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MERCURY OINTMENT.

BY C. B. JORDAN, *et al.*

In the paper by Broady and Jordan, JOUR. A. PH. A., 16 (1927), 425–430, they recommended that mercury ointment be prepared by reducing mercuric chloride to metallic mercury in colloidal form and then incorporating this with the base. The formula and procedure recommended by them are:

"Mercuric chloride	40	Gm.
Sodium hydroxide, sticks	40	Gm.
Gelatin, leaf	2.5	Gm.
Liq. formaldehyde, 40%	20	Gm.
Anhydrous lanolin	25	Gm.
White petrolatum, *q. s. ad*	100	Gm.

"Dissolve the gelatin and NaOH in 200 cc. of H_2O with heat. *Cool* and add the solution of HCHO. Dissolve the $HgCl_2$ in 200 cc. H_2O by aid of heat. While still hot, add slowly and with stirring to the solution of NaOH, HCHO and gelatin. This should be done slowly and with care. Allow the precipitate to settle completely and decant. Wash the precipitate by decantation with two successive portions of 200 cc. of H_2O, allowing the precipitate to settle each time. Filter and transfer the precipitate *while still moist* to a mortar and add 25 Gm. of anhydrous

lanolin and thoroughly mix. Add enough white petrolatum to make 100 Gm. and mix thoroughly.

"Caution. Do not allow the precipitate to dry on filter."

"All of our freshmen students made good mercurial ointments by this method, and the time required was about one hour. The portion of Hg up to 60% can be varied at will. We do claim that this method is better than the one in vogue for the following reasons:

1. The ointment can be prepared in less time.
2. It is easier to prepare it.
3. The free Hg is in a much finer divided condition and therefore of greater therapeutic value."

Mercury ointment made by the reduction process has been the subject of study at the Purdue School of Pharmacy for the past four years. C. O. Lee and H. G. Dekay have instructed their classes in manufacturing pharmacy to prepare it, using slight modifications of the original formula. The ointment offered two problems, *first*, a finely divided mercury settled slowly and time was lost in washing it; *second*, if care was not used some of the mercury was lost in the washings and the ointment was substandard. One modification that was used is as follows:

Mercuric chloride	24	Gm.
Sodium hydroxide	24	Gm.
Gelatin, leaf	1.25	Gm.
Liq. formaldehyde, 40%	12	Gm.
Anhydrous lanolin	12.5	Gm.
White petrolatum, *q. s. ad*	50	Gm.

Dissolve the gelatin and NaOH in 100 cc. of water with heat. Cool and add the solution of HCHO. Dissolve the $HgCl_2$ in 100 cc. of water by aid of heat. The gelatin, NaOH, HCHO solution should be cooled to 40° C. and the $HgCl_2$ solution to 80° C. Pour the hot $HgCl_2$ solution slowly and with stirring into the gelatin, NaOH, HCHO solution. Allow the precipitate to settle and decant. Wash the precipitate by decantation with two successive portions of 200 cc. of water, allowing the precipitate to settle each time. Transfer the moist precipitate to a pill tile and incorporate thoroughly with the anhydrous lanolin. Then add enough white petrolatum to make 50 Gm. and mix thoroughly.

TABLE I.—THEORETICAL PER CENT OF MERCURY.

Student.	31%.	31%.	32%.	32%.	50%.
No. 1	21.78	28.66	28.88	29.99	..
	21.70	28.48	28.97	29.60	..
No. 2	25.32	24.43	26.48	24.41	..
	25.37	24.64	26.91	24.43	..
No. 3	29.54	19.54	28.13	28.62	..
	29.67	19.52	28.15	28.66	..
No. 4	28.67	30.57	29.69	29.56	..
	28.62	30.35	30.00	29.29	..
No. 5	28.13	35.07	27.83	28.48	..
	28.13	35.78	27.92	28.32	..
No. 6	28.40	...	31.07	29.04	49.74
	28.47	...	31.01	29.76	49.68
No. 7	30.16	27.76	28.21	27.72	..
	30.10	27.52	28.08	27.17	..
No. 8	22.20	29.37	32.31	23.63	..
	22.07	29.72	32.10	23.84	..

