

Rotation of the flask at frequent intervals causes the buckshot to coat and recoat the sides of the flask with a thin layer of the moist powder, insuring complete extraction of the alkaloid or alkaloids by the chloroform. After carrying out the above procedure for several hours the chloroform is poured through a small filter paper and an aliquot part of 50 cc. collected.

The aliquot portion referred to is carefully transferred to a separatory funnel and extracted with dilute acid. The dilute acid is in turn made alkaline with ammonium or sodium hydroxide T. S. and extracted with chloroform. A test should be made in each case to insure complete extraction of the alkaloid. The final chloroform extractive is evaporated and the alkaloids determined either volumetrically or gravimetrically.

The weight of the alkaloid obtained multiplied by 2 gives the amount in the total sample used. The weight of the total sample used divided by the predetermined weight of one tablet gives the number of tablets containing the determined quantity of alkaloid or alkaloidal salt.

In many cases tablets containing no other chloroform-soluble material, the 50-cc. aliquot portion can be evaporated to dryness, the residue dissolved in 10 cc. of neutral dilute alcohol and directly titrated, using methyl red as the indicator, diluting the alcoholic solution to 100 cc. with distilled water after sufficient volumetric acid has been added to give a pink tint.

The following results were obtained in coated tablets by this method:

Tablet.	Theoretical Strychnine Sulphate Content.	Results.	Percentage.
A—	0.00216 Gm.	0.002088 Gm.	96.71
B—	0.00162 Gm.	0.001649 Gm.	101.25
C—	0.00216 Gm.	0.0021297 Gm.	98.60
D—	0.00108 Gm.	0.001025 Gm.	95.82
E—	0.00108 Gm.	0.001025 Gm.	95.82
F—	0.00108 Gm.	0.001022 Gm.	94.59

The theoretical Strychnine Sulphate contents above were obtained from the labeled quantity and do not make allowance for possible errors in manufacture although this in each instance was done under rigid control.

Any other solvent where chloroform is not indicated may be used with equally consistent results.

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SUGGESTED ASSAYS FOR SOME N. F. PREPARATIONS.*

STRONG RESORCINOL PASTE. MILD RESORCINOL PASTE.

BY WILLIAM B. BAKER.

The efficacy of the official resorcinol pastes as therapeutic agents is due mainly to the resorcinol and zinc oxide which they contain. It is, therefore, essential that standards be adopted fixing definitely the content limits of these ingredients, and that practical methods be developed for the quantitative determination of the

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same. With this object in view, the effort was made to adapt the methods of the U. S. P. X for the assay of resorcinol and zinc oxide, respectively, to the quantitative determination of these substances in the resorcinol pastes in question. The results obtained proved to be entirely satisfactory. These results, together with detailed descriptions of procedures, follow.

EXPERIMENTAL PART.

Preparation of Samples.—Samples of Strong Resorcinol Paste and Mild Resorcinol Paste were carefully prepared according to the directions given in the National Formulary V, assayed samples of resorcinol and zinc oxide being used in each case. Assay results showing the purity of resorcinol and zinc oxide follow:

Assay of Resorcinol and Zinc Oxide for Purity.—The methods prescribed by the United States Pharmacopœia X were followed for the assay of these materials for purity.

TABLE I.—RESULTS OF ASSAY OF RESORCINOL FOR PURITY (U. S. P. X METHOD).

Wt. of Sample in Gm.	Cc. of 0.1 N Br ₂ Added.	Cc. of 0.1 N Na ₂ S ₂ O ₃ Required.	Cc. of 0.1 N Br ₂ Consumed.	Per Cent Purity of Resorcinol.
1.67	53.92	9.31+	44.60+	98.026
1.60	53.92	11.21+	42.71—	97.96
1.583	53.92	11.62—	42.30+	98.074
1.595	53.92	11.36+	42.56—	97.923
			Average	97.99

TABLE II.—RESULTS OF ASSAY OF ZINC OXIDE FOR PURITY (U. S. P. X METHOD).

