THE ASSAY OF NATIONAL FORMULARY PREPARATIONS CONTAINING BISMUTH.*

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Glycerite of Bismuth is the only bismuth preparation in the National Formulary for which a tolerance and assay are now official. The present study was undertaken to determine whether the method of assay employed for the glycerite could be applied to the determination of the bismuth content of Solution of Bismuth, Elixir of Bismuth, Elixir of Pepsin and Bismuth and Elixir of Pepsin, Bismuth and Strychnine, and also to determine whether other methods might be applied advantageously to the assay of these preparations.

Various methods have been utilized for the quantitative determination of bismuth, namely: the official sulphide method (1) which is known to be accurate; the formaldehyde method (2) which is not suitable since the procedure does not separate other metals commonly present as impurity; the electrolytic method (3) which is not further considered since electrolytic methods in general have been deleted from the eleventh revision of the United States Pharmacopœia; and methods based on the precipitation of bismuth as the phosphate. Moser (4) reported that the phosphate process is the most advantageous method of estimating bismuth since bismuth phosphate, $BiPO_4$, is of definite composition; it forms a white, heavy crystalline precipitate which is insoluble in water and very dilute nitric acid, it deposits and filters quickly, it is not changed by ignition, and it is not readily reduced. This method was further studied by Stahler and Scharfenberg (5), Salkowski (6), Stahler (7) and Schoeller and Waterhouse (8). Schoeller and Waterhouse critically reviewed much of the earlier investigator's findings. Working with pure bismuth nitrate solutions, they concluded that the quantitative precipitation of the phosphate was a matter of rather delicate adjustment; if the acidity was low, the liquid on being heated usually deposited a heavy crystalline precipitate of oxynitrate; and if the acidity was higher than necessary to prevent deposition of oxynitrate, a small fraction of the bismuth failed to precipitate as phosphate unless an excessive quantity of alkaline phosphate was added. Mayer (9) recommended a phosphate method for the assay of bismuth without giving experimental data to indicate the accuracy of the procedure.

In the present investigation, a comparative experimental study of the official sulphide method, of the Mayer phosphate method and of the Schoeller and Waterhouse phosphate method was undertaken. The procedures followed were: (1) That of the National Formulary V for Glycerite of Bismuth in the sulphide method. (2) The Mayer phosphate method which is as follows:

"Accurately measure 5 cc. of Glycerite of Bismuth into a 400-cc. beaker, add about 100 cc. of water, heat to boiling, then add concentrated hydrochloric acid until the precipitate which at first forms redissolves and then add ammonia water until a turbidity is produced, after which sufficient concentrated hydrochloric acid is added to clear up the turbidity; to this boiling solution

* Abstracted in part from a thesis submitted by Sylvia Millett to the Graduate School of the University of Maryland in partial fulfilment of the requirements for the Degree of Master of Science.

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add an excess (about 50 cc. should be sufficient) of ten per cent ammonium phosphate solution drop by drop from a 50-cc. pipette. Allow to settle and filter the precipitate on a Gooch crucible and wash with hot water until free from chlorides and after drying crucible and contents, place in a nickel crucible and heat until the weight is constant.

"Multiply the weight of the precipitate by 0.7663 and then by 20, the result will be the grams of Bi_2O_3 in 100 cc. of sample."

(3) The Schoeller and Waterhouse phosphate method modified to adapt it to use with the official bismuth preparations as follows:

Accurately measure a portion of the preparation representing about 0.5 Gm. of Bi, dilute the solution to about 100 cc. with distilled water, and carefully add ammonia water until a slight permanent precipitate is formed. The precipitate formed in cold solution is not the crystalline oxynitrate but a flocculent basic nitrate which dissolves on the addition of nitric acid. Add 2 cc. of nitric acid, heat the solution to boiling and precipitate the bismuth while the solution is boiling by adding a 10 per cent solution of diammonium phosphate. The addition of ammonium phosphate should be made very slowly at first (preferably from a burette at the rate of about 30 drops per minute) and with constant stirring to favor the formation of a coarsely grained precipitate. When no more precipitate forms, the remainder of the precipitant may be added rapidly. A considerable excess of the ammonium phosphate solution should be used; about 60 cc. of 10 per cent solution for each 0.5 Gm. of bismuth was found to be best. After adding the precipitant, dilute the solution to 400 cc., digest the solution on a water-bath for 20 to 30 minutes, and decant the supernatant liquid through a Gooch crucible. Wash the precipitate twice with a hot 3 per cent solution of ammonium nitrate containing 0.5 cc. of nitric acid per liter, wash the precipitate into the crucible, dry and ignite gently. Each Gm. of $BiPO_4$ is equivalent to 0.6865 Gm. of Bi.

