

activity applies equally to both varieties of this drug; fourth, under proper direction there is no valid reason why American hemp cannot be collected to advantage to replace the imported article.

BIBLIOGRAPHY.

- ¹ Fraenkel—Archiv. der Path. u. Pharm., Vol. 49, 1903.
- ² U. S. Pharmacopœia, 1900.
- ³ J. A. M. A., 1897.
- ⁴ Houghton & Hamilton—Am. Jour. Pharmacy, Jan., 1908.
- ⁵ Eckler & Miller—Eighth Intern. Cong. App. Chem., Vol. 17.
- ⁶ Cushny's Pharmacology.
- ⁷ Kobert, Lehrbuch der Pharmakotherapie.
- ⁸ Die narkotische Genussmittel u. der Mensch.
- ⁹ Sollman's Pharmacology.
- ¹⁰ U. S. Dispensatory, 17th Edition.
- ¹¹ Hamilton—Jour. A. Ph. A., March, 1912.
- ¹² Scoville—Jour. A. Ph. A., March, 1912.
- ¹³ Hamilton, Lescobier, Perkins, J. A. Ph. A., Jan., 1913.
- ¹⁴ Schroof, Lehrbuch der Pharmacie.

ESTIMATION OF YELLOW PHOSPHORUS.

H. ENGELIARDT AND O. E. WINTERS.

At the Nashville meeting of the American Pharmaceutical Association we presented a paper on the estimation of Yellow Phosphorus. This paper was offered by us only as a preliminary one. Since then we have made numerous experiments in regard to the estimation of the metalloid and on the strength of these are now compelled in some instances to offer slightly modified methods. Since the paper did not appear in the Journal of the American Pharmaceutical Association up to May, 1914, we requested that the paper be not published prior to the meeting of the Association at Detroit when we would be in a position to give more details of the various methods applied by us in addition to a number of results obtained with pharmaceutic products of various kinds.

For the estimation of phosphorus several methods have been published. The distillation process for estimating phosphorus originated by Mitcherlich and later on modified by Dusart and Blondlot can be applied only when comparatively small quantities of phosphorus are present because the metalloid is not as volatile with steam as is generally accepted. It requires hours to distill as little as 50 mgms. of phosphorus. Neither the oxidation of the phosphorus in the distillate with nitric acid or bromine as carried out in Mitcherlich's method, nor the conversion of the phosphorus into silver phosphide and subsequent oxidation of the latter to phosphoric acid yield satisfactory results.

Various processes depending on the oxidation of phosphorus with nitric acid and simultaneously destroying any organic matter present, by this acid, by concentrated sulphuric acid or other chemicals were therefore recommended by Sayda,¹ Fry,² Vanderkleed and Turner,³ Woerner⁴ and others. These processes, however, have the disadvantage in that by them the total and not the elementary phosphorus alone is determined.

Reed⁵ determined the phosphorus by allowing a solution of bromine in acetone,

¹ Pharm. Zeitschr. f. Russl. XXXVI, 337.

² Pharm. Post, 1910, 969.

³ Proc. A. Ph. A., 1906, 395.

⁴ Pharm. Zeit., 1908, 398.

⁵ Analyst XXIV, 23.

previously standardized against phosphorus, to act on the phosphorus solution, until a faint but persistent yellow color was produced.

Most of the methods for estimating phosphorus depend on the property of phosphorus of forming insoluble phosphides with some of the heavy metals, especially silver and copper, which can easily be oxidized to phosphorous and phosphoric acid respectively.

The methods originated by Tothe,⁶ Louise,⁷ Stich,⁸ Fränkel,⁹ and Illes¹⁰ depend on the conversion of a solution of the phosphorus in a convenient solvent (in most cases acetone) into silver phosphide and estimating the latter as such or by oxidation into phosphoric acid.

The property of the copper salts to convert phosphorus into non-poisonous phosphide and finally into phosphoric acid has been known for years, and copper salts therefore have been used with advantage as an antidote in cases of phosphorus poisoning. The first one to use copper salts for estimating phosphorus was Straub¹¹ whose method was later modified by Katz,¹² who recommends using copper nitrate instead of copper sulphate for converting the phosphorus into phosphide, by Christimanos¹³, Korte¹⁴, Tauchert¹⁵ and others. All these investigators found that by the action of copper sulphate on phosphorus, phosphoric acid, sulphuric acid, copper phosphide and metallic copper are formed though they were not able to establish a definite equation for this reaction.

