

THE COMPOSITION OF SOME COMPLEX BISMUTH TARTRATES USED IN THE TREATMENT OF SYPHILIS.*

BY L. E. WARREN.

During the past several years a number of complex bismuth compounds have come into use in the treatment of syphilis. Their use in this disease originated in France and the majority of the pharmacological and clinical tests with these compounds have been carried out by French investigators. However, several reports have appeared in American journals.

Comprehensive reviews of the literature concerning the use of bismuth compounds in syphilotherapy¹ have appeared from time to time, so that they need not be repeated here and American chemical manufacturers have been producing some of the preparations used. The compounds commonly employed are stated to be potassium sodium bismuth tartrate, potassium bismuth tartrate and to a lesser extent, bismuth oleate, quinine bismuth iodide and finely divided metallic bismuth. Some tests have been carried out with bismuth citrate, bismuth trioxide and a few other bismuth compounds.

There is considerable confusion in the literature concerning the composition of the so-called bismuth tartrates used in the treatment of syphilis. Robert and Sauton,² who were the first to experiment with the bismuth tartrates in syphilis of animals, state that they used "sodium bismuth tartrate" which they prepared by the method published by Cowley.³ The preparation which has been most used in France is claimed by Sazerac and Levaditi⁴ to be potassium sodium bismuth tartrate, and to be prepared also by the method given by Cowley.³ It is sold in an oily suspension under the name of Trepol. An examination of Cowley's paper reveals that the product which might be expected from the reaction which he described probably would not be potassium sodium bismuth tartrate, but previous to solution in sodium hydroxide, (which he directs as part of the process) would be more likely to be a basic bismuth tartrate. This will be discussed more fully later. The error of calling this product a "potassium sodium bismuth tartrate" has continued in the literature unchallenged.

Bismuth tartrate compounds appear to have been first described by Schwarzenberg in 1847.⁵ Since then a great variety of compounds of bismuth with tartaric acid have been prepared. The composition of the finished products appears to vary with the method of manufacture, slight deviations in procedure apparently being responsible for considerable differences. Some of these compounds are briefly mentioned herewith. Following Schwarzenberg, Schneider⁶ in 1853 prepared a variety of bismuth compounds including a basic bismuth tartrate.

* From the Laboratory of the American Medical Association, Chicago, Ill.

¹ *Jour. A. M. Assoc.*, 82, 661 (1923); *Ibid.*, 83, 2087 (1924); *Am. Jour. Syph.*, 7, 352 (1923).

² A. E. Robert and B. Sauton, *Action du bismuth sur la spirallose des poules. Ann. Inst. Past.*, 30, 261 (1916).

³ R. C. Cowley, *Organic Salts of Bismuth with Alkalies. Chem. & Drug*, 82, 212 (1913).

⁴ R. Sazerac and C. Levaditi, *Action du bismuth sur la syphilis et sur la trypanosomiase du Nagana. Compt. rend. acad. sci.*, 172, 1391 (1920).

⁵ A. Schwarzenberg, *Ueber eine Verbindung von Wismuthoxyd, Kali und Weinsteinsäure. Ann. Chem. Pharm.*, 61, 244 (1847).

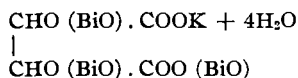
⁶ R. Schneider, *Untersuchungen über das Wismuth. Ann. Phys. Chem.*, 88, 45 (1853).

In 1866 Frisch¹ described a potassium bismuth tartrate to which he assigned the formula $K BiC_8H_2O_{12}$.

In 1894 Fischer and Grützner² prepared what they termed a neutral and an acid bismuth tartrate. The formulas ascribed to these compounds were respectively $C_4H_4O_6 \cdot 2Bi(OH)_2$ and $Bi(OH)_2 \cdot C_4H_5O_6$.

Baundran has described a variety of compounds of tartaric acid with bismuth and potassium.³

Rosenheim and Vogelsang⁴ discuss the constitution of potassium bismuth tartrate. The formula which they assign to the product is



This compound should theoretically contain 67.15 per cent of bismuth and 4.21 per cent of potassium.

