

THE ASSAY OF PHOSPHORIC ACID AND THE SODIUM PHOSPHATES.*¹

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INTRODUCTION.

The present official phosphate assay is a determination of the phosphate radical and not of the hydrogen ion. If one sodium phosphate were contaminated with another, this defect would not be revealed by the pharmacopœial assay. In addition to this, it is almost impossible to obtain checks on different samples of the same specimen when exactly the same routine is followed. Stearn, Farr and Knowlton (1) of the Mallinckrodt Chemical Company have investigated this latter problem extensively and have published a modification of the U. S. P. method which they found satisfactory. However, in my work I had no better results with the modification than with the original procedure.

Many investigators have attempted to titrate phosphoric acid directly or indirectly and consequently many methods are described in the literature. Most of these are, for various reasons, impractical for pharmacopœial testing. The most recent pharmaceutical chemists to work on the problem are Moerk and Hughes (2) of the Philadelphia College of Pharmacy and Science. They have published several methods, the best of which seems to be one in which a mixed indicator of methyl orange and indigo carmine is used for titration after sodium chloride has been added to the phosphate solution.

A survey of the literature on the subject shows that it is a well-known fact that the first hydrogen can be titrated with methyl orange and the second with phenolphthalein. The problem, then, becomes one of finding a method for complete titration. The methods studied fall, in general, into the following types:

1. Silver nitrate
2. Trinitrobenzene
3. Rosalic acid
4. Mixed indicator (Moerk and Hughes).
5. Phenolphthalein with a metallic chloride or an alkaline earth salt.

The purpose of my investigations was to find a more satisfactory method or a satisfactory modification of the above methods. I experimented more with phenolphthalein in the presence of calcium chloride than with any other method, as it seemed to be the most promising.

EXPERIMENTAL WORK.

In all my experiments I used "Baker's Analyzed" monosodium, disodium and trisodium phosphates and Merck's syrupy phosphoric acid. The di- and trisodium phosphates were very efflorescent, and monosodium phosphate was hygroscopic. As uniform samples were difficult to obtain under these conditions, I dried each to constant weight at 110° C. and made up solutions containing a definite weight of the respective salts. Phosphoric acid solutions were made by diluting a weighed sample of the concentrated acid. These solutions were determined gravimetrically for per cent of phosphate by Mahin's (3) method of precipita-

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ing the phosphate with "Magnesia Mixture" as $MgNH_4PO_4$, heating the precipitate and weighing it as $Mg_2P_2O_7$.

All alkali titrations were made with carbonate free sodium hydroxide solution, prepared by adding an excess of barium nitrate and filtering. This solution was preserved by covering it with a layer of liquid petrolatum.

FIRST EXPERIMENT WITH SILVER NITRATE METHOD.

Phosphoric Acid.—The U. S. P. determination was performed as follows:

"Pour about one gram of phosphoric acid into a tared flask, stopper and weigh accurately, transfer it to a 100-mil flask and make it up to 100 mls with distilled water. Transfer 10 mls of this solution to a 100-mil graduated flask, add a drop of phenolphthalein solution (one gram in 100 mls of alcohol) and neutralize it with potassium hydroxide solution (5%, chloride free). Add 50 mls of tenth-normal silver nitrate solution and agitate it, gradually adding zinc oxide (chloride free) in small portions until the liquid is neutral to litmus paper. Now add distilled water to make the liquid measure 100 mls, agitate it thoroughly, filter through a dry filter, collect 50 mls of the filtrate, add 2 mls of nitric acid and 2 mls of ferric ammonium sulphate (10%) and determine the excess of silver nitrate by titration with tenth-normal potassium sulphocyanate to the production of a red color. When calculated to the amount of phosphoric acid originally taken, it shows not less than 85% nor more than 88% of phosphoric acid. Each mil of tenth normal silver nitrate used corresponds to 0.0032687 grams of phosphoric acid. Each gram of phosphoric acid corresponds to not less than 260 mls nor more than 269 mls of tenth-normal silver nitrate."

The results were:

TABLE I.—U. S. P. METHOD.

