

cranberry syrup to change to a not unattractive light molasses color.

According to Table II, cranberry syrup ranked fifth in score as a vehicle for potassium iodide; tied in first place with Syrup of Citric Acid as a vehicle for chloral hydrate. As a masking agent for potassium acetate, cranberry again tied with Syrup of Citric Acid, this time in second place. As a vehicle for ammonium chloride it ranked in first place; and as a vehicle for sodium citrate, it ranked last.

Table II.—Relative Palatability of Drugs in Several Flavoring Syrups—Score Sheet

| Drug                 | Sam-<br>pler | Cherry         | Citric<br>Acid  | Cran-<br>berry  | Simple         | Rasp-<br>berry | Orange         |
|----------------------|--------------|----------------|-----------------|-----------------|----------------|----------------|----------------|
| Potassium<br>iodide  | 1            | 1              | 6               | 6               | 2              | 3              | 6              |
|                      | 2            | 6              | 6               | 6               | 6              | 1              | 2              |
|                      | 3            | 2              | 6               | 5               | 1              | 3              | 4              |
|                      | 4            | 2              | 6               | 5               | 1              | 3              | 4              |
|                      |              | —              | —               | —               | —              | —              | —              |
|                      |              | 11             | 24 <sup>b</sup> | 22 <sup>b</sup> | 10             | 10             | 16             |
| Chloral<br>hydrate   | 5            | 3              | 2               | 1               | 6              | 6              | 4              |
|                      | 6            | 2              | 3               | 4               | 6              | 5              | 1              |
|                      | 7            | 6              | 2               | 1               | 1              | 5              | 4              |
|                      | 8            | 6              | 2               | 3               | 3              | 5              | 4              |
|                      |              | —              | —               | —               | —              | —              | —              |
|                      |              | 17             | 9               | 9               | 16             | 21             | 13             |
| Potassium<br>acetate | 9            | 1 <sup>a</sup> | 2               | 6               | 6              | 6              | 1 <sup>a</sup> |
|                      | 10           | 6              | 2               | 1               | 4              | 5              | 3              |
|                      | 11           | 6              | 4               | 2               | 5              | 1              | 3              |
|                      | 12           | 4              | 3               | 2               | 6              | 4              | 3              |
|                      |              | —              | —               | —               | —              | —              | —              |
|                      |              | 17             | 11              | 11              | 21             | 16             | 10             |
| Ammonium<br>chloride | 13           | 2              | 1 <sup>a</sup>  | 1 <sup>a</sup>  | 6              | 6              | 2              |
|                      | 14           | 1              | 4               | 2               | 3              | 6              | 6              |
|                      | 15           | 5              | 4               | 3 <sup>a</sup>  | 3 <sup>a</sup> | 1              | 2              |
|                      | 16           | 1              | 3               | 2               | 4              | 6              | 5              |
|                      |              | —              | —               | —               | —              | —              | —              |
|                      |              | 9              | 12              | 8               | 16             | 19             | 15             |
| Sodium<br>citrate    | 17           | 3              | 2               | 5               | 1              | 6              | 4              |
|                      | 18           | 3              | 2               | 6               | 5              | 4              | 1              |
|                      | 19           | 2              | 5               | 6               | 3              | 1              | 4              |
|                      | 20           | 2              | 3               | 4               | 6              | 1              | 4              |
|                      |              | —              | —               | —               | —              | —              | —              |
|                      |              | 10             | 12              | 21              | 15             | 12             | 13             |

<sup>a</sup> Both rated in the same place. See Table I for method of scoring.

<sup>b</sup> Signifies that preparation was highly objectionable and counted as 6.

#### SUMMARY AND CONCLUSIONS

Two methods for the preparation of cranberry syrup were tried. The method recommended for a pharmaceutical Syrup of Cranberry is one in which the juice is expressed cold, filtered, boiled and sweetened.

Potassium acetate, sodium citrate and alkalies caused a color change in this syrup.

The estimated average cost of syrup of cranberry, excluding labor, is not over 25 cents per 1000 cc.

Syrup of cranberry is an efficient vehicle for chloral hydrate, potassium acetate and ammonium chloride. It is compatible with most alcoholic preparations.

Tin, iron, nickel and copper utensils and containers cause darkening of the syrup.

Cranberry syrup is stable in color and flavor toward sunlight under ordinary storage conditions. The syrup will not spoil readily due to high sugar content, acidity and mildly bacteriostatic substances such as benzoic acid present in the cranberries.

