

ate and light magnesium oxide are most effective while heavy magnesium oxide is less effective and talc, lactose and various starches are comparatively inefficient in preventing liquefaction. The probable explanation of the results is that powders which are light and fluffy are more effective in holding apart the particles of the substances which tend to liquefy on contact. When a light, fluffy powder is used it is somewhat more difficult to fill the capsules since the resulting powder packs less readily and has a tendency to fall out of the body of the capsule during the filling.

In some instances the use of light or heavy magnesium oxide caused the contents of the capsule to change into a hard, cement-like mass. Tests on some of the hardened masses showed that they did not disintegrate in water in four days; in 0.5 per cent solution of hydrochloric acid the solid mass was reduced slightly in size but retained its form. Since insoluble masses of this kind would probably pass through the alimentary tract without disintegrating it is important that the pharmacist take precautions to prevent their formation. In most cases cement-like masses did not form when magnesium carbonate was used as the inert powder.

SUMMARY

Experiments were carried out with various prescriptions for capsules to determine the relative efficiency of various inert powders in preventing liquefaction due to formation of a eutectic mixture. Inert powders which are light and fluffy appear to be most efficient. Magnesium carbonate and light magnesium oxide proved most effective, heavy magnesium oxide ranked next, and talc, lactose and various starches were least effective. In some cases, particularly with light and heavy magnesium oxide, the contents of the capsules assumed a cement-like hardness.

As to the various methods of compounding, the results show that it is better to first mix one incompatible ingredient with the inert powder or to mix each incompatible ingredient with a separate portion of the inert powder. **Heavy trituration hastens**

liquefaction. Likewise the use of too small a capsule hastens liquefaction due to the tightness of packing.

Apparently exposure of the filled capsules to the air usually has little or no effect when the liquefaction is due to formation of a eutectic mixture.

In most cases the use of about two grs. of magnesium carbonate or light magnesium oxide per capsule stabilized the capsules over a period of two weeks.

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The Status of Phenol in Ointment of Phenol, U. S. P.*

By William A. Prout† and A. Clifton Smith, Jr.‡

To meet the United States Pharmacopœial requirements, Ointment of Phenol must contain not less than 1.8 per cent nor more than 2.2 per cent of C_6H_5OH . As is noted, a tolerance of 0.4 per cent is allowed to take care of possible error in weighing, questionable strength of the phenol used and probable loss during manufacture of the ointment. The purpose of this investigation was to determine whether or not various samples made by different individuals actually met the requirements as designated in the United States Pharmacopœia in respect to the content of phenol.

G. R. Page (1) of England, working on the British Pharmacopœia (1932) Ointment of

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Phenol, which should contain 3 per cent of the active constituent, found that the loss of phenol during preparation may be from 3.7 per cent to 5.2 per cent of that added, and that there was a further decrease on keeping, the amount varying with the conditions of storage. He found that ointments stored in earthenware containers at room temperature lost phenol rapidly, and that the strength fell approximately 33 per cent after two years' storage. Ointments stored in collapsible tubes, however, showed little or no loss of phenol after ten months. He attributed the loss of phenol to volatilization.

EXPERIMENTAL

Two ointments of phenol were prepared, one in accordance with the United States Pharmacopœia XI directions (2) and the other according to a modified method of procedure. Following are the two formulas and directions:

Ointment of Phenol, U. S. P.

| | |
|--------------------|---------|
| Phenol..... | 2 Gm. |
| Yellow Wax..... | 5 Gm. |
| Petrolatum..... | 93 Gm. |
| To make about..... | 100 Gm. |

Melt the yellow wax and phenol on a water-bath, add the petrolatum and stir the mixture until it congeals.

Ointment of Phenol, Modified Method

| | |
|--------------------|---------|
| Phenol..... | 2 Gm. |
| Yellow Wax..... | 5 Gm. |
| Petrolatum..... | 93 Gm. |
| To make about..... | 100 Gm. |

Melt the yellow wax on a water-bath, add the petrolatum and, when liquefied, remove the source of heat. Cool to about 70° C., add the phenol and stir the mixture until congealed.

In order to reproduce as nearly as possible the ordinary conditions of manufacture as carried out by the average pharmacist, small quantities (50 Gm.) of ointment were prepared by different individuals, using phenol, which had been previously assayed, and dispensing balances to weigh the ingredients. The ointments were then immediately assayed according to the Pharmacopœia (3), which directs that the phenol be separated from the ointment base by distillation with steam, and that the phenol in the distillate be estimated by use of Koppeschaar's Solution.

The results of the assays are shown in the following tables:

Table I.—Ointment of Phenol, U. S. P.

| Sample Number | Phenol, C. P. (Baker's) Added | Found by Assay | Per Cent Loss of Phenol |
|---------------|-------------------------------|----------------|-------------------------|
| 1 | 2.0000 | 1.6395 | 18.02 |
| 2 | 2.0000 | 1.6892 | 15.54 |
| 3 | 2.0000 | 1.6405 | 17.97 |
| 4 | 2.0000 | 1.6582 | 17.09 |
| 5 | 2.0000 | 1.6281 | 18.59 |
| 6 | 2.0000 | 1.6842 | 15.79 |
| 7 | 2.0000 | 1.6482 | 17.59 |
| 8 | 2.0000 | 1.6354 | 18.23 |
| 9 | 2.0000 | 1.6784 | 16.08 |
| 10 | 2.0000 | 1.7244 | 13.78 |
| 11 | 2.0000 | 1.6982 | 15.09 |
| 12 | 2.0000 | 1.7102 | 14.46 |
| 13 | 2.0000 | 1.5984 | 20.08 |
| 14 | 2.0000 | 1.6386 | 18.07 |
| 15 | 2.0000 | 1.7236 | 13.82 |
| 16 | 2.0000 | 1.6280 | 18.60 |
| 17 | 2.0000 | 1.7423 | 12.88 |
| 18 | 2.0000 | 1.6832 | 15.84 |
| 19 | 2.0000 | 1.6204 | 18.98 |
| 20 | 2.0000 | 1.6674 | 16.63 |