H_3PO_4 .	N/10 $AgNO_3$.	N/10 KCNS.	Excess $AgNO_3$.	% H_3PO_4 .	Grav. % H_3PO_4 .
0.008698 Gm.	12.42 cc.	9.98 cc.	2.44 cc.	91.7	88.16
0.008698 Gm.	12.42 cc.	9.98 cc.	2.44 cc.	91.7	88.16
0.008698 Gm.	12.42 cc.	9.98 cc.	2.44 cc.	91.7	88.16
0.008698 Gm.	12.42 cc.	9.98 cc.	2.44 cc.	91.7	88.16
0.043488 Gm.	18.63 cc.	6.99 cc.	11.64 cc.	89.8	84.66
0.043488 Gm.	18.63 cc.	6.99 cc.	11.64 cc.	89.8	84.66
0.043488 Gm.	18.63 cc.	6.99 cc.	11.64 cc.	89.8	84.66
0.043488 Gm.	18.63 cc.	6.99 cc.	11.64 cc.	89.8	84.66

Disodium Phosphate, Exsiccated.—The directions and results were:

"Introduce about 0.15 gram of dried sodium phosphate, accurately weighed into a 100-mil graduated flask, dissolve it in 10 mls of distilled water, add 50 mls of tenth-normal silver nitrate and agitate the mixture well. Then gradually add zinc oxide (chloride free) in small portions until the mixture is neutral to litmus paper. Then add distilled water to make 100 mls, agitate the mixture thoroughly, filter through a dry filter, rejecting the first 20 mls of filtrate, collect 50 mls of the subsequent filtrate, add 2 mls of nitric acid and 2 mls of ferric ammonium sulphate (10%) and titrate with tenth-normal potassium sulphocyanate to the production of a permanent red color. It shows not less than 98% of Na_2HPO_4 . Each mil of tenth-normal silver nitrate used corresponds to 0.004735 grams of Na_2HPO_4 . Each gram of exsiccated sodium phosphate, previously dried, corresponds to not less than 207 mls of tenth-normal silver nitrate."

TABLE II.—U. S. P. METHOD.

Na_2HPO_4 .	N/10 $AgNO_3$.	N/10 KCNS.	Excess $AgNO_3$.	% Na_2HPO_4 .	Grav. % Na_2HPO_4 .
0.03515 Gm.	12.42 cc.	4.99 cc.	7.43 cc.	100.09	99.9
0.03515 Gm.	12.42 cc.	4.99 cc.	7.43 cc.	100.09	99.9
0.03515 Gm.	12.42 cc.	4.99 cc.	7.43 cc.	100.09	99.9
0.03515 Gm.	12.42 cc.	4.99 cc.	7.43 cc.	100.09	99.9

When the U. S. P. method was modified according to the directions of Stearn, Farr and Knowlton (1), my results with phosphoric acid checked almost exactly with those obtained by the U. S. P. method. Disodium phosphate was about 1% lower than the gravimetric, whereas the U. S. P. determination was 1% higher. My results were as follows:

TABLE III.—MODIFIED U. S. P. METHOD.

H ₃ PO ₄ .	N/10 AgNO ₃ .	N/10 KCNS.	Excess AgNO ₃ .	% H ₃ PO ₄ .	Grav. % H ₃ PO ₄ .
0.1044 Gm. (1/4 of it titrated)	12.42 cc.	5.1 cc.	7.32 cc.	91.6	84.66
0.1044 Gm. (1/4 of it titrated)	12.42 cc.	5.1 cc.	7.32 cc.	91.6	84.66
0.1044 Gm. (1/4 of it titrated)	12.42 cc.	5.1 cc.	7.32 cc.	91.6	84.66
0.1044 Gm. (1/4 of it titrated)	12.42 cc.	5.1 cc.	7.32 cc.	91.6	84.66
0.1044 Gm. (1/4 of it titrated)	12.42 cc.	5.1 cc.	7.32 cc.	91.6	84.66

TABLE IV.—MODIFIED U. S. P. METHOD.

Na ₂ HPO ₄ .	N/10 AgNO ₃ .	N/10 KCNS.	Excess AgNO ₃ .	% Na ₂ HPO ₄ .	Grav. % Na ₂ HPO ₄ .
0.1405 Gm. (1/4 of it titrated)	12.42 cc.	4.55 cc.	7.87 cc.	105.0	99.07
0.1405 Gm. (1/4 of it titrated)	12.42 cc.	4.66 cc.	7.76 cc.	98.2	99.07
0.1405 Gm. (1/4 of it titrated)	12.42 cc.	4.66 cc.	7.76 cc.	98.2	99.07
0.1405 Gm. (1/4 of it titrated)	12.42 cc.	4.66 cc.	7.76 cc.	98.2	99.07

Great care must be taken in titrating with KCNS as 0.1 cc. too much KCNS causes an error of about 5% in the sodium salt.

