ASSAY OF ELIXIR OF THREE BROMIDES NATIONAL FORMULARY VI.*

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Elixir of Three Bromides has been official in the last three revisions of the National Formulary. The assay provided for this galenical in the present edition of the National Formulary is merely a determination of total bromide. If a sufficiently valid reason exists for continuing the use of ammonium, potassium and sodium bromides combined in one preparation, the assay should indicate, at least approximately, the amounts of the individual bromides present. This investigation was undertaken to devise an assay procedure that would fulfil this requirement.

The direct determination of sodium and potassium in the past has been neglected, principally because the procedures recommended were tedious and unreliable. Barber and Kolthoff (1) published a method for the accurate determination of small amounts of sodium. Their method was based upon the precipitation of sodium with zinc uranyl acetate. Various modifications of this procedure, involving gravimetric and colorimetric determinations of the sodium uranyl zinc complex have appeared in the literature (2) (3) (4). Caley and Foulk (5) published a method analagous to that of Barber and Kolthoff using magnesium uranyl acetate as the precipitating agent. Caley and Foulk reported better results over a wide range (up to 0.050 Gm. sodium) with the magnesium reagent than with the zinc reagent; although the latter gave better results with small amounts of sodium (up to 0.008 Gm.). We have adapted Caley and Foulk's method for the determination of sodium in Elixir of Three Bromides National Formulary VI, and by employing the general procedures for the determination of ammonium bromide and total bromine, have calculated the amounts of ammonium, potassium and sodium bromides present.

EXPERIMENTAL.

Chemically pure ammonium, potassium and sodium bromides were dried to constant weight and then assayed. The values obtained for these salts were 99.98 per cent, 100.18 per cent and 100.40 per cent respectively. The high figures obtained in the latter two cases were probably caused by the presence of traces of chlorides. A standard Elixir was then prepared from these three salts, according to the official formula, containing ammonium bromide 80.0314 Gm., potassium bromide 80.0000 Gm. and sodium bromide 80.0492 Gm. per liter.

A dilution of the Elixir was prepared by measuring exactly 25 cc. and making up to a volume of 250 cc. with distilled water.

ASSAY FOR SODIUM BROMIDE.

Reagents. 1.—Solution of magnesium uranyl acetate. This solution is prepared as follows:

Solution A.		Solution B.	
Crystallized uranyl acetate	85 Gm.	Crystallized magnesium acetate	500 Gm.
Glacial acetic acid	60 Gm.	Glacial acetic acid	60 Gm.
Distilled water.	to 1000 cc.	Distilled water.	to 1000 cc.

Heat each solution separately to about 70° until the salts are dissolved, mix, allow to cool to 20°, and keep at this temperature for at least two hours to allow any excess to settle.

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Filter through a dry filter into a dry bottle. If further precipitation occurs on standing, filter before using.

2.—Alcohol (95 per cent) saturated with sodium magnesium uranyl acetate [$Mg(C_2H_3O_2)_2 . NaC_2H_3O_2 . 3UO_2(C_2H_3O_2)_2 . 6^1/_2H_2O$].

Experimental.—Several modifications, such as stirring the reaction mixture for five minutes and allowing to sit over night at 20°; the use of 2-cc. samples with one half the amount of reagent; and the employment of a ten minute stirring period were tried before adopting the procedure outlined below. The results of the last named assays are recorded under C in the table.

Procedure.—Pipette 5 cc. of the dilution into a 250-cc. beaker, add 100 cc. of reagent, place in a bath at 20° and stir for thirty minutes with a mechanical stirrer (or stir vigorously by hand for five minutes, then at five-minute intervals for one hour) and allow to stand until the supernatant liquid becomes clear. Wash any adhering precipitate from the stirrer-paddle with the aid of some of the reagent. Suspend the precipitate, and filter into a tared Gooch crucible, collecting the filtrate in a large clean, dry, test-tube. Transfer the remaining precipitate into the crucible with the aid of a rubber tipped rod and the first filtrate. Wash the precipitate with several 5-cc. portions of the alcoholic solution of the sodium magnesium uranyl complex, dry in an air oven at 105° for thirty minutes and weigh. The weight of the precipitate times the factor 13.66 gives the sodium bromide content of 100 cc. of Elixir. (Each Gm. of sodium bromide is equivalent to 0.7766 Gm. of bromine.)

ASSAY FOR AMMONIUM BROMIDE.