Wt. of Sample in Gm.	Cc. of N H ₂ SO ₄ Added.	Cc. of N NaOH Required.	Cc. of Excess Acid Consumed.	Per Cent Purity of Zinc Oxide.
1.6511	54.435	15.09+	39.33+	96.94
1.5083	54.435	18.49+	35.94+	96.96
1.7806	54.435	12.05+	42.38—	96.84
1.6478	54.435	15.10—	39.33+	97.13
			Average	96.97

Assay of Strong Resorcinol Paste. (1) Determination of Resorcinol.

- Reagents.—1. 0.1 N Bromine Water (Koppeschaar's Solution, U. S. P. X).
 2. Hydrochloric Acid, U. S. P. X.
 3. Potassium Iodide T.S.
 4. 0.1 N Sodium Thiosulphate Solution.
 5. Starch T.S.

Procedure.—Place 1 Gm. of the paste, accurately weighed, in a 250-cc. flask, add 40 cc. of hot water, stopper the flask tightly and shake it vigorously. Decant the supernatant liquid onto a wetted filter and collect the filtrate in a 100-cc. volumetric flask. Repeat the shaking out process with two 15-cc. portions of hot water, decanting after each extraction. Finally, rinse the contents of the flask onto the filter and wash with sufficient hot water to make 100 cc. of filtrate. Carefully preserve the filter and its contents for the determination of zinc oxide as directed below under "Assay for zinc oxide." Transfer 40 cc. of the filtrate, representing two-fifths of the weight of the paste taken, to a 500-cc. glass-stoppered flask having a long, narrow neck, add 50 cc. of tenth-normal bromine, dilute with 50 cc. of distilled water, add 5 cc. of hydrochloric acid, and at once stopper the

flask. Shake the mixture, allow it to stand for one minute, dilute it with 20 cc. of distilled water, add 5 cc. of potassium iodide T.S., allow it to stand for five minutes, and titrate the liberated iodine with tenth-normal sodium thiosulphate, using starch test solution as indicator. Each cc. of tenth-normal bromine corresponds to 0.001835 Gm. of $C_6H_4(OH)_2$.

TABLE III.—RESULTS OF ASSAY FOR RESORCINOL CONTENT.

Wt. of Sample in Gm.	Cc. of 0.1 N Br_2 Added.	Cc. of 0.1 N $Na_2S_2O_3$ Required.	Cc. of 0.1 N Br_2 Consumed.	Gm. of $C_6H_4(OH)_2$ Found per 100 Gm. Strong Resorcinol Paste.
1.0902	53.405	6.83+	46.56+	19.57
1.0446	53.405	9.11+	44.28+	19.47
1.1825	53.405	3.30-	50.10-	19.43
1.0822	53.405	7.86-	45.54-	19.53
				Average 19.50

Calculated percentage of resorcinol in sample (20×97.99) = 19.598

Average percentage of resorcinol found in sample = 19.50

Difference = 00.098

Percentage error ($00.098 \div 19.598$) $\times 100$ = 0.505

(2) Determination of Zinc Oxide.

Reagents.—1. Normal Sulphuric Acid.

2. Normal Sodium Hydroxide Solution.

3. Methyl Orange T.S.

Procedure.—Place the filter used in the preceding assay, together with its contents, into a small porcelain crucible and ignite to get rid of the liquid petrolatum and any starch which may be present. Digest the residue remaining in the crucible after ignition with 50 cc. of normal sulphuric acid until solution is complete. Then titrate the excess of sulphuric acid with normal sodium hydroxide, using methyl orange T.S. as indicator. Each cc. of normal sulphuric acid corresponds to 0.04069 Gm. of ZnO .

TABLE IV.—RESULTS OF ASSAY FOR ZINC OXIDE CONTENT.