SECOND EXPERIMENT WITH TRINITROBENZENE INDICATOR.

This indicator was obtained from Coleman and Bell Co. A solution of it was made to contain 0.5 gram in 100 cc. of alcohol. The p_H range given on the label was 13.0 to 14.3.

The phosphoric acid solution used was standardized gravimetrically, and 20 cc. of it were found to be equivalent to 18.5 cc. of an exactly *N*/10 acid. Twenty cc. were then measured into a flask to which 1 cc. of the indicator solution was added, and it was titrated directly with *N*/10 NaOH. The first appearance of a yellow color was very definite and came almost at the end-point of the second hydrogen. Eighteen and five-tenth cc. *N*/10 acid required 13 cc. of *N*/10 base to bring this color change. This was true of every one of a number of titrations and was as definite as the first appearance of a pink color when phenolphthalein is used. When the acid was heated to boiling before adding the indicator and titrating, 18.5 cc. *N*/10 acid required only 12.8 cc. *N*/10 base to bring the first yellow color of the previous titrations. Theoretically, 13.3-cc. base should have been used to neutralize two-thirds of the acid (the first two hydrogens), so the results with the cold solution were more nearly correct for this point.

As more base was added the yellow deepened to an orange and the point of complete neutralization was a brilliant orange, but it was not noticeably different from the color when 3 cc. more or less alkali had been added. In other words the change was so gradual, that even with the use of a standard (made from an acid mixture of cobalt nitrate, ferric chloride and potassium dichromate solutions) it was impossible to read the exact end-point.

Trinitrobenzene was slight yellow in a disodium phosphate solution, and as the same gradual change took place in the complete neutralization of this salt, I did no more work with it.

TABLE V.—TRINITROBENZENE.

<i>N</i> /10 H ₃ PO ₄ .	1st yellow <i>N</i> /10 NaOH.	% H ₃ PO ₄ .	Deep orange <i>N</i> /10 NaOH.	% H ₃ PO ₄ .	Grav. % H ₃ PO ₄ .
0.0696 Gm. = 18.5 cc.	13.0 cc. (cold)	61.0	16–22 cc.	75.1–103	86.8
0.0696 Gm. = 18.5 cc.	13.0 cc. (cold)	61.0	16–22 cc.	75.1–103	86.8
0.0696 Gm. = 18.5 cc.	13.0 cc. (cold)	61.0	16–22 cc.	75.1–103	86.8
0.0696 Gm. = 18.5 cc.	13.0 cc. (cold)	61.0	16–22 cc.	75.1–103	86.8
0.0696 Gm. = 18.5 cc.	12.8 cc. (boil)	60.1	16–22 cc.	75.1–103	86.8
0.0696 Gm. = 18.5 cc.	12.8 cc. (boil)	60.1	16–22 cc.	75.1–103	86.8
0.0696 Gm. = 18.5 cc.	12.8 cc. (boil)	60.1	16–22 cc.	75.1–103	86.8

Different combinations with the indicator were attempted, but none were successful. The addition of calcium chloride to the acid, before titration, raised the amount of *N*/10 NaOH to 30 cc. for the neutralization of 18.5 cc. phosphoric acid, but here again the change was so gradual that the exact point could not be determined.

TABLE VI.—TRINITROBENZENE AND CALCIUM CHLORIDE.

<i>N</i> /10 H ₃ PO ₄ .	<i>N</i> /10 NaOH.	% H ₃ PO ₄ .	Grav. % H ₃ PO ₄ .
0.0696 Gm. = 18.5 cc.	27–31 cc.	126–145	86.8
0.0696 Gm. = 18.5 cc.	27–31 cc.	126–145	86.8
0.0696 Gm. = 18.5 cc.	27–31 cc.	126–145	86.8
0.0696 Gm. = 18.5 cc.	27–31 cc.	126–145	86.8

In a mixture of trinitrobenzene with phenolphthalein, the red of the latter obliterated the yellow of the former and the end-point came at the point of two-thirds neutralization.

Following the suggestion of the Moerk and Hughes (2) mixed indicator, I mixed $\frac{1}{2}$ cc. trinitrobenzene with $\frac{1}{2}$ cc. indigo carmine solution (1 Gm. in 150 cc. water). Since the color of the latter is destroyed by warm alkali, I added my indicator mixture to a hot solution of phosphoric acid (to boiling) and titrated with NaOH to the first definite greenish color. The end-point came in the neighborhood of the theoretical but was again too indefinite to read sharply. However, the results were more promising than those of the foregoing attempts, and I have recorded them in the following table:

TABLE VII.