Eight sophomore students prepared ointments by this formula. The ointments were excellent as to appearance and smoothness, but these students had little training in technique and they lost mercury in the washing process as Table I indicates.

These ointments were assayed by E. H. Westlund, a graduate student at Purdue.

The varying results obtained by the same student indicates a lack of care in preventing loss of mercury. Student No. 4 was a Junior and a careful worker as his results indicate. Students Nos. 6 and 7 were also recognized as more careful workers than many of their classmates, and their results so indicate.

At the request of Chairman Leonard Seltzer, of the Sub-Committee on Ointments of the U. S. P. Revision Committee, further study was given to this problem last summer, using seniors and graduate students. The formula and process used were as follows:

UNGUENTUM HYDRARGYRI MITE.

Bichloride of mercury	26 Gm.
Sodium hydroxide	13 Gm.
Gelatin leaf	1.5 Gm.
Liq. formaldehyde	15 cc.
Anhydrous lanolin	18 Gm.
White petrolatum, *q. s. ad.*	60 Gm.

(1) Dissolve the sodium hydroxide and gelatin in about 100 cc. of distilled water, in a beaker.

(2) Dissolve the mercuric chloride in 125 cc. of boiling water and add it to (1) with stirring.

(3) To this add the solution of formaldehyde and stir.

(4) Cool and, when the precipitate has settled, decant the supernatant liquid.

(5) Wash the precipitate with 100 cc. of water and decant as before.

(6) Wash the precipitate into a tared porcelain dish, allow to settle, decant as closely as possible and without delay mix the precipitate with the anhydrous lanolin.

(7) Add enough white petrolatum to make 60 Gm. Heat on a water-bath until soft and mix thoroughly. Stir gently until congealed.

Table II shows results obtained.

TABLE II.

Sample Number.	Person Making.	Per Cent Hg.
10	LeBlanc	30.49
11	LeBlanc	30.78
12	LeBlanc	29.65
1	Close	31.32
2	Close	29.85
4	Close	25.53
1	Findley	31.14
2	Findley	31.55
1	Ford	27.73
1	Haines	19.51

F. J. LeBlanc assayed these ointments and his comments on these are as follows:

"Samples 10, 11, 12 were carefully made by myself.

"Samples 1, 2, 4 were made by Mr. Close. He states that one of his samples was placed in the oven for a time. He does not remember which sample. From the results obtained on assay of his ointments probably No. 1 had lost some moisture by being in the oven and, therefore, the high result. Have no explanation for the low result of No. 4 other than that directions probably were not as carefully followed as they might have been.

"Samples 1 and 2, made by Mr. Findley, show a little over 31 per cent of Hg, but he used a formula that called for a 32 per cent theoretical yield of mercury. I supervised the making of Mr. Findley's ointments and gave him several suggestions while he was working.

"Sample 1, made by Miss Haines, was made by the filter paper method. Evidently considerable Hg was lost by this method as her ointment only gave 19.51 per cent Hg on assay."

Some workers have had difficulty in getting the mercuric chloride in solution and keeping it from crystallizing out before the solutions were mixed. The staff of the Detroit City College of Pharmacy complained of this and suggested that some sodium chloride be used to make the mercuric chloride more soluble and thus permit the use of lower temperatures in the manufacturing process.

W. A. Prout, a graduate student at Purdue, worked on the problem this summer, using the suggestion of the addition of sodium chloride. He made a great many ointments, varying the amount of sodium chloride used, the temperature at which reduction was accomplished and changing the order of mixing. As a result of these many experiments he recommends the following formula and procedure:

UNGUENTUM HYDRARGYRI FORTIUS.