Greco and Muschiatti⁵ prepared potassium sodium bismuth tartrate for their use by treating bismuth oxide with a warm solution of tartaric acid adding an aqueous solution of potassium tartrate, after warming on the water bath for an hour, and finally neutralizing with an aqueous solution of sodium hydroxide, using phenolphthalein as indicator. The product was dried on porcelain plates and preserved in bottles out of the light. It was a white powder which contained 48 per cent of bismuth. These authors assign the formula $KCOO \cdot CHOH : CHO BiO \cdot COONa$ to the compound.

Calcagno⁶ disagrees with Greco and Muschiatti and believes that the formula of the product should be $KCOO(CHOH)_2(COO)_2(BiO)_2(CHOH)_2COONa + H_2O$. The formula maintained by Calcagno theoretically should contain about 33.8 per cent of bismuth.

Greco⁷ replied to Calcagno at some length and Calcagno⁸ replied to Greco, each maintaining the correctness of his first contentions but without adding anything of consequence to the discussion.

Fabregue⁹ prepared a bismuth tartrate by dissolving bismuth nitrate in acetic acid, adding an aqueous solution of sodium tartrate, washing the resultant, white precipitate with alcohol and drying it at 60°. The product was a white, microcrystalline powder; insoluble in water but soluble in ammonia water.

Only very few analyses of potassium sodium bismuth tartrate or similar com-

¹ K. Frisch, *Ueber die Basicität der Weinsäure. Jour. prakt. Chem.*, 97, 278 (1866).

² B. Fischer and B. Grützner, *Ueber die Basicität der Weinsäure. Arch. Pharm.*, 232, 462 (1894).

³ G. Baundran, *Étude sur les émétiques. Ann. chem. phys.*, 7, 19, 536 (1900).

⁴ A. Rosenheim and W. Vogelsang, *Ueber einige Salze und Komplexsalze des Wismuts. Ztschr. f. anorg. Chem.*, 48, 205 (1906).

⁵ N. V. Greco and A. H. Muschiatti, *El. Bismuto en el tratamiento de la sífilis. Sem. Med.*, 28, 849 (1921).

⁶ O. Calcagno, *A Propósito del Tartrobismutato Sodicopotássico. Sem. Med.*, 29, 5 (1922).

⁷ *Tartrobismutato Sodicopotássico, Ibid.*, 64.

⁸ *Tartrobismutato Sodicopotássico, Ibid.*, 95.

⁹ M. Fabregue, *Sur une mode de préparation du citrate et du tartrate de bismuth. J. pharm. chim.* 7, 25, 341 (1922).

pounds have been reported. In 1922 Barthe¹ analyzed two commercial specimens of potassium, sodium bismuth tartrate. They were claimed to have the formula $\text{KOO} \cdot \text{CHO} (\text{BiO}) \text{CHOH} \cdot \text{COONa}$. A compound having this formula theoretically contains 48.02 per cent of bismuth. Barthe found 48.04 and 63.41 per cent of bismuth respectively.

Klauder and Raiziss² state that they have examined several commercial samples of potassium sodium bismuth tartrate (brand names not given) and have found less than 52 per cent of bismuth. The potassium salt which Klauder employed clinically was found by Raiziss to contain about 62 per cent of bismuth. The potassium content was not determined.

Hopkins³ prepared by the Cowley method³ what he calls the "quadruple salt" *i. e.*, potassium sodium bismuth tartrate. His analyses (made by Dr. J. H. Mueller) showed 54.2 per cent of bismuth but neither sodium nor potassium were determined. This compound will be referred to again.

In making a study of some of the commercial bismuth salts used in the treatment of syphilis, the first experiments made in the Chemical Laboratory A. M. A. were undertaken with the view of gaining some information concerning the composition of the compound made by the Cowley process.³ Accordingly a quantity of the salt was prepared by his method with the modification that the precipitate was dried at 100° instead of being dissolved in sodium hydroxide solution as Cowley directs. The yield from 70 Gm. of bismuth subnitrate was 81 Gm. of the dried product.

Cowley³ prepared his complex bismuth salt as follows:

Bismuth subnitrate.....	70	Gm.
Potassium sodium tartrate.....	64.5	Gm.
Nitric acid (specific gravity, 1.430).....	57	cc.
Sodium bicarbonate.....	57	Gm.