Table II.—Ointment of Phenol, Modified Method

| Sample Number | Phenol, C. P. (Baker's) Added | Found by Assay | Loss of Phenol |
|---------------|-------------------------------|----------------|----------------|
| 1 | 2.0000 | 1.9702 | 1.49 |
| 2 | 2.0000 | 1.9742 | 1.29 |
| 3 | 2.0000 | 1.9849 | 0.75 |
| 4 | 2.0000 | 1.9502 | 2.49 |
| 5 | 2.0000 | 1.9498 | 2.51 |
| 6 | 2.0000 | 1.9784 | 1.08 |
| 7 | 2.0000 | 1.9836 | 0.82 |
| 8 | 2.0000 | 1.9827 | 0.86 |
| 9 | 2.0000 | 1.9588 | 2.06 |
| 10 | 2.0000 | 1.9672 | 1.64 |
| 11 | 2.0000 | 1.8580 | 2.10 |
| 12 | 2.0000 | 1.9546 | 2.27 |
| 13 | 2.0000 | 1.9468 | 2.66 |
| 14 | 2.0000 | 1.9322 | 3.39 |
| 15 | 2.0000 | 1.9406 | 2.97 |
| 16 | 2.0000 | 1.9398 | 3.01 |
| 17 | 2.0000 | 1.9782 | 1.09 |
| 18 | 2.0000 | 1.9688 | 1.56 |
| 19 | 2.0000 | 1.9842 | 0.79 |
| 20 | 2.0000 | 1.9764 | 1.18 |

DISCUSSION

The results of this investigation have shown conclusively that there is a decided loss of phenol during the manufacture of the ointment when made as directed by the United States Pharmacopœia XI, while the loss of phenol was much smaller in the ointment made according to the modified procedure of manufacture. The average loss of phenol in the pharmacopœial ointment amounts to 16.65 per cent while the average

loss of phenol in the ointment made by the modified method was only 1.80 per cent.

While possible error in weighing, and improper mixing may also contribute to the loss of phenol, volatilization appears to be the outstanding factor responsible for so great a loss of phenol during the manufacture of the ointment.

Phenol (4), as described in the French Pharmacopœia, is slightly hygroscopic, slowly volatilized at room temperature and very rapidly volatilized at 100° C. As the United States Pharmacopœia directs that the yellow wax (5), which has a melting point of 62° C. to 65° C., and the phenol be melted on a water-bath, evidently the heat is great enough to volatilize some of the phenol before the remainder of the base is finally added.

CONCLUSIONS

1. Ointments manufactured in accordance with the United States Pharmacopœia directions lose phenol rapidly during preparation and the strength may fall to as low as 1.59 per cent.

2. Ointments of phenol when made according to a modified procedure show much less loss of phenol during the preparation. All samples of this series fell within the pharmacopœial limits of the active constituent.

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Notes on the Preparation of Lotio Flava, N. F. VI*

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In a course dealing with the pharmacy of inorganic substances and preparations the writer has assigned, among other official

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preparations involving chemical reactions, Lotio Flava to be made by the students in the laboratory. It has been observed over a period of several years that a goodly number of the individual products handed in for grading showed, instead of the expectant yellow precipitate, a reddish brown one. This has occurred with such frequency that it could not be explained entirely on the basis of faulty technique by the individual worker and it was decided to attempt an explanation of this variation in the appearance of the product.

It was at first thought that the variation might be due to an inferior or impure mercuric chloride used in the formula. However, products from different manufacturers purchased at various times yielded similar results in the final product. One writer states that the reddish or brownish precipitate may be a basic compound which forms because the lime water was deficient in calcium hydroxide (hence too much HgCl₂) or too much mercuric chloride has been used (1). He further states that there is very little difference in the composition of the two oxides (?) formed. The yellow oxide is more finely divided and reflects the yellow rays of light and the red form is crystalline (hence of large size) and reflects the red rays of light (2).

EXPERIMENTAL

The following experiments were performed:

- (1) The N. F. formula and procedure were followed using freshly prepared lime water decanted from the excess of calcium hydroxide.
- (2) Repeat (1) using freshly prepared lime water filtered.
- (3) Repeat (1) using freshly prepared lime water shaken.
- (4) The N. F. procedure was employed using freshly prepared and filtered Liquor Calcis and 3.25 Gm. mercuric chloride per 1000 cc. (0.25 Gm. more than the N. F. formula).
- (5) Same as (4) using 2.75 Gm. HgCl₂ per 1000 cc. (0.25 Gm. less than the N. F. formula).
- (6) Same as (1) but using lime water that had been exposed to the air for several days, then filtered.
- (7) Same as (2) after bubbling carbon dioxide through the lime water for a time.
- (8) Same as (2) adding 0.1% sodium bicarbonate.
- (9) Same as (2) using 0.3% sodium bicarbonate.