Finally Enell's method must be mentioned. This process which is exceptionally suitable for the estimation of phosphorus in phosphoretted oil depends on the oxidation of phosphorus by standardized iodine solution, titrating back the excess of the latter with thiosulphate solution then estimating alkalimetrically the amount of phosphoric acid formed by the oxidation and deducting from this the amount of acid originally present in the oil.

For estimating the phosphorus in commercial yellow phosphorus and in galenical preparations we have applied both Louise's silver method as modified by Fränkel and Straub's copper method with Katz's modification.

Yellow Phosphorus.—The phosphorus was carefully deprived of any oxidation products by scraping, then dried in an atmosphere of carbonic acid and weighed. It was then dissolved in chloroform free from air and the solution was made up with chloroform to a certain volume.

10 cc. of the solution corresponding to .03656 gm. of phosphorus was mixed in a bottle with 15 cc. of 10 *per cent.* copper nitrate solution from which the air previously had been expelled by heating. The air in the bottle was replaced by carbonic acid gas and the mixture shaken for about one-quarter hour. Hydrogen peroxide was then added and the mixture shaken again until the black color of the copper phosphide had disappeared. The aqueous solution was separated from the

⁶ Chem. Zeit., 1893, 1244.

⁷ Compt. rend., 1899, 394.

⁸ Chem. Zeit. Rep., 1901.

⁹ Pharm. Post, 1901, 117.

¹⁰ Wien. med. Pract., 1901, No. 2.

¹¹ Archiv der Pharm., 1903, 5, 535.

¹² Apoth. Zeit., 1903, 683.

¹³ Zeitschr. anorg. Chem., 1904, 303.

¹⁴ Inaugural Dissertation, Berne, 1906.

¹⁵ Zeitschr. anorg. Chem., 1912, 350.

chloroformic solution, the latter washed out twice with about 15 cc. of water and the combined aqueous solutions and wash-waters after the addition of nitric acid were evaporated to about 5 cc. testing from time to time for unoxidized phosphorous acid. When oxidation was complete the phosphoric acid was estimated in the aqueous liquid as magnesium pyrophosphate. Should any copper salt separate together with the ammonium magnesium phosphate, the latter is re-dissolved and re-precipitated.

In this way we obtained magnesium pyrophosphate corresponding to 101.5 *per cent.* of the phosphorus taken for the estimation. In order to find out whether the phosphorus contained any appreciable amount of oxidation products, the chloroformic solution of the phosphorus was shaken out with various quantities of carbonated water but the amount of magnesium pyrophosphate obtained from the aqueous solution and calculated for phosphorus, showed the phosphorus to have a purity of 99.2 *per cent.* In other words, only traces of oxidation products were present in the phosphorus used for this test.

In another series of experiments 15 cc. of a solution of phosphorus in chloroform containing .1064 gm. of phosphorus were treated in the same way, and the results obtained, calculated for phosphorus, were 100.5, 98.7, 99.8 and 100.0 *per cent.*

When substituting the copper nitrate by silver nitrate and filtering the silver phosphide, we obtained in the first experiments magnesium pyrophosphate corresponding to only 78.6, 77.1, 81.6 and 82.4 *per cent.* of the amount of phosphorus used. This amount was not materially decreased by previously washing the chloroformic solution with water. The results were 78.6, 80.9 and 79 *per cent.* The estimation was carried out by mixing the chloroformic phosphorus solution in a bottle filled with carbonic acid gas with about 10 cc. of a 50 *per cent.* silver nitrate solution, shaking the mixture for about one-half hour, and, after allowing to settle, collecting the silver phosphide in a Gooch crucible. The silver phosphide was then oxidized with 25 *per cent.* nitric acid and in the resulting solution the silver was removed by hydrochloric acid. The mixture was filtered again, the filtrate evaporated to dryness, the residue taken up in water and the phosphoric acid precipitated in the regular way.