Mix the nitric acid with an equal volume of water and dissolve the bismuth subnitrate in the mixture. Add the Rochelle salt dissolved in a little water and then the sodium bicarbonate also dissolved in water. Heat to expel carbon dioxide, filter and wash the precipitate until the filtrate no longer gives a test for nitrates. Lastly dissolve the precipitate in normal sodium hydroxide solution.

It appears probable that the precipitate produced by this reaction is a basic bismuth tartrate insoluble in water but soluble in sodium hydroxide solution. Cowley called his finished product "a solution of sodium bismuth-tartrate" and never at any time claimed it to be a potassium sodium bismuth tartrate. From the rather indefinite statements in the literature, it would seem probable that the active substance in Trepol is the basic bismuth tartrate as prepared by Cowley (before solution in sodium hydroxide) and that it is not a potassium sodium bismuth-tartrate as is claimed by the French manufacturers and clinicians. This (the insoluble salt) is the preparation used by Hopkins in this country³ (mentioned

¹ L. Barthe, *Le. tartrobismuthate de potassium et de sodium*. *Bull. Soc. pharm. Bord.*, 60, 20 (1922).

² J. V. Klauder and G. W. Raiziss, "Bismuth in the Treatment of Syphilis," *Arch. Derm. & Syph.*, 7, 721 (1923).

³ J. V. Hopkins, "Bismuth in the Treatment of Syphilis." *Arch. Derm. & Syph.*, 7, 745 (1923).

earlier in this paper) but Hopkins calls his preparation the "quadruple salt," evidently believing that it contains both potassium and sodium. In a later paper Hopkins¹ refers to this compound as the "potassium sodium bismuth tartrate (soluble)" but gives no clew to his method of rendering the substance soluble.

Klauder² employed "the potassium salt because" he states "its chemical constitution is probably more definite, its preparation easier, and because its spirocheticidal action was regarded as efficient as the 'sodium potassium tartrobismuthate' which is probably a mixture of the potassium and sodium salts." This salt contained 62 per cent of bismuth.

LABORATORY SPECIMEN.

After being passed through a No. 30 sieve, the compound prepared in the laboratory by the Cowley³ method was a white, finely granular, odorless powder. It was insoluble in water but soluble in dilute alkalis; soluble in acids without effervescence. On exposure to air for several days, a weighed sample of the salt gained about 2.3 per cent of its weight. The compound was submitted to analysis by the following method:

Bismuth.—A weighed quantity of the bismuth salt was dissolved by agitation in weak ammonia water, the bismuth precipitated as bismuth sulphide from the warmed solution by hydrogen sulphide, the precipitate collected in a weighed Gooch crucible, washed successively with water, alcohol, ether, carbon disulphide, alcohol and ether in the order named, dried at 100° and weighed.

In three determinations the weight of the bismuth sulphide obtained corresponded to 60.64, 60.97 and 61.83 per cent of bismuth respectively.

Tartaric Acid.—The filtrate from which the bismuth sulphide had been removed was slightly acidulated with hydrochloric acid, the solution evaporated to half its volume, the residue placed in a graduated flask and made up to volume. An aliquot portion of the solution was evaporated to about 25 cc., an excess of potassium chloride added, followed by 2 cc. of glacial acetic acid and, after stirring, two volumes of alcohol. After standing over night the precipitate (potassium bitartrate) was collected in a Gooch crucible and washed with 50 per cent alcohol until free from acetic acid. The crucible was then placed in a beaker containing hot water and the acidity titrated with normal sodium hydroxide, using phenolphthalein as indicator. The results were calculated to tartaric acid, $H_2C_4H_4O_6$.

The results of two determinations were respectively 32.0 per cent and 31.95 per cent of tartaric acid.

Potassium and Sodium.—An aliquot portion of the diluted filtrate from the bismuth determination was evaporated to dryness in the presence of an excess of sulphuric acid, the residue heated to low redness, cooled, a fragment of ammonium carbonate added and the residue again heated. The mixture of potassium sulphate and sodium sulphate was weighed, its sulphate content determined as barium sulphate in the usual way and the relative proportions of potassium and sodium calculated by the method described in the reports of the Chemical Laboratory A. M. A. vol. 6, p. 44, 1913.

