their opinion as to the relative value of lard and petrolatum as a base for this ointment, many claiming that, since zinc oxide is a mild antiseptic and astringent, an absorbent base is indicated. A very satisfactory ointment was prepared by thoroughly triturating the zinc oxide (20 Gm.), adding a small amount of molten hydrogenated oil, triturating until a smooth mass results, and adding the balance of the molten hydrogenated oil (70 Gm. total) and white wax (10 Gm.). The mixture is stirred thoroughly, strained through muslin and stirred constantly while cooling. The product is a beautiful, smooth, white ointment.

SUMMARY.

Hydrogenated oil (with an iodine number of 75) appears to be a fairly absorbent fat and a very good substitute for lard in pharmaceutical ointments. The physical and chemical properties of the fat also indicate its use. Many U. S. P. ointments were found to be very satisfactory when hydrogenated oil or a mixture of hydrogenated oil with wax were substituted for the official base. Its use is particularly indicated in those ointments which are susceptible to rancidity since hydrogenated oil and ointments containing it did not develop rancidity after exposure in open containers to air and light in a warm place for 25 weeks, while the same ointments prepared with lard became very rancid.

THE REVIVAL OF STUDY IN CHINESE MEDICINE.

The following is from *The Japanese Weekly Druggist.*

While people pursue after novelties, they also show their reverence for the past. This is the situation in the Japan of the Showa Era. And the drug world is no exception to this rule. While, on one hand, western medicine has been making a vast progress, much headway is also being made in the world of Chinese medicine. This was most clearly shown by the recent convention of dealers in prepared medicines held in Tokyo, whose committee resolved to present a petition to the Government in favor of establishing courses in Chinese medicine in colleges of pharmacy. The resolution contains the following:

"Among the numerous Chinese herbs, there are some which have been found to be efficacious through actual experience although their ingredients have not been examined as yet. This is why their use has continued to this day, and are found in the prepared medicines very extensively. But the majority of pharmacists lack proper knowledge in Chinese herbs to their great detriment in the execution of their professional duties, because they are not taught in their professional education. Because of this lack of knowledge, a maximum efficiency in medical efficacy is not gained. We urge the establishment of courses in Chinese herbs and pharmacology in addition to that in pharmacy."

[1] Wood and LaWall, "*U. S. Dispensatory*" (1926), 1144.

[2] *Jour. A. M. A.*, 75 (1920), 1420.