The discrepancies in the results obtained by the copper nitrate method and the silver nitrate method were probably due to the fact that on adding to a solution of phosphorus in chloroform, silver nitrate or copper nitrate, some oxidation products of nitrogen are formed in addition to the respective phosphides, which in turn dissolve any metallic phosphide formed or inhibit the formation of the phosphide to some extent.*

In order to prove this, 15 cc. of the chloroformic phosphorus solution, containing .1064 gm. of phosphorus, were treated in an atmosphere of carbonic acid gas with copper nitrate, the mixture was shaken for one-half hour and after settling, the copper phosphide was collected in a Gooch crucible. It was oxidized with hydrogen peroxide solution with the addition of traces of nitric acid, and the solution was evaporated to dryness on a water-bath after the addition of more

* According to Bird and Diggs (Journ. Amer. Chem. Soc., 1914, page 1383), nitric acid is formed when converting the phosphorus into phosphides with copper nitrate or silver nitrate. They also found that nitric acid even when very diluted acts on the phosphorus.

nitric acid in order to convert all the lower oxidation products of phosphorus into phosphoric acid. The residue was then taken up with water and the phosphoric acid estimated in the usual way. By this method we obtained .224, .231 gm. of magnesium pyrophosphate. The filtrate from the copper phosphide was oxidized in the regular way by evaporation in the presence of nitric acid, the residue taken up in water and the phosphoric acid determined as magnesium pyrophosphate; .161, and .153 gm. of magnesium pyrophosphate were obtained. The combined magnesium pyrophosphate obtained from the precipitate and the filtrate therefore was .385 and .384 gm. respectively, corresponding to 100.7 and 100.6 *per cent.* of phosphorus. In another experiment 15 cc. of the phosphorus solution were treated with silver nitrate solution, the silver phosphide was collected in a Gooch crucible, oxidized with nitric acid, etc. The following results were obtained: .307, .303, .305, .308 gm. of magnesium pyrophosphate. In the filtrate .065, .064, .069, .064 gm. of magnesium pyrophosphate was found. This gives a total .372, .371, .374, .372 gm. respectively of magnesium pyrophosphate, corresponding to 97.9, 97.6, 98.1, 97.6 *per cent.* of phosphorus.

These experiments show that the phosphorus cannot be estimated by collecting the copper phosphide or silver phosphide on a filter, because in the reaction some substances are formed which dissolve a part of the phosphide already formed or convert the phosphorus into oxidation products which naturally do not form phosphides.

For the estimation of phosphorus in a solution in chloroform or any other suitable solvent, the copper nitrate method therefore is to be preferred, because the mixture of copper phosphide, copper nitrate, water, chloroform, etc., can be treated directly with hydrogen peroxide solution, while in the silver nitrate method the silver phosphide cannot be well oxidized with nitric acid in the presence of chloroform. In the silver method the silver phosphide is preferably collected in a Gooch crucible and in the filtrate the oxidation products are to be estimated separately thus involving two manipulations instead of one as in the copper method. In our previous paper we expressed the opinion that copper phosphide is more stable than silver phosphide. This, however, is not the case as has developed in the course of later experiments.

Phosphorus Resin.—In our previous paper we reported that for estimating the phosphorus in phosphorus resin we applied the following methods to a sample which was several years old and reputed to have contained originally 10 *per cent.* of phosphorus. About 4 gms. of the resin (accurately weighed) were dissolved in 50 cc. of air-free chloroform in a separator, 20 cc. of air-free water were added, the air in the separator replaced by carbonic acid gas and the mixtures shaken for one-quarter hour. An aliquot part of the chloroformic solution was then drawn off and treated with copper nitrate solution as given above. The resin was found to contain 7.33 and 7.45 *per cent.* respectively of phosphorus, thus showing that about 25 *per cent.* of the latter had been lost either by volatilization or oxidation.

Since then we have made quite a number of experiments in regard to estimating the phosphorus in phosphorus resin, especially for the purpose of finding out whether or not the ammonium magnesium phosphate is free from magnesium

abietate and also to what extent phosphoric acid is formed when treating the copper phosphide with hydrogen peroxide solution only.

The resin used for these experiments was dried over sulphuric acid in an atmosphere of carbonic acid gas for one week. One gramme was dissolved in 50 cc. of air-free chloroform, the solution was shaken out with various small portions of water in order to remove any oxidation products, and was then shaken well for one-half hour with 10 cc. of a 10 *per cent* copper nitrate solution. After the addition of an excess of hydrogen peroxide solution the mixture was shaken again until the copper phosphide had been oxidized, i. e., until the black color of the latter had disappeared. The aqueous solution was then separated in the usual way, mixed with nitric acid and evaporated to dryness. The residue was taken up in water with the addition of hydrochloric acid and the phosphoric acid precipitated with magnesia mixture.

