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

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(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:

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

Melting point	41.5° C.
Softening point	30.0° C.
SO_3 content	10%
p_H (5% solution)	6.0–6.3

The fact that it has a p_H of 6, very slightly on the acid side, is valuable because this is approximately the p_H of the skin (3). Also, it makes an ideal vehicle for substances such as salicylic acid which are not readily compatible with bases of an alkaline nature.

Its solubility in water is a distinct advantage. Perspiration does not interfere with the ointment as, for example, it would in the case of official Whitfield's Ointment. It may be readily incorporated with many substances which are not soluble or readily suspended in other ointment bases. Also, it incorporates readily with aqueous, alcoholic, glycerin, glycol, liquid petrolatum, etc., solutions without precipitation, as well as other bases such as petrolatum, fats, spermaceti, wax, etc. Of minor dispensing importance is the fact that apparatus used to prepare ointments may be readily cleansed with water. Likewise any excess ointment can be removed from the skin with water.

Because it is made from completely hydrogenated castor oil, free from unsaturated fatty acids, it is not subject to rancidity. Clinical Patch tests in two clinics indicate that it is non-irritating, thus well suited for an ointment base. Like other sulfated oils it possesses wetting properties. This should make it more readily absorbed by the skin. Likewise it possesses definite detergent properties, either alone or with added petrolatum to give it an oily consistency.

EXPERIMENTAL

Official Ointments.—SHCO can be used as an ointment base without addition of other substances if an adhesive ointment is desired. The material possesses a peculiar stickiness which is very advantageous when it is desired to produce an ointment which will adhere to the skin. This ointment is often applied after the skin has been moistened with water or a small amount of water may be rubbed into the ointment after it has been applied to the skin.

Preliminary tests indicated that medicaments could be readily incorporated with SHCO using manipulation with a spatula and pill tile, trituration in a mortar and trituration with previously melted SHCO. All three methods were satisfactory. Trituration with fused SHCO was the simplest method and therefore used in all cases unless otherwise specified; for dispensing, however, it might be less trouble to use the SHCO cold. When incorporating with medicaments, it was sometimes not necessary to use the solvent employed by the official formula. In all cases a small amount of the base or the diluent was incorporated with the medicament and then the balance of the base added. Rapid trituration or use of a mechanical mixer produced a lighter colored ointment due to incorporation of air. Since SHCO in most cases needed no additional solidifiers, such as wax, in large scale manufacture, the ointments could be poured while hot and allowed to cool in ointment jars without danger of separation of solidifier or the medicament which in most cases was well suspended or dissolved in the base.

For many ointments, however, a smooth, less adhesive ointment is desired. The stickiness can be removed by the addition of many substances, thus any desired ointment base can be obtained. Among such substances are petrolatum, liquid petrolatum, fats and fixed oils, glycerin, glycols or water. If the resultant ointment is too soft, it may be made stiffer by addition of solidifiers such as wax, spermaceti, hydrogenated castor oil, hydroxystearic acid, stearic acid, etc.

In most cases the medicament readily incorporates with the SHCO-petrolatum mixture. Often, however, slightly better dispersion is obtained if the material is triturated with the SHCO and the petrolatum added. The amount of petrolatum may vary with the individual ointment. Twenty-five per cent of petrolatum makes a smooth ointment; even though as little as twenty-five per cent of SHCO is employed, the ointment is still hydrophilic and may be readily removed with water.

For many purposes an emulsified ointment base is indicated. SHCO is a good emulsifying base and numerous types of emulsified creams can be prepared. The simplest type may be made by melting 28.5 parts each of SHCO and petrolatum and adding 43 parts of water, heated to the same temperature. Agitation results in a very good emulsion which is compatible with most medicaments. Other creams may be prepared using substances such as diethylene glycol monostearate, glyceryl monostearate, triethanolamine and its soaps, etc.

If making ointments with this emulsified cream, in many cases the emulsified ointment base will readily incorporate the medicament. In other cases, the medicament may be dissolved in the water or, in the case of substances such as coal tar, incorporated first with the SHCO.