<i>N</i> /10 H ₃ PO ₄ .	<i>N</i> /10 NaOH.	% H ₃ PO ₄ .	Grav. % H ₃ PO ₄ .
0.0696 Gm. = 18.5 cc.	19.0 cc.	89.2	86.8
0.0696 Gm. = 18.5 cc.	18.6 cc.	87.6	86.8
0.0696 Gm. = 18.5 cc.	22.0 cc.	103.0	86.8
0.0696 Gm. = 18.5 cc.	19.5 cc.	91.5	86.8
0.0696 Gm. = 18.5 cc.	18.6 cc.	87.6	86.8
0.0696 Gm. = 18.5 cc.	20.5 cc.	96.2	86.8
0.0696 Gm. = 18.5 cc.	20.0 cc.	93.9	86.8
0.0696 Gm. = 18.5 cc.	20.5 cc.	96.2	86.8

THIRD EXPERIMENT WITH ROSOLIC ACID.

In this experiment a method recommended by Schimpf (4) was used. To 20 cc. phosphoric acid (equivalent to 18.8 cc. *N*/10), were added 29.82 cc. *N*/10 NaOH, three drops of rosolic acid (one gram in 10 cc. diluted alcohol, and water to make 100 cc.) and 25 cc. of approximately *N*/10 neutral barium nitrate solution. The

mixture was heated to boiling and titrated hot with *N*/10 HCl to determine the excess of NaOH. The color change was very gradual and concordant results were not obtained with uniform procedure. The results were:

TABLE VIII.

H ₃ PO ₄ .	BaCl ₂ .	<i>N</i> /10 NaOH.	<i>N</i> /10 HCl.	% H ₃ PO ₄ .	Grav. % H ₃ PO ₄ .
20 cc. = 0.0696 Gm.	25 cc.	29.82 cc.	15.12 cc.	69.0	88.16
20 cc. = 0.0696 Gm.	25 cc.	29.82 cc.	13.70 cc.	75.6	88.16
20 cc. = 0.0696 Gm.	25 cc.	29.82 cc.	15.12 cc.	69.0	88.16
20 cc. = 0.0696 Gm.	25 cc.	29.82 cc.	13.50 cc.	76.6	88.16
20 cc. = 0.0696 Gm.	25 cc.	29.82 cc.	13.70 cc.	75.6	88.16
20 cc. = 0.0696 Gm.	25 cc.	29.82 cc.	13.70 cc.	75.6	88.16

FOURTH EXPERIMENT WITH MIXED INDICATOR.

In this method I followed the directions of Moerk and Hughes (2) as to solutions and procedure. The method for phosphoric acid is:

"To liquid (100 cc. NaCl solution), add 0.2 cc. each of methyl orange and indigo carmine solutions. Add *N*/10 HCl drop by drop until green color changes without producing a violet color. Divide into two parts. To (1) add measured quantity phosphoric acid solution and titrate with *N*/10 NaOH until color matches reserve."

The following results were obtained:

TABLE IX.

H ₃ PO ₄ .	<i>N</i> /10 NaOH.	NaCl (10%)	% H ₃ PO ₄ .	Grav. % H ₃ PO ₄ .
20 cc. = 0.06958 Gm.	19.63 cc.	50 cc.	92.20	84.66
20 cc. = 0.06958 Gm.	19.20 cc.	50 cc.	91.90	84.66
20 cc. = 0.06958 Gm.	19.00 cc.	50 cc.	89.20	84.66
10 cc. = 0.03479 Gm.	9.30 cc.	50 cc.	87.37	84.66
10 cc. = 0.03479 Gm.	9.20 cc.	50 cc.	86.40	84.66
10 cc. = 0.03479 Gm.	9.30 cc.	50 cc.	87.37	84.66
10 cc. = 0.03479 Gm.	9.30 cc.	50 cc.	87.37	84.66
10 cc. = 0.03479 Gm.	9.20 cc.	50 cc.	86.40	84.66
10 cc. = 0.03479 Gm.	9.30 cc.	50 cc.	87.37	84.66
10 cc. = 0.03479 Gm.	9.30 cc.	50 cc.	87.37	84.66
10 cc. = 0.03479 Gm.	9.30 cc.	50 cc.	87.37	84.66
10 cc. = 0.03479 Gm.	9.30 cc.	50 cc.	87.37	84.66
10 cc. = 0.03479 Gm.	9.20 cc.	50 cc.	86.40	84.66