By this process the following results were obtained:—

.224 gm. of $Mg_2P_2O_7$ = 6.25 *per cent.* of phosphorus
 .219 gm. of $Mg_2P_2O_7$ = 6.13 *per cent.* of phosphorus
 .224 gm. of $Mg_2P_2O_7$ = 6.25 *per cent.* of phosphorus
 .225 gm. of $Mg_2P_2O_7$ = 6.26 *per cent.* of phosphorus

In the next series of experiments the copper phosphide was treated in the same way, the phosphoric acid precipitated with ammonium molybdate solution, the ammonium phospho-molybdate dissolved in ammonia water and the phosphoric acid again precipitated with magnesia mixture. We then obtained:—

0.225 gm. of $Mg_2P_2O_7$ = 6.26 *per cent.* of phosphorus
 0.220 gm. of $Mg_2P_2O_7$ = 6.15 *per cent.* of phosphorus

In still another series of experiments, the phosphoric acid obtained by oxidizing the copper phosphide and further oxidizing the resulting solution with nitric acid was precipitated with magnesia mixture, the ammonium magnesium phosphate was dissolved in hydrochloric acid, and this solution was shaken out with ether to remove any abietic acid. The phosphoric acid was then precipitated with magnesia mixture. This yielded:—

.227 gm. of $Mg_2P_2O_7$ = 6.34 *per cent.* of phosphorus
 .224 gm. of $Mg_2P_2O_7$ = 6.25 *per cent.* of phosphorus

These results clearly show that in precipitating the aqueous solution with magnesia mixture no magnesium abietate is carried down with the ammonium magnesium phosphate.

That by oxidizing the copper phosphide with hydrogen peroxide solution alone, only a part of the phosphorus is oxidized to phosphoric acid is shown by the following experiment:—

One gramme of the above resin was treated as given before and the aqueous solution obtained after decomposing the copper phosphide with hydrogen peroxide solution was precipitated with magnesia mixture.

.140 gm. of $Mg_2P_2O_7$ = 3.92 *per cent.* of phosphorus
 .140 gm. of $Mg_2P_2O_7$ = 3.92 *per cent.* of phosphorus
 .143 gm. of $Mg_2P_2O_7$ = 4.05 *per cent.* of phosphorus

were obtained, thus showing that only 50 *per cent.* of the copper phosphide had been oxidized to phosphoric acid. It is, therefore, absolutely necessary to oxidize the aqueous liquid containing the oxidation products of the phosphorus with a strong oxidizing agent, preferably nitric acid.

When applying the silver method to the resin only

.153 gm. of $Mg_2P_2O_7$ = 4.27 per cent. of yellow phosphorus
 .153 gm. of $Mg_2P_2O_7$ = 4.27 per cent. of yellow phosphorus
 .148 gm. of $Mg_2P_2O_7$ = 4.14 per cent. of yellow phosphorus

were obtained, or only about 65 per cent. of the amount obtained by the copper method. With another old resin the following figures were obtained:—

Copper method	5.57 per cent.	Silver method	3.88 per cent.
	5.85 per cent.		3.82 per cent.
	5.85 per cent.		4.02 per cent.

thus again showing that by the silver method only about two-thirds of the phosphorus as found by the copper method is obtained.

For estimating the oxidation products present in the resin, the following experiments were made with a preparation containing

7.33 per cent. of phosphorus; 7.45 per cent. of phosphorus

when assayed by the copper nitrate method.

4 gms. of resin were dissolved in 50 cc. of air-free chloroform and the solution was shaken out in a separator filled with carbonic acid gas with several portions of air-free water. The chloroformic solution was transferred to a 100 cc. graduated flask and the volume of the liquid was made up with air-free chloroform to the mark. In aliquot parts of the chloroformic solution the phosphorus was determined by the copper nitrate method directly, without separating the copper phosphide. The aqueous solution after expelling any dissolved carbonic acid by heating was titrated with N/10 caustic potash solution of which 51.3 cc. 50.4 cc. were required for neutralization, using phenolphthalein as indicator. This amount corresponds to 12.8 and 12.6 cc. respectively for one gramme of resin. In another series of experiments only 2 gms. of resin were used for the estimation, when 26.6 and 26.0 cc. of N/10 KOH were used, corresponding to 13.3 and 13.0 cc. for one gramme of resin. Since the alkali is used for the various oxidation products of the phosphorus, it was impossible to calculate the amount of phosphorus present as oxidation products from the amount of alkali used in the titration. The aqueous liquids were therefore evaporated after the addition of nitric acid and in the residue the phosphoric acid was estimated as magnesium pyrophosphate. Thus the following results were obtained:—