Formulas are given for the three types of ointments, using the official formula modified only in that the SHCO bases replace the official base. In the following list of formulas, the one marked "1" is an adhesive base; "2" is a smooth base; and "3" is an emulsified base. In many cases the preparation can be prepared by merely incorporating the medicament with the appropriate simple ointment

and different formulas are not necessary. For large-scale manufacturing, however, a slightly better ointment often results if the material (unless soluble in the amount of water in the cream base) is first incorporated with the SHCO and then the petrolatum and, if a cream base, the water incorporated. The SHCO tends to suspend insoluble substances better such as zinc oxide, mercurial salts, etc.

OFFICIAL OINTMENTS (U. S. P.)

Simple Ointment: 1 Sulfated hydrogenated castor oil.

2 SHCO 75 Gm., white petrolatum 25 Gm. Triturate the bases, with or without previously melting them.

3 SHCO 28.5 Gm., white petrolatum 28.5 Gm., distilled water 45 Gm. Melt the SHCO and petrolatum, heat the water to the same temperature and added to the molten bases with agitation.

Boric Acid Ointment: Boric acid 10 Gm., simple ointment 90 Gm. Triturate the acid with the simple ointment, with or without fusion.

Tannic Acid Ointment: Tannic acid 20 Gm., Glycerin 20 Gm., simple ointment 60 Gm. Triturate the acid with the glycerin, incorporate the molten simple ointment. (This ointment was not satisfactory when made with the emulsified base.)

Belladonna Ointment: 1. Pilular extract of belladonna 10 Gm., SHCO 90 Gm. Triturate the extract with a small amount of the molten SHCO, gradually incorporating the balance.

2. Pilular extract of belladonna 10 Gm., SHCO 67.5 Gm., petrolatum 22.5 Gm. Triturate the extract with a small amount of the molten SHCO, gradually incorporating the balance and the molten petrolatum.

3. Pilular extract of belladonna 10 Gm., SHCO 25.5 Gm., petrolatum 25.5 Gm., distilled water 39 cc. Triturate the belladonna with a small amount of the molten SHCO, following with the balance and the molten petrolatum. Heat the water to approximately the same temperature and add it to the mixture with trituration.

Chrysarobin Ointment: 1. Chrysarobin 6 Gm., chloroform 4 Gm., liquid petrolatum 6 Gm., SHCO 84 Gm. Triturate the chrysarobin with the liquid petrolatum and the chloroform, add the molten SHCO and triturate.

2. Chrysarobin 6 Gm., chloroform 4 Gm., petrolatum 22.5 Gm., SHCO 67.5 Gm. Triturate the chrysarobin with the molten petrolatum and chloroform, add the molten SHCO and triturate.

3. Chrysarobin 6 Gm., simple ointment 94 Gm. Triturate.

Nutgall Ointment: Nutgall 20 Gm., glycerin 20 Gm., simple ointment 60 Gm. Triturate the nutgall with the glycerin, incorporate the molten simple ointment. (This ointment was not satisfactory when made with the emulsified base.)

Ammoniated Mercury Ointment: Ammoniated mercury 10 Gm., simple ointment 90 Gm. Triturate.

Strong Mercurial Ointment: Mercury 50 Gm., oleate of mercury 2 Gm., simple ointment 48 Gm. Triturate the mercury with the oleate until dispersed, incorporate the simple ointment.

Mild Mercurial Ointment: Strong mercurial ointment 60 Gm., simple ointment 40 Gm. Triturate.

Yellow Mercuric Oxide Ointment: Yellow mercuric oxide 1 Gm., liquid petrolatum 1 Gm., simple ointment 98 Gm. Triturate the oxide with the liquid petrolatum until smooth, incorporate with the simple ointment.