When phosphoric acid was added to the solution containing the indicator, the color was deep purple. At the one-third point (first hydrogen) it changed quickly to a blue. This changed to a more greenish blue as more alkali was added and the final end-point came at the first distinct green. After one learns this point it is quite easy to obtain concordant results as the change always comes at the same point; but for one who is not familiar with the determination, this point is very difficult to distinguish as the change is gradual. My first results were high for this reason.

The residual method for determining Na₂HPO₄ is:

"Use same directions as were used for phosphoric acid until the solution is divided into two parts. To (1) add a measured quantity of *N*/10 acid (excess) and titrate with *N*/10 NaOH to match reserve. Add to reserve 10 cc. disodium phosphate solution and same quantity of *N*/10 acid as was added to solution (1). Titrate to same color with *N*/10 NaOH."

My results were:

TABLE X.

Na_2HPO_4	<i>N</i> /10 HCl	¹ <i>N</i> /10 NaOH	² <i>N</i> /10 NaOH	Dif. 1 and 2.	% salt.	Grav. %.
10 cc. = 0.1406 Gm.	25 cc.	22.3 cc.	13.80 cc.	8.50 cc.	85.30	99.07
10 cc. = 0.1406 Gm.	25 cc.	22.3 cc.	13.50 cc.	8.80 cc.	88.80	99.07
10 cc. = 0.1406 Gm.	25 cc.	22.3 cc.	13.50 cc.	8.80 cc.	88.80	99.07
10 cc. = 0.1406 Gm.	25 cc.	24.0 cc.	14.98 cc.	9.02 cc.	91.12	99.07
10 cc. = 0.1406 Gm.	25 cc.	22.3 cc.	13.50 cc.	8.80 cc.	88.80	99.07
10 cc. = 0.1406 Gm.	25 cc.	24.0 cc.	14.98 cc.	9.02 cc.	91.12	99.07
10 cc. = 0.1406 Gm.	25 cc.	24.0 cc.	14.98 cc.	9.02 cc.	91.12	99.07
10 cc. = 0.1406 Gm.	25 cc.	24.0 cc.	14.98 cc.	9.02 cc.	91.12	99.07
10 cc. = 0.1406 Gm.	25 cc.	24.0 cc.	14.98 cc.	9.02 cc.	91.12	99.07

Although I titrated to the same end-point as in the phosphoric acid determination, the final per cent does not check so well with the gravimetric.

FIFTH EXPERIMENT WITH PHENOLPHTHALEIN AND CALCIUM CHLORIDE.

In my first experiments I followed the suggestions of Blitz and Marcus (5) and determined the first hydrogen with methyl orange, the second with phenolphthalein, and the third with phenolphthalein after calcium chloride had been added. No heat was used in the first series, but the effect of increasing amounts of calcium chloride was tried. The calcium chloride solution was measured only approximately. The indicators were made according to U. S. P. IX and three drops were used in a titration. The end-point of methyl orange was the first yellow, and of phenolphthalein, the first pink.

My results were:

TABLE XI.—ROOM TEMPERATURE.

H_2PO_4	<i>N</i> /10 CaCl ₂	M. O. <i>N</i> /10 NaOH	M. O. <i>N</i> /10 NaOH calc.	Phen. <i>N</i> /10 NaOH	Phen. <i>N</i> /10 NaOH calc.	% acid.	Grav. %.
25.0 cc. = 0.09006 Gm.	0.0 cc.	7.8 cc.	7.8 cc.	15.4 cc.	15.4 cc.	83.01
25.0 cc. = 0.09006 Gm.	12.5 cc.	7.8 cc.	7.8 cc.	18.9 cc.	23.4 cc.	68.3	83.01
25.0 cc. = 0.09006 Gm.	25.0 cc.	7.8 cc.	7.8 cc.	22.2 cc.	23.4 cc.	80.5	83.01
25.0 cc. = 0.09006 Gm.	50.0 cc.	7.8 cc.	7.8 cc.	22.7 cc.	23.4 cc.	82.3	83.01
25.0 cc. = 0.09006 Gm.	75.0 cc.	7.8 cc.	7.8 cc.	22.5 cc.	23.4 cc.	81.6	83.01
12.5 cc. = 0.04503 Gm.	50.0 cc.	3.9 cc.	3.9 cc.	11.4 cc.	11.7 cc.	82.7	83.01
12.5 cc. = 0.04503 Gm.	75.0 cc.	3.8 cc.	3.9 cc.	11.6 cc.	11.7 cc.	84.2	83.01
12.5 cc. = 0.04503 Gm.	100.0 cc.	3.8 cc.	3.9 cc.	11.4 cc.	11.7 cc.	82.7	83.01
12.5 cc. = 0.04503 Gm.	125.0 cc.	3.7 cc.	3.9 cc.	11.5 cc.	11.7 cc.	83.4	83.01
12.5 cc. = 0.04503 Gm.	200.0 cc.	3.6 cc.	3.9 cc.	12.3 cc.	11.7 cc.	89.2	83.01