¹ J. V. Hopkins, "Antisyphilitic Action of Bismuth." *Jour. Am. Med. Assoc.*, 83, 2087 (1924).

The results from two determinations were 0.34 per cent and 0.22 per cent for potassium and 0.34 per cent and 0.30 per cent for sodium.

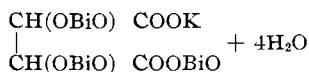
A salt having the composition $K_3Na_3Bi_2O_{16}H_{12}O_{24}$ ¹ when dried should contain 34.95 per cent of bismuth, 9.85 per cent of potassium and 5.80 per cent of sodium. According to the Powers, Weightman, Rosengarten Co., this compound should be soluble in water. It is very evident that a salt insoluble in water and containing 61 per cent of bismuth and considerably less than 1 per cent of total potassium and sodium, cannot be correctly called a "potassium sodium bismuth tartrate." Therefore, it is concluded that the salt prepared by Cowley's method as modified in the A. M. A. Laboratory is not a potassium sodium bismuth tartrate, but is, essentially, a bismuth tartrate containing small amounts of potassium and sodium compounds as impurities. A comparison between the formula suggested by the Powers, Weightman, Rosengarten Co., as well as the formulas for some other theoretical compounds, and the findings for the laboratory specimen are given in the following table:

TABLE I.—COMPARISON OF A LABORATORY SPECIMEN OF BISMUTH TARTRATE WITH THEORETICAL FORMULA.

Theory.	Potassium.	Sodium.	Bismuth.	Yield of tartaric acid.	Water of hydration.
$K NaBiC_4H_3O_7$	9.02	5.31	48.02	34.6	
$K NaBiC_8H_8O_{14} + H_2O$	6.34	3.73	33.75	48.7	2.92
$K_3Na_3Bi_2C_{16}H_{12}O_{24}$	9.85	5.80	34.95	50.4	
Laboratory Specimen	0.28	0.32	61.1	32.0	0

SPECIMEN FROM DERMATOLOGICAL RESEARCH LABORATORIES.

A specimen of potassium bismuth tartrate was received from the Dermatological Research Laboratories. It was a white, odorless powder, easily soluble in water. The aqueous solution had a very faintly alkaline reaction to litmus and gave precipitates with solutions of a number of alkaloidal salts and local anesthetics. The manufacturer stated that the compound was believed to have the composition approximately represented by the formula:



A compound having the formula indicated theoretically should contain 67.15 per cent of bismuth, 4.21 per cent of potassium and 7.75 per cent of water of hydration. Evidently this preparation is intended to correspond to that described by Rosenheim and Vogelsang.¹⁰ Analysis by the method used in the examination of the specimen prepared in the laboratory, omitting the treatment with ammonia water to produce a solution, gave 65.73 per cent of bismuth, 5.26 per cent of potassium, 20.5 per cent of tartaric acid liberated and 4.53 per cent of water of hydration. The examination indicates that the composition of the product is essentially as claimed by the manufacturer. A comparison of the theoretical composition with the findings is shown in Table II:

¹ This formula was suggested by the Powers, Weightman, Rosengarten Co. It is again referred to in this paper.

TABLE II.—ANALYSIS OF A SPECIMEN OF POTASSIUM BISMUTH TARTRATE COMPARED WITH THE THEORETICAL FORMULA.

Theory for.	Potassium.	Bismuth.	Tartaric acid liberated.	Water of hydration.
$\text{KBi}_3\text{C}_4\text{H}_2\text{O}_9 + 4\text{H}_2\text{O}$	4.21	67.15	16.15	7.75
D. R. L. Specimen	5.26	65.73	20.50	4.53

Potassium bismuth tartrate D. R. L. was accepted by the Council on Pharmacy and Chemistry for inclusion with New and Nonofficial Remedies and a description of the product published.¹

POWERS-WEIGHTMAN-ROSENGARTEN SPECIMEN.