Iodine Ointment: 1. Iodine 4 Gm., potassium iodide 4 Gm., glycerin 12 Gm., SHCO 80 Gm. Dissolve the potassium iodide in the glycerin, triturate with the iodine until dissolved, and incorporate with the SHCO. A stiffer ointment may be prepared by dissolving the potassium iodide in 92 Gm. molten SHCO, followed by the iodine, with no glycerin.

2. Iodine 4 Gm., potassium iodide 4 Gm., glycerin 12 Gm., SHCO 60 Gm., petrolatum 20 Gm. Prepare as above; a stiffer ointment can also be prepared as above; the petrolatum should be incorporated last.

3. Iodine 4 Gm., potassium iodide 4 Gm., distilled water 40 cc., SHCO 26 Gm., petrolatum 26 Gm. Dissolve the potassium iodide in the water; dissolve the iodine in this solution. Melt the SHCO and petrolatum and incorporate the aqueous solution.

Phenol Ointment: Phenol 2 Gm., simple ointment 98 Gm. Incorporate.

Pine Tar Ointment: 1-2. Pine tar 50 Gm., yellow wax 20 Gm., simple ointment 30 Gm. Melt the wax and add to the previously warmed simple ointment. Incorporate the pine tar, previously warmed.

3. Pine tar 50 Gm., yellow wax 20 Gm., SHCO 8.5 Gm., petrolatum 8.5 Gm., water 13 cc. Melt the wax and petrolatum. Mix the molten SHCO with warm pine tar. Mix them and incorporate the water.

Sulfur Ointment: Sulfur 15 Gm., simple ointment 85 Gm. Triturate with or without melting the simple ointment.

Zinc Oxide Ointment: 1. Zinc oxide 20 Gm., SHCO 55 Gm., water 25 cc. Triturate the zinc oxide with the molten SHCO, incorporate the water.

2. Zinc oxide 20 Gm., SHCO 41 Gm., petrolatum 14 Gm., water 25 cc. Triturate the zinc oxide with the molten SHCO, incorporate the molten petrolatum and finally the water.

3. Zinc oxide 20 Gm., simple ointment 80 Gm. Triturate.

OFFICIAL OINTMENTS (N. F.)

Compound Ointment of Benzoic Acid: Benzoic acid 12 Gm., salicylic acid 6 Gm., simple ointment 82 Gm. Triturate the acids with the molten base. (This ointment was not satisfactory when prepared with the emulsified base.)

Calamine Ointment: 1. Prepared calamine 15 Gm., SHCO 65 Gm., water 25 cc. Triturate the calamine with the molten SHCO, incorporate the water.

2. Prepared calamine 15 Gm., SHCO 64 Gm., petrolatum 21 Gm. Triturate the calamine with the molten SHCO and incorporate the molten petrolatum.

Modification (similar to N. F. VII): Prepared calamine 15, SHCO 45, petrolatum 15, compound spirit of rose geranium 1 cc., distilled water 25 cc. Triturate the ingredients in the order named, melting the bases.

3. Prepared calamine 15, simple ointment 85. Triturate.

Camphor Ointment: Camphor 22 Gm., alcohol *q. s.*, simple ointment 78 Gm. Powder the camphor with the alcohol, allow the latter to evaporate and incorporate with the base. (In the case of "2" and "3," the camphor may be dissolved without alcohol treatment, in the warm, molten petrolatum.)

Capsicum Ointment: Oleoresin of capsicum 5 Gm., simple ointment 95 Gm. Incorporate.

Mild Mercurous Chloride Ointment: Mild mercurous chloride 30 Gm., simple ointment 70 Gm. Triturate.

Colloidal Mercurous Chloride Ointment: Magma of colloidal mercurous chloride 30 Gm.,[2] simple ointment 70 Gm. Incorporate.

Mercuric Nitrate Ointment, Half-Strength: Mercuric nitrate ointment 50 Gm., simple ointment 50 Gm. Incorporate. (This ointment is commonly employed by the dermatologist in half strength; dilution with SHCO makes a hydrophilic ointment.)