This procedure entirely obviates the formation of crystalline oxynitrate caused by deficiency of nitric acid, while the subsequent dilution of the liquid reduces the concentration of the nitric acid so that all of the bismuth is precipitated as phosphate.

ASSAY OF GLYCERITE OF BISMUTH.

Two samples of Glycerite of Bismuth prepared by the method of the National Formulary V were assayed by the three methods. Five-cc. samples of the glycerite were accurately measured from a pipette calibrated to contain 5 cc. and the glycerite adhering to the wall of the pipette was washed out with distilled water. The results given in the following table are expressed in terms of per cent Bi W/V.

TABLE I.—ASSAY OF GLYCERITE OF BISMUTH.

Method.	Analyst A. Sample 1.	Analyst A. Sample 2.	Analyst B. Sample 1.	Analyst B. Sample 2.
Sulphide	14.33, 14.77	12.35, 12.48	14.36, 14.40	12.45, 12.52
Mayer phosphate	14.29, 14.32	12.43, 14.47	14.38, 14.35	12.50, 12.46
Schoeller Waterhouse phosphate	14.69, 14.68	12.90, 12.60	14.60, 14.42	12.78, 12.82

The results show that the sulphide and the Mayer phosphate methods yield equally accurate and comparable results and that the Schoeller Waterhouse phosphate method yields slightly high results. Consequently, the Schoeller Waterhouse phosphate method was eliminated and further study was limited to the sulphide and Mayer phosphate methods. Samples of solution of bismuth, elixir of bismuth, elixir of pepsin and bismuth and of elixir of pepsin, bismuth and strychnine were prepared from the respective glycerites and assayed with results as follows:

TABLE II.

Preparation and Method.	Analyst A. Sample 1.	Analyst A. Sample 2.	Analyst B. Sample 1.	Analyst B. Sample 2.
Solution of Bismuth				
Sulphide	1.83, 1.79	1.61, 1.59	1.78, 1.80	1.57, 1.64
Mayer phosphate	1.81, 1.75	1.60, 1.63	1.83, 1.86	1.54, 1.58
Calculated	1.80	1.60	1.80	1.60
Elixir of Bismuth				
Sulphide	1.78, 1.79	1.58, 1.59	1.79, 1.80	1.62, 1.60
Mayer phosphate	1.81, 1.80	1.61, 1.60	1.82, 1.82	1.61, 1.60
Calculated	1.80	1.60	1.80	1.60
Elixir of Pepsin and Bismuth				
Sulphide	1.81, 1.80	1.59, 1.59	1.79, 1.79	1.61, 1.60
Mayer phosphate	1.78, 1.79	1.58, 1.57	1.78, 1.80	1.58, 1.59
Calculated	1.80	1.60	1.80	1.60
Elixir of Pepsin, Bismuth and Strychnine				
Sulphide	1.83, 1.79	1.61, 1.62	1.82, 1.80	1.63, 1.59
Mayer phosphate	1.81, 1.78	1.60, 1.58	1.78, 1.79	1.57, 1.58
Calculated	1.80	1.60	1.80	1.60

SUMMARY AND CONCLUSIONS.

1. A comparative study has been made of the accuracy of the sulphide, Mayer phosphate and Schoeller Waterhouse phosphate methods of estimating bismuth in bismuth containing liquid preparations of the National Formulary.

2. The Schoeller Waterhouse phosphate method does not yield accurate results when applied to these preparations.

3. Either the sulphide method or the Mayer phosphate method yields accurate and comparable results when applied to the glycerite, solution or elixirs of bismuth.

4. Since the Mayer phosphate method is simple and accurate, it might advantageously replace the sulphide method now official for the assay of glycerite of bismuth and be made official for the assay of the solution and elixirs containing bismuth.

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