A STUDY OF THE ABSORPTION AND ANTISEPTIC PROPERTIES OF SEVERAL TYPES OF IODINE OINTMENTS.

BY W. H. ZEIGLER.

This investigation was undertaken at the request of the United States Pharmacopœial Committee on Therapeutics and Pharmacologic Research.

The questions asked were: Is Stainless Ointment of Iodine (as **Unguentum Iodi Denigrescens,** N. F.) equivalent to the U. S. P. Ointment?

a. Determine the absorbability of iodine through skin.

b. Which ointment is best absorbed?

c. Are the antiseptic qualities of the two ointments identical?

The following preparations were used throughout the experiments.

Unguentum Iodi, U. S. P.

Unguentum Iodi Denigrescens, N. F.

Petroxolinum Iodi, N. F.

An ointment in which petrolatum was used as the base, and an ointment in which the Potassium Iodide was omitted were also studied.

ABSORPTION THROUGH SKIN.

Method.—Eighteen dogs and a number of human subjects were used in the experiments. The procedure consisted of applying certain amounts of the ointment under consideration, and testing the urine for iodides. Six dogs were used for each experiment. Six Gm. of the ointment were rubbed into the axillae daily and the animal bandaged securely. This was continued over a period of four to six days. The urine was tested daily by the following method:

Sulphuric acid and sodium nitrite were added to the urine after which it was shaken out with chloroform. A pink color develops if iodine is present. Witzel and Sollman (2) found that this test would give in 0.08 cc. of urine representing 0.008 mg. of iodine, a definite pink color. In the preliminary experiments it was observed that unless the animal was bandaged securely, after applying the ointment, the test for iodides would be positive in every instance. This was due to the animal licking the ointment or because of contact with the bottom of the cage.

Chloroform was used in one group to clean the site of application. In the experiments in which human subjects were used, only one application was made; the urine being collected and tested four or five times daily over a period of two days.

ANTISEPTIC QUALITIES OF THE TWO OINTMENTS.

Method.—The following method recommended by Reddish (1) of the Bureau of Chemistry, Department of Agriculture, for the testing of antiseptic salves, ointments, etc., was used.

M. aureus of normal resistance is grown at 37° C. in a special broth and transferred in this medium for 3 consecutive days. One-tenth of a cubic centimeter of this culture is added to 15 cc. of melted nutrient agar at 45° C. (1.5% agar in the above broth base), the culture is thoroughly mixed with the agar and poured into a sterile Petri dish and allowed to cool at room temperature. As soon as this inoculated agar has hardened, the salves and ointments, previously melted at 37° C., are spread over a small surface of the inoculated agar with a sterile glass rod. Melted sterile vaseline is spread on another part of the inoculated agar in the same manner and the plate inverted and incubated at 37° C. for 48 hours. A duplicate test is made at the same

time in which the melted salve or ointment is streaked on the bottom of a sterile Petri dish with a sterile glass rod and 15 cc. of nutrient agar inoculated with 0.1 cc. of *M. aureus* broth culture poured over it. The test also includes a vaseline control streaked in the same way. After being incubated it will be noted that colonies of *M. aureus* grow immediately adjacent to the vaseline control and even under or above it, according to whether it is streaked on top of the agar or on the bottom of the plate. There is no active ingredient in pure vaseline which will prevent the growth of *M. aureus*. However, in effective antiseptic salves and ointments a part of the active ingredients contained in them is absorbed into the agar and by their presence prevent the organisms present from growing. Therefore, the plate will show a clear zone around the antiseptic salve or ointment which is in marked contrast to the turbidity of the surrounding medium caused by the heavy growth of the organism.

Commenting on this method, Reddish says (1):

"When such preparations as these are used in practice, the active ingredients are held in intimate contact with the infective micro-organisms and can render them innocuous by simply preventing their activity. Since these preparations do remain in contact with the infected surfaces for long periods of time when used in practice, laboratory tests for their efficiency should simulate these conditions as nearly as possible. If an antiseptic salve, for example, does prevent the growth of micro-organisms in an infected area, it will not only prevent them from doing harm, but will also render them easy prey for the leucocytes.