Experiment I. (4 grams.)	.281 gm. of $Mg_2P_2O_7$	
corresponding to	.288 gm. of $Mg_2P_2O_7$	
	.07024 gm. of $Mg_2P_2O_7$	in one gm. of resin or to
	.072 gm. of $Mg_2P_2O_7$	
	1.96 per cent. of phosphorus	
	2.03 per cent. of phosphorus	
Experiment II. (2 grams.)	.146 gm. of $Mg_2P_2O_7$	
corresponding to	.149 gm. of $Mg_2P_2O_7$	
	.073 gm. of $Mg_2P_2O_7$	
	.0745 gm. of $Mg_2P_2O_7$ or to	
	2.04 per cent. of phosphorus	
	2.065 per cent. of phosphorus	

These experiments show that the direct copper method can be used for estimating the percentage of elementary phosphorus in phosphorus resin. They also show that it is quite easy to estimate the amount of oxidation products of phosphorus present in the preparation.

Phosphorus Paste.—For phosphorus paste such as is used for making pills the following method was applied. About one gramme of the paste, exactly weighed, was mixed in a bottle filled with carbonic acid gas, with 25 cc. of air-free chloroform and 25 cc. of air-free water and the mixture shaken for fifteen minutes. After allowing the mixture to separate, the aqueous layer was siphoned off, and the chloroform was shaken once more with 15 cc. of air-free water to remove the last traces of oxidation products of phosphorus. The water was again separated from the chloroformic solution and the latter was treated with copper nitrate and silver nitrate respectively and the estimation carried out as outlined above.

In a paste supposed to contain 7 per cent. of phosphorus, 6.86 and 6.7 per cent. were found by the copper method. By the silver method, only 5.78 and 5.86 per cent. of phosphorus were found. The above method applied for the estimation of phosphorus in another paste supposed to contain 10 per cent. of phosphorus was modified in that the aqueous solution after separating was shaken out with two portions of 25 cc. each of chloroform in order to remove any phosphorus suspended in the liquid. The combined chloroformic liquids were then treated in the regular way with copper nitrate solution. Thus 9.29 and 9.64 per cent. of phosphorus were obtained, by the silver method only 7.19 and 7.24 per cent.

Spirit of Phosphorus.—The N. F. directs that spirit of phosphorus be made by boiling 1.2 gms. of phosphorus with 1000 cc. of absolute alcohol until solution has taken place, and after cooling replacing any alcohol lost by evaporation. No requirements are given for the finished spirit, and it is probably understood that the spirit contain about 0.1 per cent. of phosphorus. In our previous paper we reported that we had been unable to prepare a spirit containing even approximately the amount of phosphorus required and we ascribed this shortage to oxidation of the phosphorus taking place during the boiling.

The method which we applied at that time was the following:—25 cc. of the spirit were transferred to a separator, mixed with air-free copper nitrate solution and the air in the separator replaced by carbonic acid gas. The mixture was then shaken well for a short time and allowed to stand until complete separation of the copper phosphide had taken place. The latter was collected on a filter in an atmosphere of carbonic acid gas, washed with a little air-free copper nitrate solution, decomposed by hydrogen peroxide solution preferably with the addition of a few drops of nitric acid, the solution evaporated in the presence of nitric acid to about 5 cc. and the phosphoric acid estimated as magnesium pyrophosphate. In the filtrate from the copper phosphide the oxidation products present in the spirit were estimated in the regular way. We thus obtained the following results with a spirit which was prepared by boiling phosphorus in excess with absolute alcohol for 12 hours and preserving the spirit in a bottle filled with carbonic acid gas.

<i>Phosphorus converted into copper phosphide.</i>	<i>Phosphorus present as oxidation products in filtrate from copper phosphide.</i>
0.068 per cent.	0.123 per cent.
0.073 per cent.	0.116 per cent.
0.0678 per cent.	
0.0704 per cent.	
0.069 per cent.	
0.0708 per cent.	