Procedure.—Pipette exactly 10 cc. of the Elixir into a distillation flask provided with a trap and a condenser, add 250 cc. of distilled water and an excess of 50 per cent sodium hydroxide solution. Distil the ammonia into 20 cc. of *N*/2 sulfuric acid, and titrate the excess acid with *N*/2 sodium hydroxide, using methyl red T.S. as an indicator. Each cc. of *N*/2 sulfuric acid is equivalent to 0.04898 Gm. of ammonium bromide or 0.03996 Gm. of bromine.

ASSAY OF POTASSIUM BROMIDE.

Procedure.—Pipette exactly 10 cc. of the dilution (1:10) into a suitable vessel, add slowly and with agitation, 30 cc. of *N*/10 silver nitrate, 2 cc. of nitric acid and 2 cc. of ferric ammonium sulfate T.S. Titrate the excess silver nitrate with *N*/10 thiocyanate. Each cc. of *N*/10 silver nitrate is equivalent to 0.00799 Gm. of bromine. The amount of potassium bromide (x) in 100 cc. Elixir may be calculated by the following formula:

$$x = 1.489\ [A - (B + C)]$$

in which

A = Total Bromine in 100 cc. Elixir
B = Bromine as NH_4Br in 100 cc. Elixir
C = Bromine as NaBr in 100 cc. Elixir.

The factor 1.489 converts bromine to potassium bromide.

The presence of potassium may be verified by the official tests.

The Gm. of sodium bromide per 100 cc. of standard Elixir determined by the several procedures tested are given in the following table.

TABLE I.

	Procedure. A.		Procedure. B.		Procedure. C.	
	Gm. NaBr Found.	% NaBr Recovered.	Gm. NaBr Found.	% NaBr Recovered.	Gm. NaBr Found.	% NaBr Recovered.
	7.920	98.92	7.941	99.19	7.999	99.93
	7.864	98.24	7.819	97.68	7.785	97.25
	7.834	97.86	7.954	99.37	7.878	98.41
	7.781	97.20	7.893	98.60		
	7.835	97.88	7.917	98.90		
	7.931	99.08	7.986	99.76		
	7.863	98.22	8.027	100.27		
Average	7.861	98.20	7.934	99.11	7.887	98.53

A—Stirred for 30 minutes with mechanical stirrer.
B—Stirred vigorously for 5 minutes, then stirred at 5 minute intervals for 1 hour, and let stand until clear.
C—Stirred vigorously for 10 minutes, then as in B.

The assay for sodium bromide showed the presence of 7.898 Gm. of sodium bromide per 100 cc. of Elixir (average of results) which is 98.7 per cent of the theoretical, and is equivalent to 6.134 Gm. of bromine. The assay for ammonium bromide showed the presence of 7.984 Gm. of ammonium bromide per 100 cc. of Elixir (99.8 per cent of theoretical), equivalent to 6.513 Gm. of bromine. The total bromine content per 100 cc. of Elixir was found to be 18.038 Gm. of bromine. Bromine present as potassium bromide = 18.038 Gm. − (6.134 + 6.513) Gm., or 5.391 Gm. of bromine; which is equivalent to 8.027 Gm. of potassium bromide. The value found for this salt is 100.3 per cent of the theoretical.

DISCUSSION.

In the determination of sodium the stirring must be quite vigorous at all times to obtain a quantitative precipitation of the complex. The employment of the first filtrate as a transferring agent minimizes the use of alcohol. In the official assay the National Formulary provides 50 cc. of N/10 silver nitrate to assay an aliquot containing a maximum of 0.250 Gm. of mixed bromides equivalent to 23.6 cc. of the silver solution. As this is an excess greater than 100 per cent, the amount of N/10 silver nitrate employed was reduced to 30 cc.

The estimation of potassium bromide yields results in good agreement with the theoretical.

SUMMARY.

A procedure is recommended for the determination of ammonium bromide and sodium bromide and the estimation of potassium bromide in the Elixir of Three Bromides National Formulary VI.

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A STUDY OF MASTIC IN THE PREPARATION OF ENTERIC MEDICAMENTS.*[1]

BY F. S. BUKEY[2] AND C. J. KLEMME.[3]

The object of this study was to determine the efficiency of mastic-talc and mastic-magnesium stearate as enteric coating materials. The use of talc as a drying agent is of common commercial practice in the application of an enteric coating. In one part of this study, magnesium stearate was used in place of talc, as it was

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[1] An abstract of a thesis presented to the faculty of the School of Pharmacy, Purdue University, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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