Storage is recommended in well-filled, tightly-stoppered, amber glass containers.

It is suggested that further research on Syrup of Cranberry be carried out to ascertain its value as a carrier for other drugs.

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## Ointment of Mercuric Nitrate\*

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#### INTRODUCTION

Ointment of Mercuric Nitrate has long been in use as an antiseptic preparation and is widely employed to-day as an antiseptic application in various skin diseases such as impetigo, sycosis, ring worm and in certain forms of chronic eczema. It was originally derived from an ointment of lard and nitric acid, called Alyon's Ointment after the man who first prepared it. The Ointment of Nitric Acid of the former Edinburgh and Dublin Pharmacopœias was of this character

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(1). Ointment of Mercuric Nitrate was official in U. S. P. IX and is now official in the N. F. VI. The first preparation under this name appeared in the London Pharmacopœia, of 1650. It contained no mercury however, but was made from a number of mineral ingredients including coral, quartz, sea shells, marble, white lead and tragacanth incorporated with lard, suet and chicken fat. The first ointment of record containing mercuric nitrate was in the Edinburgh Pharmacopœia, of 1722. A variety of ingredients and processes have appeared in the many revisions down to the present time (2).

It has been proven that Ointment of Mercuric Nitrate, N. F. VI, has the highest anti-septic potency of any U. S. P. or N. F. ointment which is now official (3). It is also well known that Ointment of Mercuric Nitrate, N. F. VI, has very poor keeping qualities. After a short time the ointment changes from citrine yellow to a brown color and liberates pungent fumes due to certain oxides of nitrogen. After a long time the ointment acquires a dirty greenish and mottled color, and becomes very hard. In this condition it can only be used when mixed with additional lard. The ointment is very sticky. It is evident that the creation of Ointment of Mercuric Nitrate, *i. e.*, the suspending of substantial quantities of the electrolyte, mercuric nitrate and an excess of nitric acid in lard, was the work of a novice. In a relatively short time the nitric acid is entirely decomposed and therefore can serve no purpose in holding the mercuric nitrate in solution or in suspension. The lard likewise undergoes a change as is evidenced by an alteration both in color and physical properties. The previous explanation that the citrine color of freshly prepared ointment of mercuric nitrate is due to the formation of elaidin from olein can no longer be accepted since the same shade of yellow color is obtained when the ointment is made with petrolatum as a base.

#### EXPERIMENTAL

With the foregoing facts in mind the following work was undertaken in an attempt to prepare a stable form of ointment of mercuric nitrate. This was accomplished by dispersing an aqueous mercuric nitrate phase in a proposed cholesterol-petro-

latum base capable of holding large quantities of aqueous solutions or suspensions in a rather permanent form (4).

After some experimentation the following formula for ointment of mercuric nitrate was developed.

|                  |            |
|------------------|------------|
| Mercuric nitrate | 11.34 Gm.  |
| Nitric acid      | 1.35 Gm.   |
| Distilled water  | 32.31 Gm.  |
| White wax        | 5.00 Gm.   |
| Cholesterol      | 1.50 Gm.   |
| White petrolatum | 48.50 Gm.  |
| To make          | 100.00 Gm. |

Mix 11.34 Gm. of finely powdered mercuric nitrate with 1 cc. of water, preferably in a mortar, and add 1.35 Gm. of nitric acid, accurately weighed. Triturate in the mortar until solution is effected and add 31.31 Gm. of water, slowly and with constant stirring.

Melt the white petrolatum, the cholesterol finely powdered and the white wax in a suitable dish. Continue the heat until the temperature of the mixture is raised to 80° C. and the cholesterol has completely dissolved. Stir the mixture until it congeals. By trituration, slowly incorporate the aqueous solution of mercuric nitrate into the ointment base. Care should be taken to avoid contact with metallic instruments or containers.

An ointment made according to the above formula has the same mercuric nitrate content as the one described in N. F. VI, *i. e.*, 11.34 Gm. per 100 Gm.