At that time we made a number of experiments by precipitating the phosphorus from the spirit in the presence of varying amounts of alcohol and water, and since

we found that the strength of the alcohol did not have any material influence on the yield of copper phosphide we concluded that the phosphorus was precipitated quantitatively as phosphide. However, we did not take into consideration the amount of phosphorus not converted into phosphide, nor the amount of phosphide redissolved by the oxidation products of nitrogen which are formed in the reaction.

Since then (see results below) we have found that in making spirit of phosphorus only about 10 *per cent.* of the phosphorus is converted into oxidation products during the boiling process. The above spirit therefore contained

0.172 *per cent.*

0.170 *per cent.*

of phosphorus instead of about 0.07 *per cent.* as reported at that time.

After numerous experiments we finally found the following method to be quite reliable for estimating the yellow phosphorus in the spirit:—

25 cc. of the spirit (prepared by boiling an excess of phosphorus with ordinary alcohol) was mixed with 50 cc. of air-free chloroform and 50 cc. of water. The mixture was shaken well and when complete separation had taken place the chloroformic solution was drawn into a flask filled with carbonic acid gas. The aqueous liquid was shaken out with two more portions of 25 cc. each of chloroform in order to remove any phosphorus suspended in the aqueous solution and the combined chloroformic liquids were then treated with copper nitrate in the usual way. The copper phosphide mixture was oxidized with H_2O_2 and the phosphoric acid estimated in the usual way. In the aqueous liquid obtained by shaking out the diluted spirit with water, the oxidation products of phosphorus were estimated. We thus obtained the following results:—

Phosphorus as such in the Spirit
.133 gm. $Mg_2P_2O_7$ = .149 *per cent.*
.137 gm. $Mg_2P_2O_7$ = .153 *per cent.*

Oxidation Products.
0.0123 *per cent.*
0.0121 *per cent.*

In another series of experiments the spirit diluted with water was shaken out with chloroform, the chloroformic solution was treated with copper nitrate, the copper phosphide separated by filtration in an atmosphere of carbonic acid gas and the phosphorus estimated both in the precipitate and filtrate. We obtained

Phosphorus from precipitate.
0.071 gm. $Mg_2P_2O_7$ = 0.0795 *per cent.*
0.071 gm. $Mg_2P_2O_7$ = 0.0795 *per cent.*

Phosphorus from filtrate.
0.062 gm. $Mg_2P_2O_7$ 0.0693 *per cent.*
0.066 gm. $Mg_2P_2O_7$ 0.0715 *per cent.*

Replacing copper nitrate by silver nitrate, filtering the silver phosphide, etc., we obtained:—

Phosphorus from precipitate.
.102 gm. $Mg_2P_2O_7$ = .114 *per cent.*
.100 gm. $Mg_2P_2O_7$ = .116 *per cent.*

Phosphorus from filtrate.
0.026 gms. $Mg_2P_2O_7$ 0.0297 *per cent.*
0.026 gms. $Mg_2P_2O_7$ 0.0291 *per cent.*

These results clearly show that copper phosphide is more soluble than silver phosphide in the oxidation products of nitrogen formed by the action of copper nitrate on a chloroformic solution of phosphorus in the presence of alcohol.

We have made a series of experiments with the purpose in view to reduce the amount of soluble phosphorus compounds by filtering the silver phosphide in an atmosphere of carbonic acid gas, but this seems to have no influence whatever on the results. In our previous paper we pointed out that the spirit of phosphorus is a rather unstable preparation even when kept in an atmosphere of carbonic acid, and this statement has been verified by recent experiments.

A spirit assaying at the time of manufacture .137 *per cent.* assayed, after one week's standing, only 0.117 *per cent.* and the oxidation products, calculated as phosphorus, had increased from 0.0123 *per cent.* to 0.0313 *per cent.* After three week's standing the percentage of phosphorus had been decreased to 0.088 *per cent.* A spirit prepared under exactly the same conditions, which, however, was not assayed at the time of manufacture, showed after four months standing only 0.0415 *per cent.* of yellow phosphorus and 0.087 *per cent.* of phosphorus present as oxidation products.

Only freshly prepared spirit of phosphorus should therefore be used.

Phosphorus Pills:—The process applied for assaying phosphorus pills and tablets both of plain and complex composition, is almost identical with that given for the assay of phosphorus paste.

