REVISION OF THE MONOGRAPHS OF OFFICIAL CHEMICALS*

BY H. V. ARNY.

In discussing this phase of the pharmacopoeial revision attention must be called to the importance of the correct wording of the text of official chemicals because of the frequent scrutiny given the chemical monographs by attorneys attempting to get clients out of tight phases when their products are being subjected to the scrutiny of the law.

Two of many such cases might be cited by way of illustration. In one case, the attorney asked the chemist whether mercury was volatile. "I would not consider it so," was the response. The attorney forthwith asked the chemist to read page 220 of U. S. P. IX, where it is stated "at ordinary temperatures mercury volatilizes very slowly," and forthwith began to expatiate upon the possibility of the ointment of mercury, upon the weakness of which the case was based, losing strength by volatilization during the manipulations directed in the official assay.

In another case, the defense in a case of shortage of strength of a solution of magnesium citrate attempted to confuse the issue by the following argument:

Each 100 mils of the Solution should contain 1.5 Gm. magnesium oxide.

Each 100 Gm. magnesium carbonate U. S. P. should contain 39.2 Gm. magnesium oxide.

$$\text{Since } \frac{100}{39.2} \times 1.5 = 3.8,$$

each 100 mils of the Solution should contain 3.8 Gm. magnesium carbonate U. S. P. and a bottle of the Solution (350 mils) should contain 3.8×3.5 or 13.3 Gm. magnesium carbonate U. S. P. instead of 15 Gm. directed in the official formula.

Such arguments were, of course, merely quibbling, but they do point out the need of great explicitness in wording the monographs of the official chemicals and great care in making the prescribed tests as nearly "fool-proof" as possible.

Such thoughts actuated the talented chairman of the two sub-committees entrusted with the preparation of the monographs on inorganic and organic chemicals in the present Pharmacopoeia, Charles H. LaWall and George Rosengarten, and no one realizes this more than does the former's successor, the present writer. There are but few invitations to legal quibbles found in the carefully prepared texts and carefully worked out tests, and what changes I have to suggest are largely because of changed conditions coming into being since U. S. P. IX has been published.

"Faint Turbidity" Tests.—A prolific source of misunderstandings between analysts are time-honored tests of the Pharmacopoeia where it is stated that when a solution of the chemical under examination is mixed with a certain test solution "not more than a faint turbidity" or "not more than a slight opalescence" should rest. If distinct turbidity or opalescence is shown, the presence of some impurity is indicated. In such test the question arises, "What is a faint turbidity?" The chemist in the chemical works is apt to consider as a "faint turbidity" what the chemist of the pure drug enforcement bureau might consider an extremely

* Read before Scientific Section A.Ph. A., City of Washington meeting, 1920.

turbid and, until the wording of such tests is made more precise, the controversy will continue and provoke trouble in pure drug litigation.

The sub-committee on inorganic chemicals during the past year gave its attention to this matter and, as a result, a grant was made by the U. S. P. Board of Trustees permitting John M. Williams to study the question under the supervision of the writer of this paper.

We first established the sensitivity of the tests involved finding that:

Silver nitrate shows chlorides in a dilution of 1 in 500,000
Barium chloride shows sulphates in a dilution of 1 in 100,000
Magnesium mixture shows phosphates in a dilution of 1 in 40,000
Ammonium molybdate shows phosphates in a dilution of 1 in 400,000
Potassium sulphate shows barium in a dilution of 1 in 40,000.

We next examined several samples of each of the following commercial chemicals for which "faint turbidity" tests are provided and found the following limits of impurity easily attained.