A specimen of potassium sodium bismuth tartrate was submitted to the Council on Pharmacy and Chemistry by Powers-Weightman-Rosengarten Company. This product as manufactured by Poulenc Freres of Paris, had been sold abroad under the name of "Luatol." The American manufacturers (P. W. R.) stated that the product was believed to have the composition represented by the formula



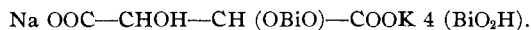
The theoretical composition of this compound may be seen by an examination of Table III. According to the submitted formula the product should contain no water of hydration. The product was a white, odorless powder, easily soluble in water to form a colorless solution having an alkaline reaction. Analysis of the salt by the methods previously described, omitting the treatment with ammonia water to produce solution, gave 8.74 per cent of potassium, 5.13 per cent of sodium, 31.41 per cent of bismuth and 12.53 per cent of loss on drying. The analysis shows that the product conforms reasonably closely with the theoretical formula if calculated as containing 9 molecules of water of hydration. A comparison of the findings and the theoretical formula is given in Table III.

TABLE III.—COMPARISON OF THE P. W. R. SPECIMEN OF POTASSIUM SODIUM BISMUTHO-TARTRATE WITH THEORETICAL FORMULAS.

Theory for.	Potassium.	Sodium.	Bismuth.	Water of hydration.
$\text{K}_3\text{Na}_3\text{Bi}_2\text{C}_{16}\text{H}_{12}\text{O}_{24}$	9.85	5.80	34.95	0
$\text{K}_3\text{Na}_3\text{Bi}_2\text{C}_{16}\text{H}_{12}\text{O}_{24} + 9\text{H}_2\text{O}$	8.67	5.10	30.75	11.98
P. W. R. Specimen	8.74	5.13	31.41	12.53

TREPOL.

Trepol is manufactured by Chenal, Douilhet & Co., of Paris. A specimen of Trepol in dry form was submitted to the Council on Pharmacy and Chemistry by the manufacturer's American agent, The Anglo-French Drug Co., of New York with the claim that it is "a tartro bismuthate of potassium and sodium containing 64 per cent of active bismuth." The formula claimed for the product is given herewith:



A compound of the formula claimed should contain 74.4 per cent of bismuth, whereas the amount claimed by the manufacturer is "64 per cent of active bismuth."

¹ *Jour. A. M. A.*, 82, 209 (1924).

Since this formula contains but one tartrate radical, every bond of which is saturated without allowance for the four (BiO_2H) groups, the formula as submitted at first appeared untenable. The manufacturer explained that both of the acidic functions of the tartaric acid are blocked—one by potassium and the other by sodium. This combination is rendered insoluble by an excess of bismuth oxide so as to form a basic compound. This portion of the formula (BiO_2H) may be considered as bismuth hydroxide which has been partially dehydrated.

The specimen of Trepol examined was a pale yellowish white, finely granular, odorless powder. It was nearly insoluble in water, but soluble in acids with effervescence. On analysis, the preparation lost about 2.6 per cent by drying at 100° . No statement was made in the submission concerning the presence or absence of water hydration. Determinations indicated about 72 per cent of bismuth¹ instead of 64 per cent as claimed. The product contained only about 1.3 per cent of potassium and only about 0.9 per cent of sodium instead of 2.79 per cent and 1.65 per cent respectively as is required by the formula submitted. Further, Trepol contained calcium, equivalent to 3.3 per cent of calcium carbonate. The presence of this substance was not declared in the submission and there appears to be no justification for its presence.

The analytical findings are tabulated herewith together with the composition as claimed by the formula:

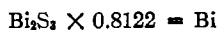
TABLE IV.—ANALYSIS OF TREPOL, COMPARED WITH THE COMPOSITION CLAIMED.

	Theory for submitted formula. %	Found. %
Loss on drying	0	2.59
Bismuth	74.44	72.10
Potassium	2.79	1.31
Sodium	1.65	0.89
Calcium (equivalent to calcium carbonate)	0	3.32

The findings for Trepol were brought to the attention of the manufacturer, who replied that the percentage of bismuth as found by the American Medical Association Laboratory was correct. While the theory of the formula required 74 per cent of bismuth, the manufacturer stated that the actual content may vary between 70 and 74 per cent, the average being from 72 to 73 per cent. The firm promised that the claim of 64 per cent of bismuth as made in the Trepol literature would be changed. The manufacturer claimed that not a trace of calcium could possibly be present in Trepol as none had been used in the manufacture of the product. The manufacturer also challenged the Laboratory's findings for potassium and sodium, claiming that the quantities as shown by the submitted formula were those actually present.