A quantity of pills equivalent to about one grain of phosphorus is mixed in a bottle with 25 cc. of air-free water and 100 cc. of air-free chloroform. The air in the bottle is replaced by carbonic acid gas and the mixture is then shaken well until the pills are disintegrated. After allowing the liquids to separate as much as possible the aqueous layer is siphoned off. The mixture is then shaken with sufficient tragacanth to eliminate the remaining water, an aliquot part of the chloroformic solution is filtered off, treated with copper nitrate, etc.

We have examined a great number of pills and tablets and the following results may therefore be of interest:—

Phosphorus Pills plain 1/100 gr.

1/92, 1/92.7, 1/92, 1/93, 1/90 gr.

Phosphorus Pills plain 1/25 gr., 1/23.4, 1/24.2, 1/25.

Phosphorus Pills plain 1/50 gr.

1/48, 1/45, 1/46.5 1/46.2 gr.

Pills claimed to contain 1/30 gr. of phosphorus in addition to extract of damiana and extract of nux vomica, were found to contain 1/30 gr. and 1/31 gr. of phosphorus respectively.

Four lots of Aphrodisiac pills which contained, in addition to 1/100 gr. of phosphorus, extract of damiana and extract of nux vomica assayed 1/102 gr., 1/112, 1/98, 1/101 gr.

Another kind of Aphrodisiac pills which contained, in addition to the above ingredients, powdered muirapuana were found to contain 1/93 and 1/94 gr. of phosphorus instead of 1/100 gr. claimed on the label.

Pills coated with sugar, showed that no loss of phosphorus is entailed in the coating process as shown by the assay of four lots of Aphrodisiac pills which assayed, instead of 1/100 gr. of phosphorus, 1/102, 1/98, 1/101 and 1/102 gr.

All these assays were carried out with the copper method without filtering the copper phosphide. These results were obtained with freshly-made pills. In the manufacture of these pills an excess of 10 *per cent.* of phosphorus had been added to the pill mass in order to meet any loss of phosphorus by volatilization and oxidation.

That, however, phosphorus pills are not absolutely stable may be shown by the following results:—Plain phosphorus pills which were one year old showed only 86.2 *per cent.* of the amount of phosphorus claimed on the label; pills containing 1/50 gr. after one and one-half years showed only 83.5 *per cent.*; one year old 1/100 gr. pills assayed 76 *per cent.*; nine months old 1/150 gr. pills only 79 *per*

cent. These results seem to show that the greater the dilution of the phosphorus in the pill mass the greater the loss of phosphorus.

While the loss of the metalloid is not very great in plain pills it is quite marked in complex pills. Aphrodisiac pills which were one year old and which contained 1/100 gr. of phosphorus, in addition to extract of nux vomica and extract of damiana, contained after one year only 42 *per cent.* of the phosphorus present.

In a lot of Aphrodisiac pills one year old, which contained nux vomica and damiana with 1/100 gr. of phosphorus, only 57 *per cent.* of the phosphorus was found.

A lot of the same kind of pills 11 years old showed only 16 *per cent.* of the phosphorus as claimed on the label.

Pills containing in addition to 1/100 gr. of phosphorus, 1/4 gr. of extract of nux vomica, showed after three years 46.5 *per cent.* Pills containing in addition to 1/50 gr. phosphorus, 1/4 gr. of extract of nux vomica, showed after one and one-half years 42.5 *per cent.* of phosphorus, while other pills which contained in addition to 1/50 gr. of phosphorus, 1/8 gr. of extract of nux vomica, after the expiration of three years still showed 75 *per cent.* of phosphorus.

Pills containing 1/50 gr. of phosphorus in addition to 1 gr. powdered cantharides and 1 gr. of powdered nux vomica, showed after two years 68.5 *per cent.* of the amount of phosphorus originally present.

Phosphorus, Quinine and Nux Vomica pills containing 1/50 gr. phosphorus, 1 gr. quinine sulphate and 1/4 gr. extract of nux vomica contained after one year 45 *per cent.* of phosphorus. On the other hand pills containing 1/40 gr. phosphorus, 1 gr. zinc sulphate, 2 grs. extract valerian, still showed after three years 91 *per cent.* of the phosphorus originally present.