Chemical.	Impurity.		
Magnesium sulphate	chloride	2	parts in 100,000
Sodium phosphate	chloride	2	" " "
Ammonium carbonate	chloride	0.50	" " "
Calcium glycerophosphate	chloride	10	" " "
Zinc sulphate	chloride	0.01	" " "
Bismuth subnitrate	chloride	0.01	" " "
Sodium bromide	sulphate	10	" " "
Sodium iodide	sulphate	20	" " "
Lithium bromide	sulphate	50	" " "
Ammonium bromide	sulphate	15	" " "
Ammonium carbonate	sulphate	50	" " "
Calcium bromide	sulphate	20	" " "
Calcium glycerophosphate	sulphate	500	" " "
Zinc chloride	sulphate	20	" " "
Potassium iodide	sulphate	20	" " "
Sodium hypophosphite	phosphate	50	" " "
Calcium glycerophosphate	phosphate	1	" " "
Sodium glycerophosphate	phosphate	1	" " "
Potassium bromide	barium	25	" " "
Potassium iodide	barium	25	" " "
Sodium bromide	barium	25	" " "
Sodium iodide	barium	25	" " "
Ammonium bromide	barium	25	" " "
Calcium bromide	barium	25	" " "
Strontium bromide	barium	25	" " "

After a study of these findings, the sub-committee decided to recommend to the incoming sub-committee the adoption in the next Pharmacopoeia of more precise turbidity tests. Such tests could direct, for instance, that a five percent solution of the salt mixed with definite amounts of the appropriate reagents and diluted to a definite volume, say 10 mils, should show no more turbidity than a 5 percent solution of the C. P. chemical to which has been added a definite volume of a standard solution of the impurity plus definite amounts of the appropriate reagents and diluted to the definite 10 mil volume, the two fluids compared in test-tubes.

Chlorides in Bromides and Iodides.—This is one of the most troublesome and unsatisfactory tests of the Pharmacopoeia and presents a subject that should be

given further study. Such a recommendation has been made by the present sub-committee to the incoming committee.

Miscellaneous Suggestions.—In the extremely important list of pharmacopoeial suggestions published by the Committee on Revision in the March and April numbers of the JOURNAL are found many references to changes needed in the phraseology of the monographs of, and tests for, the official chemicals. To these at this place I will add a few that have come to the notice of Dr. Hugo H. Schaefer and myself in our daily routine of chemical testing.

Alkaloidal Assays.—In these days when chloroform is very expensive, attention should be given to the use of other "shaking-out" solvents which are cheaper and are equally efficient.

Camphorated Oil.—While the polarimetric assay given in the present Pharmacopoeia is scientifically correct, it is not only time-consuming but also demands a larger amount of the sample than is feasible to collect in a drug law enforcement case. We find the evaporation method of the German and Swiss pharmacopoeias entirely satisfactory, although giving somewhat higher results than really obtain. This, however, is a blending of mercy with justice, a quality not entirely out of place in a court proceeding. Of course in carrying out the evaporation assay the analyst must see that the sample is freed from water, alcohol or ether before the assay is carried out.

Mild Mercurous Chloride.—In the assay of calomel tablets, the official method does not work satisfactorily, since the calomel dissolves very slowly in the tenth-normal iodine solution. Dr. A. B. Lyons (J. AM. PHARM. ASSOC., 7, 1918, 939) has suggested the use of a fifth-normal iodine solution but in the discussion of the matter before the sub-committee on inorganic chemicals it was pointed out that instead of introducing a new volumetric solution into the Pharmacopoeia the same result can be obtained by lessening the amount of calomel used. In U. S. P. IX it is said "Mix . . . . about 1 gramme of mild mercurous chloride." If this direction is changed to "about 0.5 gramme" the assay will be performed without trouble.

Quinine Hydrobromide.—We have found that the differentiation of quinine hydrobromide from the hydrochloride of that alkaloid is not easy, which perhaps explains why the present Pharmacopoeia presents no test of distinction. We have worked out a method that brings the desired result and will publish it elsewhere within the next few months.

Solution of Magnesium Citrate.—There is being sold a considerable quantity of this solution containing a shortage of citric acid and it is therefore desirable that the next Pharmacopoeia provide assays for the magnesium oxide and for citric acid. For the latter, the assay suggested by J. L. Mayer,[1] which is an adaptation of the present blanket assay for alkali salts of organic acids, has in our hands produced satisfactory results. Incidentally, as mentioned above, attempts should be made to reconcile more accurately, than at present obtains, the statements made as to the MgO content of this Solution and of the magnesium carbonate from which it is made.

[1] JOURNAL A. PH. A., March 1920, p. 253.