Wt. of Sample in Gm.	Cc. of N H_2SO_4 Taken.	Cc. of N $NaOH$ Used.	Cc. of Excess Acid.	Gm. of ZnO per 100 Gm. Strong Resorcinol Paste.
1.0902	48.385	43.08-	5.30-	19.79
1.0446	48.385	43.31+	5.06+	19.73
1.1825	48.385	42.61+	5.76+	19.85
1.0822	48.385	43.19+	5.18+	19.49
				Average 19.715

Average percentage of zinc oxide found in sample = 19.715

Calculated percentage of zinc oxide in sample (20×96.97) = 19.394

Difference = 00.321

Percentage error ($00.321 \div 19.394$) $\times 100$ = 1.65

DISCUSSION.

The methods for the quantitative determination of resorcinol and zinc oxide described above, as previously stated, are essentially those given in the U. S. P. X for the determination of the purity of these substances, and no great difficulty was experienced in carrying them out after the substances were isolated. The isolation of the substances, likewise, presented little difficulty, as the resorcinol is

completely removed from the paste by shaking out with hot water and passing the washings through a filter. The zinc oxide and other insoluble matter composing the base of the paste are retained by the filter. After ignition, the zinc oxide content can readily be determined by titration.

The above methods were also applied to the quantitative determination of resorcinol and zinc oxide in Mild Resorcinol Paste and they were found to be equally as well suited to the assay of this preparation as to the assay of the strong paste.

Since the methods described above are comparatively simple, give accurate and concordant results, it is recommended that they be adopted for admission to the National Formulary, and that the following standards be prescribed for the resorcinol pastes contained therein:

Suggested Standards: Strong Resorcinol Paste.—One hundred grams of Strong Resorcinol Paste contain not less than 19 Gm. and not more than 21 Gm. of $C_6H_4(OH)_2$, and not less than 19 Gm. and not more than 21 Gm. of ZnO.

Mild Resorcinol Paste.—One hundred grams of Mild Resorcinol Paste contain not less than 9.5 Gm. and not more than 10.5 Gm. of $C_6H_4(OH)_2$, and not less than 24 Gm. and not more than 26 Gm. of ZnO.

STUDIES ON THE PREPARATION, TOXICITY AND ABSORPTION OF BISMUTH COMPOUNDS. II. BISMUTH SALTS OF ALI- PHATIC HYDROXY ACIDS.*

BY W. M. LAUTER, A. E. JURIST AND W. G. CHRISTIANSEN.

A great deal of work has been done with one acid of this series, namely, tartaric acid. The sodium and potassium salts of this acid in combination with bismuth have been used extensively in the treatment of syphilis both in aqueous solution and in oil suspension. Also a number of investigators have studied both the preparation of these compounds and their absorption, excretion and toxicity in animals.

The composition of bismuth tartrates and their preparation by different methods have been described by Rosenheim and Vogelsang (1), Cowley (2), Bauer (3), Maschman (4), Warren (5), Corfield and Adams (6, 7), Barthe (8), Fabregue (9), Picon (10), Godfrin (11), Von Oettingen and Ishikawa (12), Volmer (13), Hehner and Likiernik (14), Kober (15), Von Oettingen, Sollmann and Schweid (16), and Yoe and Mote (17). The toxicity, absorption and excretion of these compounds have been discussed by Ducrey (18), Pautrier (19), Didry (20), Pomaret and Didry (21), Raiziss and Brown (22), Raiziss and Severac (23), Giemsa (24), Giemsa and Weise (25), Lomholt (26), and Pacella (27). Also Browning, Cohen, Gulbransen, Phillis and Snodgrass (28) studied the comparative therapeutic action of the bismuth salts of several organic hydroxy acids including tartaric acid, gluconic acid, mannonic acid and others. An investigation of the effect of different solvent media on the absorption of and local reactions produced by bismuth tartrates in dogs was reported by Jurist and Christiansen (29).

The purpose of this investigation was to compare the toxicity and absorption of bismuth tartrates in aqueous solution and in oil suspension with bismuth tartrates and bismuth mucates combined with mannite, and with bismuth mucates

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