That the presence of extracts has a greater influence on the dissipation of the phosphorus than plain ingredients such as alkaloids, etc., may be shown by the following results. Phosphorus and Strychnine pills supposed to contain 1/50 gr. phosphorus and 1/60 gr. strychnine showed after one year 89.5 *per cent.* of phosphorus; pills containing 1/100 gr. of phosphorus and 1/60 gr. of strychnine still showed after three-quarters of a year, 93 *per cent.* of the amount of phosphorus. Phosphorus, Quinine and Strychnine pills containing 1/50 gr. of phosphorus, 1 gr. quinine sulphate, 1/60 gr. strychnine, after two years still contained 85 *per cent.* of phosphorus.

As has been pointed out in our previous paper, the presence of iron salts seem to favor the dissipation of the phosphorus, because in four lots of pills containing varying amounts of iron in the form of iron carbonate or reduced iron, phosphorus was found only in very small amounts. We have again made quite a number of experiments with Aphrodisiac pills containing in addition to the other ingredients, phosphorus and iron bromide. We have tried the copper nitrate, silver nitrate and copper acetate methods, but in no case have we been able to obtain trustworthy results. The phosphorus seems to act on the iron bromide and thus make the assay extremely difficult, if not impossible.

Of tablets we examined only a few lots containing extract of damiana and extract of nux vomica in addition to 1/30 gr. of phosphorus. In freshly made tablets we found 1/29, 1/31, 1/28, 1/33 gr. of phosphorus. On reassaying the tablets after 1, 2, 4 and 6 months we found the amount of phosphorus originally

present in the tablets had decreased considerably. This seems to show that the phosphorus keeps better in pill mass than in tablet mass and also better in coated than in uncoated pills.

Elixir of Phosphorus.—In our previous paper we reported that we had applied the following process for estimating yellow phosphorus in elixirs of phosphorus, especially in those which are largely used as aphrodisiacs, such as Elixir Phosphorus, Nux Vomica and Damiana.

25 cc. of the elixir under examination are mixed with 100 cc. of air-free chloroform in a 150 cc. bottle, the air in the bottle is replaced by carbonic acid gas and the mixture is shaken well for one-quarter hour. An aliquot part of the chloroformic solution (taking into consideration the amount of alcohol present in the preparation) is then separated, shaken with copper nitrate and the assay is then finished in the usual way. We reported at that time that elixirs of this kind made with freshly-prepared spirit of phosphorus do not retain the phosphorus for any length of time. This could be proven not only by assaying the elixir according to the copper method, but also by applying Mitcherlich's test.

Quite recently we have modified the method in the following way:—25 cc. of the elixir is mixed with 50 cc. of air-free water in a separator, the air in the separator is replaced by carbonic acid gas and the mixture is shaken out with 50, 25 and 25 cc. of air-free chloroform. By this process the alcohol present in the elixir does not need to be taken into consideration. The combined chloroformic liquids were then shaken out once with 10 cc. of air-free water in order to remove any oxidation products of the phosphorus suspended in the chloroformic solution, and the latter was then treated with copper nitrate in the regular way. An elixir which contained in addition to the other ingredients 24.40 *per cent.* of spirit of phosphorus, yielded when assayed by the copper method only 0.0198 *per cent.* of phosphorus. The spirit used for making this elixir assayed .09 *per cent.* of elementary phosphorus. After three weeks standing in an ice-chest the percentage of phosphorus had been reduced to 0.0179 *per cent.*, thus showing a loss of about 10 *per cent.* It is rather difficult to estimate the amount of phosphorus in the regular Elixir Phosphorus, Nux Vomica and Damiana which contains only about 6 *per cent.* of spirit of phosphorus. We have made a great number of experiments with various lots of this elixir, but the results obtained, although agreeing very well when made with the same lot of elixir, varied considerably from those obtained with other lots of the elixir. This is probably due to the presence of traces of phosphates in the various ingredients used for manufacturing the elixir, which, considering the small amount of phosphorus present in the preparation, are liable to upset the results considerably.

Having found that a reliable method is available for estimating phosphorus in most pharmaceutical preparations, we expect to determine the rate of deterioration of such products. We shall also apply other copper salts, copper sulphate, acetate, chloride, etc., for converting the phosphorus into phosphide, and we hope to be able to report on these experiments at the next meeting of the Association.

Analytical Laboratory of Sharp & Dohme, Baltimore, Md., July, 1914.