When this ointment is first prepared it is snow white, gradually, however, assuming a beautiful light yellow color which it retains permanently. It has an excellent consistency, appreciably enhanced by the five per cent of white wax it contains. After a period of several months the ointment shows no signs of deterioration. It holds its

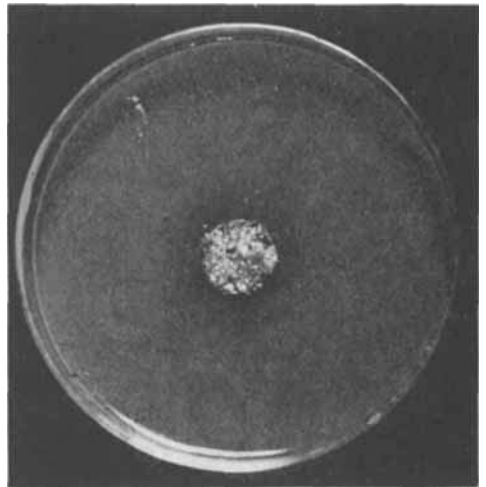


Fig. 1.—Ointment of Mercuric Nitrate, N. F. VI. Test Organism: *Staphylococcus aureus* of 24 hour broth culture at 37° C. Width of Zone: 4 mm. Mercury Coefficient: 0.61.

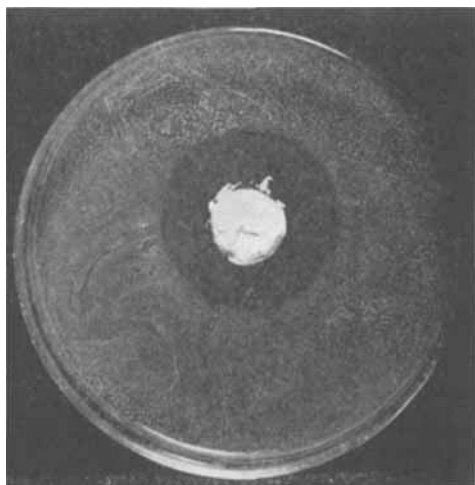


Fig. 2.—Proposed Ointment of Mercuric Nitrate. Test Organism: *Staphylococcus aureus* of 24 hour broth culture at 37° C. Method: Agar-cup. Period of Incubation: 48 hours at 37° C. Width of Zone: 13 mm. Mercury Coefficient: 2.0.

aqueous phase completely and retains its light yellow color and its original antiseptic potency.

The proposed ointment was tested for antiseptic potency in comparison with the N. F. VI ointment using *Staphylococcus aureus* as the test organism. The results were quite satisfactory as the accompanying photographs show.

#### MERCURY COEFFICIENT

Reddish and Wales (3), in 1929, experimenting with Ointment of Ammoniated Mercury U. S. P. X, obtained a zone 5 mm. wide using *Staphylococcus aureus* as the test organism on plain agar medium. Bryan (5) in 1936, made the same ointment with lanolin as a base, and obtained an inhibited zone having a width of 8 mm. It was this figure he used to compute the mercury coefficient of forty different ointments. Li and Kuever (4) tested U. S. P. Ointment of Ammoniated Mercury and obtained an inhibited zone of 6.5 mm. To find the mercury coefficient of an ointment, using U. S. P. XI Ointment of Ammoniated Mercury as a standard, divide the width of the inhibited zone of the ointment tested by 6.5.

| Name           | N. F. Ointment               | Proposed Ointment            |
|----------------|------------------------------|------------------------------|
| Organism       | <i>Staphylococcus aureus</i> | <i>Staphylococcus aureus</i> |
| Method         | Agar-cup                     | Agar-cup                     |
| Zone           | 4 mm.                        | 13 mm.                       |
| Mercury coeff. | 0.61                         | 2.00                         |

#### SUMMARY

The proposed Ointment of Mercuric Nitrate is more than three times as potent as Ointment of Mercuric Nitrate N. F. VI, when tested against *Staphylococcus aureus*.

The proposed Ointment of Mercuric Nitrate is a relatively permanent preparation which will retain its antiseptic potency and its original physical properties.

The proposed Ointment of Mercuric Nitrate is noticeably superior in consistency and texture when compared with the ointment made according to the process given in the N. F. VI.

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## A Rapid Procedure for the Manufacture of Saponated Solution of Cresol\*

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Saponated Solution of Cresol, formerly known as Compound Solution of Cresol, did not make its appearance in the United States Pharmacopœia until the Eighth Revision. However its chief constituent, cresol, had been in use as a germicide for many years prior to the issuance of the Eighth Revision of the Pharmacopœia.

The fact that cresol is readily miscible with soap solution has led to its popularity in detergents. It is natural enough then, that Saponated Solution of Cresol should have found its way into foreign Pharmacopœias, such as the British, German and others. Due, no doubt, to its relatively high

\* Senior thesis required for graduation from the School of Pharmacy, The Medical College of the State of South Carolina, Charleston.

Presented before the Section of Practical Pharmacy and Dispensing, A. PH. A., Atlanta meeting, 1939.

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