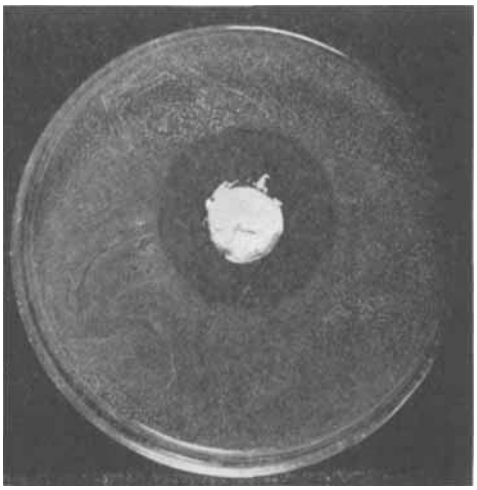

Fig. 2.—Proposed Ointment of Mercuric Nitrate. Test Organism: *Staphylococcus aureus* of 24 hour broth culture at 37° C. Method: Agar-cup. Period of Incubation: 48 hours at 37° C. Width of Zone: 13 mm. Mercury Coefficient: 2.0.

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	*Staphlococcus aureus*	*Staphlococcus aureus*
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*

By Lawell F. Martin† and William A. Proul‡

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

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phenol coefficient, this widely employed preparation is retained in the Eleventh Revision of the United States Pharmacopœia. Little or no decided change has been made in this monograph since its initial appearance, although many changes have been proposed from time to time as difficulties were encountered in the manufacture of the solution. Kaufman and Lee (1) have pointed out some of the objectionable features of the official formula and procedure, namely; the variability of time usually required for its preparation; the use of two alkalies, when one should suffice; and the probable loss of cresol due, no doubt, to the prolonged heating which is often necessary in order to bring about complete reaction between the reacting substances.

Table I.—Ingredients of Saponated Solution of Cresol, U. S. P.

United States Pharmacopœia Constituents	VIII	IX	X	XI
Cresol	500 Gm.	500 Gm.	500 cc.	500 cc.
Linsced oil	350 Gm.	300 Gm.	350 cc.	350 cc.
Potassium hydroxide (85%)	80 Gm.	80 Gm.	...	14.52 Gm.
Potassium hydroxide dekanormal sol.	...	...	22 cc.	....
Sodium hydroxide (95%)	...	...	...	37.05 Gm.
Sodium hydroxide dekanormal sol.	...	...	88 cc.	....
Alcohol	...	30 mils	...	....
Water, *q. s.* to make	1000 Gm.	1000 Gm.	1000 cc.	....
Distilled water, *q. s.* to make	...	...	...	1000 cc.

EXPERIMENTAL

Investigation of this preparation was undertaken to eliminate these objectionable factors by combining, if possible an already prepared soap, such as sodium stearate or sodium oleate directly with the cresol, rather than manufacturing the soap within the solution.

In substituting an already prepared constituent in place of one manufactured in a preparation, the amount to be used is generally based upon the quantity produced between the reacting agents. The equivalent amount of sodium stearate or sodium oleate was therefore substituted for the alkalies and linseed oil designated in the pharmacopœial formula. As a result of this combination, gelatinization occurred in almost every instance. Contrary to the report of Kaufman and Lee, (1) gelatinization occurred regardless of the quality of the cresol used.[1] It was decided, if possible, to trace the cause of gelatinization, since the question of the quality of cresol was apparently not involved. It was noted that preparations made as outlined on the basis of the pharmacopœial formula showed an excess of soap in the finished product, which led to the belief that too much soap was being used. Hilton's formula (2) which has proved to be a very satisfactory one, was finally decided upon as the basis of calculation of the amount of soap to use. Hilton's formula is as follows:

Cresol	500 Gm.
Oleic acid	226 Gm.
Sodium hydroxide	35 Gm.
Water, *q. s. ad*	
to make	1000 mils

From this it was calculated that 240 Gm. of sodium oleate or sodium stearate were required to replace the amount of oleic acid and sodium hydroxide in the above formula. This was considerably less than the amount calculated upon the basis of the official formula. The revised formula is as follows:

Cresol	500 cc.
Sodium oleate or Sodium stearate	240 Gm.
Distilled water, *q. s. ad*	
to make	1000 cc.