"In treating infected surfaces with preparations of this nature, it is necessary that the active ingredients leave the inert base and become free to surround the infective organisms. It is only in this way that the preparation will be of benefit in preventing the growth of these micro-organisms. If the antiseptics were so securely incorporated into the inactive base that it could not become free to attack the micro-organisms or if the base were of such a nature that the antiseptic could not separate from it, the value of such preparations so far as the antiseptic ingredient is concerned would be lost. Plain 1.5% agar simulates fairly closely the conditions met in skin and wounds. It is permeable, semisolid, isotonic and constitutes a valuable laboratory means of approximating the conditions found in human and animal tissues, at least so far as the preparations under consideration are concerned."

DISCUSSION.

Witzel and Sollman (2) after a study of iodine absorption from human skin in which tincture of iodine was the principal form used, found that the amount absorbed by the normal human skin was very small.

Herzfeld and Elin (3) found that petrolatum secures the best absorption.

Bartenbach (4) found that absorption was better when lard was used as a base.

The experiments as outlined were carefully planned and executed with the following results: **Unguentum Iodi,** U. S. P. was readily absorbed, the test for iodides being positive after a single application. The same ointment made up with a base of petrolatum also was found to be as readily absorbed. The test for iodides after the application of the **Unguentum Iodi Denigrescens,** N. F., was negative.

Petroxolinum Iodi, N. F. also was used with positive results.

Unguentum Iodi without iodide of potash, while more irritating, also was readily absorbed.

ANTISEPTIC VALUE OF THE IODINE OINTMENTS.

The results obtained by the test mentioned were as follows: The U. S. P. Iodine Ointment shows complete inhibition. The N. F. Stainless Ointment of Iodine did not inhibit the growth of the organisms. The vaseline control was used throughout the test and in every instance Staphylococcus colonies were all over the plate.

CONCLUSIONS.

1. **Unguentum Iodi,** U. S. P. is readily absorbed through the skin.

2. **Unguentum Iodi Denigrescens,** N. F. is apparently not absorbed through the skin as shown by absence of iodides in the urine.

3. **Petroxolinum Iodidi,** N. F. is absorbed through the skin.

4. **Unguentum Iodi,** U. S. P. possesses antiseptic properties.

5. **Unguentum Iodi Denigrescens,** N. F. apparently does not possess antiseptic properties.

The author wishes to express his appreciation for the valuable assistance of C. B. Woods; also E. C. Hood and Dr. T. H. Byrnes of the Department of Pharmacology and Dr. R. E. Lee of the Department of Bacteriology of this college.

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(2) Witzel and Sollman, *Journ. Pharm. and Exp. Ther.* (1920), 15.

(3) Herzfeld and Elin, *Zentr. Bioch. Bioph.*, 13 (1912), 251.[1]

(4) Bartenbach, *Bioch. Bioph.*, 10 (1909), 278.[1]

LABORATORY OF PHARMACOLOGY OF THE MEDICAL COLLEGE
OF THE STATE OF SOUTH CAROLINA,
CHARLESTON, S. C.

THE EFFECT OF SUNLIGHT ON CITRIC ACID IN THE PRESENCE OF FERRIC SALTS.

WITH SPECIAL REFERENCE TO THE ELIXIR OF IRON QUININE AND STRYCHNINE AND ELIXIR OF IRON QUININE AND STRYCHNINE PHOSPHATES.*

BY JOSEPH B. BURT.

This study was suggested by the investigations of Chilson[1] and of Mueller.[2] The principal reason for modification of the pharmacopœial formula for the elixir of iron, quinine and strychnine phosphates was because of the unstable character of the preparation manifested by precipitation and color changes upon standing. Chilson made a search of the literature for suggested changes and new formulas for the elixir and prepared samples in accordance with each method or modification found, without obtaining a single sample of the elixir which was entirely satisfactory. A review of the literature on the elixir of iron, quinine and strychnine shows that this preparation has also been subjected to the same criticism, and chiefly for the same reasons. In attempting to classify the suggested remedies for the incompatibility in the elixir of iron, quinine and strychnine phosphates, it

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[1] From "Manual of Pharmacy," Sollman, as original articles could not be obtained.

* Scientific Section, A. PH. A., St. Louis meeting, 1927.

[1] Thesis, "Suggested Modifications of the United States Pharmacopœial Formula for Elixir of Iron, Quinine and Strychnine Phosphates," University of Wisconsin, 1914.

[2] Thesis, "The Action of Light on Solutions of Soluble Ferric Phosphate," University of Wisconsin, 1915.