Mercuric chloride	42.25 Gm.
Sodium chloride	5.00 Gm.
Sodium hydroxide	21.00 Gm.
Leaf gelatin	2.4 Gm.
Liq. formaldehyde	25.00 cc.
[1] Purdue base, *q. s. ad.*	60.00 Gm.

[1] Purdue base consists of the following:

White wax	5 Gm.
Anhydrous lanolin	5 Gm.
Petrolatum, white	90 Gm.

Melt the wax on a water-bath, add the petrolatum and allow it to melt and then add the lanolin. When all is melted, stir just enough to insure thorough mixing and set aside to congeal.

(1) Dissolve the sodium hydroxide and gelatin in 100 cc. of distilled water in a beaker.

(2) Dissolve the mercuric chloride and sodium chloride in 100 cc. of distilled water heated to 60° C.

(3) Immediately pour Solution 2 into Solution 1 with gentle stirring. Add the formaldehyde and stir rapidly with a rubber-tipped rod, to insure thorough mixing. Place the beaker in cold water and continue stirring until the temperature is down to 40° C.

(4) Allow the precipitate to settle. Decant the supernatant liquid and wash with 200 cc. of distilled water with a minimum disturbance of the precipitate. Again decant after settling.

(5) Wash the precipitate into a tared dish using about 150 cc. of distilled water. When the precipitate has settled, decant the supernatant liquid as closely as possible and immediately add the required amount of base and mix thoroughly.

This gives a fine ointment of good texture, smooth and uniform. Mr. Prout made a number of samples by this procedure and assayed them for mercury content.

His results are shown in Table III.

TABLE III.

Sample No.	Assay.	Sample No.	Assay.
1	52.09%	4	50.7 %
	52.18%		50.8 %
2	49.2 %	5	50.1 %
	49.5 %		50.04%
3	49.4 %	6	50.1 %
	49.1 %		49.84%

All of these ointments except the first fall within the U. S. P. purity rubric limits and, therefore, meet the U. S. P. requirements for this ointment.

The dilute ointment of mercury can easily be made by mixing a sufficient amount of the stronger ointment with sufficient base to produce the required percentage of mercury. The larger the amount of ointment that is prepared at any one time, the less the danger of error. It is, therefore, recommended that the stronger ointment be prepared and the dilute ointment made from it when needed.

The advantages of this method of preparing mercury ointment are:

(1) The ointment can be prepared in less time. (Requires about one hour.)

(2) It is easier to prepare. The old trituration procedure was not only time-consuming but also very tiresome.

(3) The free mercury is in a much finer divided condition and therefore ought to be of greater therapeutic value.

The disadvantage of the method is in the danger of loss of mercury in washing. However, in the hands of a careful worker, this disadvantage is reduced to a minimum, as shown by the work of LeBlanc, Prout and others. This formula and procedure are recommended for the favorable consideration of the Sub-Committee on Ointments of the U. S. P. Revision Committee.

AN OINTMENT BASE FOR OFFICIAL OINTMENTS.*

BY C. O. LEE AND H. G. DEKAY.

The criticisms of the official ointments are in a large measure traceable to their bases. The usual story about them is that they become rancid or grainy or both, or are too stiff or too soft. It is too much to expect any class of preparations to be without fault, but constant effort to improve them is the pharmacist's responsibility.

In his "Summary of Comments," Seltzer,[1] among other things, reported on thirteen ointments of the Pharmacopœia. Ten of the thirteen comments are definite proposals for changes in the present bases. To us the suggested changes are well founded.

An ideal ointment base is, of course, a pharmaceutical dream that has never come true and perhaps never will. We should, however, continue to dream and to strive for galenical ideals. If the present Committee of Revision takes cognizance of the suggestions that are now being made with reference to ointments, the forthcoming Pharmacopœia will have an improved list of preparations from the pharmaceutical point of view. Formulas that have remained unchanged through a

* Section on Practical Pharmacy and Dispensing, A. PH. A., Toronto meeting, 1932.

[1] U. S. P. XI Bulletins, Sub-Committee 13, Bull. 14, page 19 (1931).