¹ The method for the determination of bismuth which was found to give the best results is as follows:

Weigh about 1 Gm. of the material, suspend it in 800 cc. of water, add 2 Gm. of potassium chloride, warm the mixture to 80° and saturate with hydrogen sulphide. Keep the mixture warm for three hours, passing in more hydrogen sulphate if necessary, collect the precipitate in a tared Gooch crucible, wash it respectively with water, alcohol, ether, carbon disulphide, alcohol and ether, dry to constant weight at 100° and weigh.



In view of the fact that the Laboratory findings had been challenged, a reëxamination of the submitted specimen of Trepol was undertaken. The findings for the second analysis are given in Table V.

TABLE V.—SECOND ANALYSIS OF TREPOL.

Loss on Drying.....	2.31 per cent
Bismuth.....	72.69 per cent
Calcium.....	1.51 per cent
Potassium.....	1.63 per cent
Sodium.....	0.86 per cent
Carbon dioxide (CO ₂).....	4.79 per cent*

* The specimen contained about 8 per cent of water-soluble material. This was found to consist almost entirely of potassium sodium tartrate.

From the results of the analysis it was calculated that the composition of the submitted specimen of Trepol was probably essentially as follows:

Water of hydration.....	2.3 per cent
Calcium carbonate.....	3.7 per cent
Potassium sodium tartrate.....	8.0 per cent
Bismuth subcarbonate (U. S. P. IX).....	36.7 per cent
Basic bismuth tartrate.....	49.3 per cent

In these calculations all of the calcium is assumed to be in combination with carbon-dioxide, and the balance of the carbon dioxide is assumed to be present in the form of bismuth subcarbonate having the approximate composition given in the U. S. Pharmacopœia. The balance of the bismuth is considered as a basic bismuth tartrate roughly approximating the composition claimed by Chenal, Douilhet & Co.

The findings for the second analysis of Trepol were submitted to the manufacturer. It was pointed out in the analytical report that the presence of calcium had been positively identified, notwithstanding the manufacturer's claim that not a trace of it could be present. The fact that the product contained nearly 5 per cent of carbon dioxide was mentioned and, as had been shown in the first analysis, the report emphasized further that the content of potassium and sodium was much lower than that indicated by the formula given by the manufacturer. The firm replied that their present analysis (made after the second report from the A. M. A. Chemical Laboratory had been received) confirmed the analysis of the A. M. A. chemists. They admitted the presence of calcium and of carbon dioxide but were unable to offer any satisfactory explanation for their presence.

The examination of Trepol reveals that its manufacturers, Chenal, Douilhet & Co., were ignorant of the composition of the product which they were selling. Its bismuth content was higher than claimed, it contained potassium sodium tartrate and calcium carbonate as impurities, and a considerable amount of other, carbonate probably bismuth subcarbonate, was present.

METZ SPECIMEN.

A specimen said to be potassium sodium bismuth tartrate was received from the H. A. Metz laboratories. This substance was not a market product, but its analysis was included as a matter of record. The manufacturer stated that the specimen contained 32 per cent of bismuth but that no determinations of potassium or of sodium had been made.

The product was a cream colored, hygroscopic powder, easily soluble in water forming a colorless solution which had an alkaline reaction to litmus. Determinations of bismuth, potassium, sodium and tartrate radicle were made. The analytical results are tabulated herewith:

TABLE VI.—ANALYSIS OF THE METZ SPECIMEN.

Bismuth.....	34.09 per cent
Potassium.....	0.59 per cent
Sodium.....	15.31 per cent
Yield of tartaric acid.....	44.22 per cent

The great excess of sodium over potassium in the Metz specimen as compared with the Dermatological Research Laboratories specimen recorded earlier in this report, indicates that the product is not potassium sodium bismuth tartrate, but a sodium bismuth tartrate, containing small amounts of potassium salts.

SPECIMENS FROM SYNTHETIC DRUG CO., LTD.