Red Mercuric Oxide Ointment: Red mercuric oxide 10 Gm., simple ointment 90 Gm. Triturate.

Ichthammol Ointment: Ichthammol 10 Gm., simple ointment 90 Gm. Incorporate.

Stainless Iodized Ointment: Iodine 5 Gm., oleic acid 20 Gm., simple ointment 75 Gm. Warm the iodine with the oleic acid until the red color disappears, incorporate with the simple ointment.

Compound Menthol Ointment: Menthol 10 Gm., methyl salicylate 10 Gm., white wax 10 Gm., simple ointment 70 Gm. Melt the wax, incorporate it with the warmed simple ointment. Dissolve the menthol in the methyl salicylate and incorporate with the base.

Coal Tar Ointment: 1. Coal tar 5 Gm., SHCO 95 Gm. Incorporate with the molten SHCO.

2. Coal tar 5 Gm., SHCO 71 Gm., petrolatum 24 Gm. Incorporate the coal tar with the molten SHCO; incorporate the petrolatum.

3. Coal tar 5 Gm., SHCO 27 Gm., petrolatum 27 Gm., distilled water 41 cc. Triturate the coal tar with the molten SHCO, add the molten petrolatum, mix and triturate with the water, previously warmed.

Compound Tar Ointment: 1-2. Rectified oil of tar 4 Gm., tincture of benzoin 2 Gm., zinc oxide 3 Gm., simple ointment 91 Gm. Triturate the zinc oxide with the molten base, incorporate the oil and the tincture.

[2] Courtesy of Research Dept., The Upjohn Co., Kalamazoo, Michigan.

3. Rectified oil of tar 4 Gm., tincture of benzoin 2 Gm., oxide of zinc 3 Gm., SHCO 26 Gm., petrolatum 26 Gm., water 39 cc. Triturate the zinc oxide with molten SHCO, incorporate the tincture, oil and molten petrolatum, finally the water, previously warmed.

Ointment of Potassium Iodide: Potassium iodide 10 Gm., sodium thiosulfate 1 Gm., distilled water 9 Gm., simple ointment 80 Gm. Dissolve the salts in water; incorporate with the simple ointment. (A stiffer ointment may be prepared by triturating the salts with SHCO, using no water, and incorporating the petrolatum in the case of "2." This ointment was not satisfactory when prepared with the emulsified base.

Compound Resorcinol Ointment: Resorcinol, zinc oxide, bismuth subnitrate, rectified oil of birch tar, of each 6 Gm., wax 6 Gm., simple ointment 70 Gm. Triturate the solids with warm simple ointment; incorporate the oil and the melted wax.

Scarlet Red Ointment: Scarlet red 5 Gm., simple ointment 95 Gm. Triturate.

Mustard Ointment: Volatile oil of mustard 2 Gm., simple ointment 98 Gm. Incorporate.

Stramonium Ointment: 1. Pilular extract of stramonium 10 Gm., SHCO 90 Gm. Triturate.

2. Pilular extract of stramonium 10 Gm., SHCO 74 Gm., petrolatum 21 Gm. Triturate the extract with the SHCO, incorporate the petrolatum.

3. Pilular extract of stramonium 10 Gm., SHCO 25.5 Gm., petrolatum 25.5 Gm., distilled water 39 cc. Triturate the extract with molten SHCO, add the molten petrolatum and incorporate the water, previously warmed.

Alkaline Sulfur Ointment: This ointment was not satisfactory when prepared with the emulsified base.

Compound Sulfur Ointment: Precipitated calcium carbonate 10 Gm., sublimed sulfur 15 Gm., juniper tar 15 Gm., simple ointment 60 Gm. Triturate.

Zinc Stearate Ointment: Zinc stearate 35 Gm., liquid petrolatum 10 Gm., simple ointment 55 Gm. Mix the liquid petrolatum with the warm simple ointment, and incorporate the zinc stearate by trituration. If a stiffer ointment is desired, the liquid petrolatum may be replaced by simple ointment.