Dissolve the soap in the cresol, to which about 200 cc. of distilled water have been added. Heat the mixture, with constant stirring, to about 65° C., and maintain this temperature until solution is effected. Cool the liquid, add sufficient distilled water to make the product measure 1000 cc. and mix well.

DISCUSSION

Approximately five minutes were required to prepare the solution using either sodium stearate or sodium oleate. Gelatinization did not occur in any of the solutions made by this formula. The initial appearance of the solution is practically the same regardless of which soap is used. The solution made with the sodium oleate, however, presents an extremely slight precipitate which forms after several hours standing, but no increase is noted upon further standing. The precipitate does not appear objectionable, as it is so very slight and can be easily dispersed by agitating the solution. The initial color of the solutions (light amber) prepared as above is much lighter than that of the official preparation, probably because of the

[1] U. S. P. Cresol (Baker's), fresh stock.

fact that much less heat is required in its manufacture. They do become darker, however, upon standing unless well protected from light.

Objections have been raised relative to the dark color of the pharmacopœial solution. As it usually requires an indefinite interval, generally an hour, to prepare the official solution by heating at 70° C., this suggested the probable cause of the dark color of the finished product. Experiments were carried out, therefore, to ascertain to what extent, if any, prolonged heating had upon the color. Cresol, U. S. P. (fresh stock) whose initial color is very light amber, was used as the control. It, along with the Saponated Solution of Cresol made in accordance with the revised formula, was heated at 70° C., for one hour. At the end of this time, both the cresol and the Saponated Solution of Cresol had acquired a very deep amber color. This color appeared to be about the same shade as that of the official preparation. These heating experiments confirm the report of O'Day and Jones (3) who investigated the Saponated Solution of Cresol, employing both the hot and cold method of manufacture. Ordinary light also affects the color of the solutions containing cresol. Even in dilutions of 1:250, the solutions become decidedly pink, and after having stood several days, the color deepens. The present revision of the pharmacopœia designates that cresol be preserved in well-closed containers and protected from light, yet, no such provision is made for the preparation of the Saponated Solution of Cresol with respect to the protection from light.

Prolonged heating also appears to affect the content of cresol as is shown by analyses carried out according to Handke's (4) method. The United States Pharmacopœia X Compound Solution of Cresol assayed approximately forty-four per cent cresol, the present official Saponated Solution of Cresol assayed approximately forty-six per cent cresol, while the Saponated Solution of Cresol made according to the revised formula assayed approximately forty-nine per cent cresol.

The following specific gravities of the cresol solutions were determined with the Mohr-Westphal Balance: U. S. P. Compound Solution of Cresol 1.0356; U. S. P. Saponated Solution of Cresol 1.0350; and Saponated Solution of Cresol (revised formula) 1.0272. These figures show how closely the specific gravity of the solution prepared in accordance to the revised formula compares with the specific gravities of the U. S. P. X and U. S. P. XI preparations.

CONCLUSIONS

1. Saponated Solution of Cresol can be easily and speedily prepared by using either sodium stearate or sodium oleate in direct combination with the cresol.

2. Very little heat is required in the manufacture using the revised formula, thus assuring a relatively high per cent of cresol in the finished product.

3. Prolonged heating affects the color of the solution. The preparation made according to the revised formula presents a much lighter-colored solution than the official product.

4. Ordinary light also affects the color of the finished preparation, therefore, provision should be made to protect preparations containing cresol from light during storage.

5. Gelatinization does not occur in the Saponated Solution of Cresol when made according to the revised formula, regardless of the grade of cresol used. While the cause of gelatinization is apparently not entirely solved, it is suggested that possibly too much soap is produced and too much heating is required in the official formula.

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NOTICE

Please send in immediately completed manuscripts for papers read at the Richmond meeting.