According to Blitz, Marcus (5) and Prideaux (6) when calcium chloride is added to phosphoric acid, the precipitate consists almost entirely of tertiary calcium phosphate. If this be true one should be able to titrate the HCl formed and obtain accurately the per cent of acid present. However, the percentages fall below the gravimetric, indicating incomplete precipitation of tertiary calcium phosphate. The amount of calcium chloride present did not affect the titration very much unless a great excess was added. With methyl orange and calcium chloride the solution remained perfectly clear at the end-point, but phenolphthalein and calcium chloride gave a finely divided white precipitate which did not form until NaOH was added. This does not obscure the end-point.

Next I heated the phosphoric acid and calcium chloride solutions to boiling, added three drops of phenolphthalein and titrated with *N*/10 NaOH. The results were:

TABLE XII.—HEATED TO BOILING.

H ₃ PO ₄ .	CaCl ₂ .	Phen. N/10 NaOH calc.	Phen. N/10 NaOH.	% H ₃ PO ₄ .	Grav. %.
12.5 cc. = 0.04503 Gm.	25.0 cc.	12.3 cc.	11.7 cc.	89.2	85.01
12.5 cc. = 0.04503 Gm.	37.5 cc.	12.3 cc.	11.7 cc.	89.2	85.01
12.5 cc. = 0.04503 Gm.	50.0 cc.	12.2 cc.	11.7 cc.	88.5	85.01
12.5 cc. = 0.04503 Gm.	62.5 cc.	11.8 cc.	11.7 cc.	85.6	85.01
12.5 cc. = 0.04503 Gm.	75.0 cc.	11.7 cc.	11.7 cc.	84.9	85.01
12.5 cc. = 0.04503 Gm.	87.5 cc.	12.1 cc.	11.7 cc.	87.8	85.01
12.5 cc. = 0.04503 Gm.	100.0 cc.	11.7 cc.	11.7 cc.	84.9	85.01
12.5 cc. = 0.04503 Gm.	25.0 cc.	12.2 cc.	11.7 cc.	88.5	85.01
12.5 cc. = 0.04503 Gm.	50.0 cc.	12.2 cc.	11.7 cc.	88.5	85.01
12.5 cc. = 0.04503 Gm.	75.0 cc.	12.2 cc.	11.7 cc.	88.5	85.01
12.5 cc. = 0.04503 Gm.	100.0 cc.	11.7 cc.	11.7 cc.	84.9	85.01

The majority of the titrations in this series ran high, although several checked perfectly. Since cold solutions gave low percentages and boiling gave high ones, I next tried 75° C., then 60–65° C. and the respective results were:

TABLE XIII.—75° C.

H ₃ PO ₄ .	CaCl ₂ .	Phen. N/10 NaOH.	Phen. N/10 NaOH calc.	% H ₃ PO ₄ .	Grav. %.
12.5 cc. = 0.04503 Gm.	25 cc.	11.8 cc.	11.7 cc.	85.6	85.01
12.5 cc. = 0.04503 Gm.	50 cc.	11.8 cc.	11.7 cc.	85.6	85.01
12.5 cc. = 0.04503 Gm.	75 cc.	11.8 cc.	11.7 cc.	85.6	85.01
12.5 cc. = 0.04503 Gm.	100 cc.	11.6 cc.	11.7 cc.	84.1	85.01

TABLE XIV.—60–65° C.