A specimen said to be potassium sodium bismuth tartrate (insoluble) and a specimen stated to be the soluble form of the first compound were submitted to the Council on Pharmacy and Chemistry by the Synthetic Drug Co., Ltd., of Toronto. The second product was stated by the manufacturers to have been prepared by dissolving the insoluble form in sodium hydroxide. The insoluble product was a white, bulky, odorless powder, practically insoluble in water. The aqueous suspension of the material was neutral to litmus paper. The soluble form was a white, odorless powder, soluble in water to form a clear, colorless solution which had an alkaline reaction to litmus. The products were analyzed and the findings are tabulated herewith:

TABLE VII.—ANALYSIS OF SYNTHETIC DRUG CO. SPECIMENS.

Sample.	Bismuth.	Potassium.	Sodium.	Water of hydration.
Insoluble	62.08	0.35	0.49	3.06
Soluble	57.06	0.35	6.33	1.78

From the results of the analysis it is evident that the first specimen is not a potassium sodium bismuth tartrate, but is probably a basic bismuth tartrate containing small amounts of potassium and sodium as impurities. The second specimen (soluble) is a sodium bismuth tartrate containing traces of potassium salts as impurities. When the analysis was brought to the attention of the firm it accepted that its insoluble product was not a potassium sodium bismuth tartrate but was probably a bismuth tartrate and voluntarily decided to change the name.

SUMMARY.

The results of this examination reveal that there is considerable diversity in the composition of the bismuth tartrate compounds used in syphilotherapy. Some appear to be potassium sodium bismuth tartrate. These are relatively low in bismuth content, are soluble in water and their solutions have an alkaline reaction to litmus. Others are potassium bismuth tartrate. These also are relatively low in bismuth and are soluble in water. Still others appear to be sodium bismuth tartrate which contains small amounts of potassium salts. They are soluble in water

to form solutions which are slightly alkaline to litmus. Their bismuth content is low. Others appear for the most part to be basic bismuth tartrates of unknown constitution but containing small amounts of sodium and potassium salts probably as impurities. Their bismuth content is relatively high and they are insoluble in water.

It is a reflection on manufacturing pharmacy that the error of Sazerac and Levaditi in calling the Cowley product potassium sodium bismuth tartrate has been allowed to remain in the literature for several years without challenge, whereas proper chemical control by the makers of Trepol would have revealed the error before any of the first batch of material had been marketed. The fact that some of these compounds have been used in so-called scientific research without their composition being known to the users is a reflection on research.

THE DISINFECTANT ACTION AND TOXICITY OF TRICHLOR-ISOPROPYL ALCOHOL.*

BY J. W. HOWARD AND F. D. STIMPERT.

INTRODUCTION.

A number of compounds containing the trichlor-methyl group have proven of interest because of their physiological action. One of these, trichlor-isopropyl alcohol (often called "isoprol" for practical purposes) has been investigated only to a limited extent. Impens¹ has found it to be a hypnotic. He also states that 0.10% solution of isoprol inhibits the fermenting action of the yeast cell.

It was the object of this investigation to add to this data a study of its disinfectant action and toxicity.

For this purpose we have compared it with isopropyl alcohol as this shows the effect of replacing a methyl by a tri-chlor-methyl group.

The toxicity of isopropyl alcohol has been studied by Macht² who found it to be less toxic than propyl alcohol but twice as toxic as ethyl alcohol. His study was made by intravenous injection in the cat. A different method and animal was used by us. Our study of its disinfectant action, however, is entirely new.

EXPERIMENTAL PART.

Preparation of Materials.—The isopropyl alcohol was obtained from the Research Laboratories of the Eastman Kodak Company.

The trichlor-isopropyl alcohol has previously been prepared by the combination of chloral and zinc dimethyl³ or methyl magnesium salts.⁴ The latter method

* Contribution from the Departments of Chemistry and Biology of the State University of Montana.

¹ *Therapeutische Monatshefte*, 17, 533 (1903).

² *J. Pharm. and Expt. Therapeutics*, 16, 1 (1921).

³ Garzarolli-Thurnlockh, *Ann.*, 210, 77 (1881).

⁴ Henry, *Compt. rend.*, 138, 205 (1904); *Rec. Trav. Chim.*, 24, 331 (1905); *Victoria Rec. trav. Chim.*, 24, 265 (1905).