DISCUSSION

The above formulas merely serve to indicate the compatibility of SHCO as an ointment base. In some cases the ointment might not be stiff enough for warm climates; this can be remedied by addition of a solidifier such as wax.

Ointments prepared with SHCO are usually much easier to prepare than the official ointment. In most cases the medicaments may be incorporated with the SHCO

base without regard to proper pharmaceutical technique.

SHCO can be used to overcome incompatibilities; coal tar or balsam of peru, for instance, previously triturated with SHCO may readily be incorporated with petrolatum, lard, lanolin, etc.

The emulsified base is an oil-in-water emulsion. This is a distinct advantage as such an emulsion would absorb perspiration or serous fluid better than a water-in-oil emulsion. A less greasy base (semi-vanishing) may be obtained by substituting diethylene glycol monostearate up to about 50% of the SHCO.

Ointments prepared with SHCO are recommended particularly in cases where there is serous discharge or perspiration, or in cases where a washable ointment is indicated. An example of the latter is scalp ointments; SHCO ointments have proved very satisfactory for this purpose since they are readily removed by simple washing with water.

SUMMARY

Sulfated hydrogenated castor oil is recommended as an ointment base. It is water-soluble, semi-solid, compatible with medicaments used in ointments and produces, when used in quantities of twenty-five per cent or more, hydrophilic ointments. An emulsified base comprised of sulfated hydrogenated castor oil, petrolatum and water is described. Formulas are given for the official ointments prepared with adhesive base, smooth base and emulsified base.

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"When the archer misses the center of the target, he turns around and seeks for the cause of his failure within himself."—Kong Fu Tsze.

Book Reviews

A New Dictionary of Chemistry, edited by STEPHEN MIALL. 544 pages. Longmanns, Green & Co. Price, $15.00.

This dictionary is intended for both chemist and layman and it provides a reference source of chemical terms and facts relating to chemicals and drugs for use in special fields. It contains a vast number of entries which include the latest advances in chemistry, inorganic, organic and physical. Many of the entries include references to books and papers in which further information can be found. Trade names are included in many cases. There are many short biographical sketches of eminent chemists in which their outstanding achievements are given. The volume also contains a classified reading list of 85 volumes and a table of physical constants of organic compounds.—A. G. D.

Handbook for Chemical Patents, by EDWARD THOMAS. 270 pages, $5^1/_2$ x $8^1/_4$. 1940. New York: Chemical Publishing Company. Price, $4.00.

The author of this book is a former employee of the U. S. Patent Office and is, therefore, well qualified to explain the essential details of patent procedures, which he has done. Included in the explanations are suggestions for writing patent specifications, anticipation of a patent based on previous facts, types of infringement, process of taking out a patent from the patent office, assignments, licenses, etc. Explanatory references to cases are numerous. The book should prove to be an invaluable aid to those seeking to obtain a patent on a chemical process or composition of matter.—A. G. D.

The Essentials of Physiology and Pharmacodynamics, by GEORGE BACHMANN and A. RICHARD BLISS, JR. 3rd Edition. xiv + 508 pages, $6^1/_2$ x 10. 1940. Philadelphia: The Blakiston Co. Price, $4.50.

This, the third edition of this well-known textbook on physiology and pharmacodynamics, follows along the lines of preceding editions. The anatomic viewpoint is maintained and the pharmacologic activity of drugs is explained at the appropriate point. This edition includes the newer drugs, such as ergonovine, sulfapyridine, etc.—A. G. D.

Mathematics in Bacteriology, by OTTO RAHN. ii + 63 pages, $8^1/_4$ x $10^3/_4$. 1939. Minneapolis: Burgess Publ. Co. Price, $1.75.

This book gives the application of mathematics to the interpretation of such subjects as cell division and growth, unrestricted and restricted multiplication and fermentation, and the death rate in disinfection. The probable error computed on a statistical basis and the use of graphs are discussed. It contains a sufficient amount of elementary calculus and information on the use of graphs to enable