H ₃ PO ₄ .	CaCl ₂ .	N/10 NaOH.	N/10 NaOH calc.	% H ₃ PO ₄ .	Grav. %.
12.5 cc. = 0.04503 Gm.	25 cc.	11.7 cc.	11.70 cc.	84.90	85.01
12.5 cc. = 0.04503 Gm.	50 cc.	11.7 cc.	11.70 cc.	84.90	85.01
12.5 cc. = 0.04503 Gm.	75 cc.	11.7 cc.	11.70 cc.	84.90	85.01
12.5 cc. = 0.04503 Gm.	100 cc.	10.0 cc.	11.70 cc.	72.60	85.01
10.0 cc. = 0.03479 Gm.	10 cc.	9.4 cc.	9.38 cc.	88.31	88.16
10.0 cc. = 0.03479 Gm.	10 cc.	10.5 cc.	9.38 cc.	98.60	88.16
10.0 cc. = 0.03479 Gm.	20 cc.	9.4 cc.	9.38 cc.	88.31	88.16
10.0 cc. = 0.03479 Gm.	20 cc.	9.0 cc.	9.38 cc.	84.50	88.16
10.0 cc. = 0.03479 Gm.	30 cc.	9.4 cc.	9.38 cc.	88.31	88.16
10.0 cc. = 0.03479 Gm.	30 cc.	9.4 cc.	9.38 cc.	88.31	88.16
10.0 cc. = 0.03479 Gm.	40 cc.	9.4 cc.	9.38 cc.	88.31	88.16
10.0 cc. = 0.03479 Gm.	40 cc.	9.4 cc.	9.38 cc.	88.31	88.16
10.0 cc. = 0.03479 Gm.	50 cc.	10.5 cc.	9.38 cc.	98.60	88.16
10.0 cc. = 0.03479 Gm.	50 cc.	9.4 cc.	9.38 cc.	88.31	88.16
10.0 cc. = 0.03479 Gm.	30 cc.	9.4 cc.	9.38 cc.	88.31	88.16
10.0 cc. = 0.03479 Gm.	30 cc.	9.1 cc.	9.38 cc.	85.40	88.16
10.0 cc. = 0.03479 Gm.	30 cc.	9.4 cc.	9.38 cc.	88.31	88.16
10.0 cc. = 0.03479 Gm.	30 cc.	9.4 cc.	9.38 cc.	88.31	88.16
10.0 cc. = 0.03479 Gm.	30 cc.	9.0 cc.	9.38 cc.	84.50	88.16

The following series is one of titrations on a sample of unknown strength, which was determined gravimetrically after the volumetric results had been obtained. The percentages were all too high but were fairly uniform.

Practically the same procedure was followed with disodium phosphate as with the acid. It was heated with calcium chloride to various temperatures, as

TABLE XV.—60–65° C. UNKNOWN SAMPLE.

H ₃ PO ₄ .	CaCl ₂ .	N/10 NaOH.	% H ₃ PO ₄ .	Grav. %.
0.0695 Gm.	50 cc.	18.57 cc.	87.2	84.66
0.0695 Gm.	50 cc.	18.70 cc.	87.8	84.66
0.0695 Gm.	50 cc.	18.45 cc.	86.6	84.66
0.0695 Gm.	50 cc.	18.57 cc.	87.2	84.66
0.0695 Gm.	50 cc.	18.57 cc.	87.2	84.66

indicated below, three drops of phenolphthalein were added and the hot solution was titrated with N/10 NaOH. The results were:

TABLE XVI.—65° C.

Anhyd. Na ₂ HPO ₄ .	N/10 CaCl ₂ .	N/10 NaOH.	N/10 NaOH calc.	% Na ₂ HPO ₄ .	Grav. %.
20 cc. = 0.2812 Gm.	35 cc.	17.80 cc.	19.6 cc.	89.90	99.07
20 cc. = 0.2812 Gm.	35 cc.	18.00 cc.	19.6 cc.	90.90	99.07
20 cc. = 0.2812 Gm.	35 cc.	18.23 cc.	19.6 cc.	92.08	99.07
20 cc. = 0.2812 Gm.	35 cc.	19.00 cc.	19.6 cc.	95.90	99.07
20 cc. = 0.2812 Gm.	50 cc.	18.80 cc.	19.6 cc.	95.30	99.07
20 cc. = 0.2812 Gm.	50 cc.	18.45 cc.	19.6 cc.	93.20	99.07
20 cc. = 0.2812 Gm.	50 cc.	18.80 cc.	19.6 cc.	95.30	99.07

TABLE XVII.—TO BOILING.

Anhyd. Na ₂ HPO ₄ .	CaCl ₂ .	N/10 NaOH.	N/10 NaOH calc.	% Na ₂ HPO ₄ .	Grav. %.
10 cc. = 0.1406 Gm.	20 cc.	10.3 cc.	9.8 cc.	104	99.07
10 cc. = 0.1406 Gm.	20 cc.	10.3 cc.	9.8 cc.	104	99.07

TABLE XVIII.—70–75° C.

Na ₂ HPO ₄ .	CaCl ₂ .	N/10 NaOH.	N/10 NaOH calc.	% Na ₂ HPO ₄ .	Grav. %.
0.1406 Gm.	20 cc.	9.85 cc.	9.8 cc.	99.5	99.07
0.1406 Gm.	20 cc.	9.00 cc.	9.8 cc.	90.9	99.07
0.1406 Gm.	20 cc.	9.80 cc.	9.8 cc.	99.0	99.07
0.1406 Gm.	20 cc.	9.80 cc.	9.8 cc.	99.0	99.07
0.1406 Gm.	20 cc.	9.85 cc.	9.8 cc.	99.5	99.07
0.1406 Gm.	20 cc.	9.80 cc.	9.8 cc.	99.0	99.07
0.1406 Gm.	20 cc.	9.90 cc.	9.8 cc.	100.0	99.07
0.1406 Gm.	20 cc.	9.80 cc.	9.8 cc.	99.0	99.07
0.1406 Gm.	20 cc.	9.85 cc.	9.8 cc.	99.5	99.07
0.1406 Gm.	20 cc.	9.80 cc.	9.8 cc.	99.0	99.07
0.1406 Gm.	20 cc.	9.80 cc.	9.8 cc.	99.0	99.07
0.1406 Gm.	20 cc.	9.80 cc.	9.8 cc.	99.0	99.07
0.1406 Gm.	20 cc.	9.80 cc.	9.8 cc.	99.0	99.07

In this case the white precipitate appeared as soon as the calcium chloride was added. The temperature was 70–65° C. as in the titration of the acid.

Although monosodium phosphate is not official, I experimented with it and found that this method gave practically the same results as with the acid and the disodium salt. The following results were obtained:

TABLE XIX.

Anhyd. Na ₂ HPO ₄ .	N/10 CaCl ₂ .	N/10 NaOH.	% NaH ₂ PO ₄ .	Grav. %.	Temperature.
0.1192 Gm.	20 cc.	20.6 cc.	103.7 cc.	100.06	60–65° C.
0.1192 Gm.	35 cc.	20.6 cc.	103.7 cc.	100.06	60–65°
0.1192 Gm.	35 cc.	20.3 cc.	102.2 cc.	100.06	60–65°
0.1192 Gm.	35 cc.	19.5 cc.	98.2 cc.	100.06	50°

0.1192 Gm.	35 cc.	19.8 cc.	99.7 cc.	100.06 cc.	55-60°
0.1192 Gm.	35 cc.	19.8 cc.	99.7 cc.	100.06 cc.	55-60°
0.1192 Gm.	35 cc.	19.7 cc.	99.2 cc.	100.06 cc.	55-60°
0.1192 Gm.	35 cc.	19.8 cc.	99.7 cc.	100.06 cc.	55-60°
0.1192 Gm.	35 cc.	19.9 cc.	100.2 cc.	100.06 cc.	55-60°
0.1192 Gm.	35 cc.	19.9 cc.	100.2 cc.	100.06 cc.	55-60°
0.1192 Gm.	35 cc.	19.8 cc.	99.7 cc.	100.06 cc.	55-60°

The optimum temperature for the titration of this salt is 55-60° C.

SUMMARY.

A consideration of the data which I have submitted shows that there is no known indicator which will completely titrate phosphoric acid or the sodium phosphates. Theoretically, trinitrobenzene should be satisfactory as the p_H range is the required one, but in practice, the gradual change of color after the first yellow, renders it worthless.

In my opinion the only remaining solutions to the problem are, first, complete precipitation of the phosphate with the formation of a strong acid which can be titrated and, second, the addition of sodium chloride to increase the hydrogen-ion dissociation of the acid.

In the first method a number of precipitants may be used. My experiments and those of Stearn, Farr and Knowlton have shown that there are discrepancies when silver nitrate is added to precipitate the phosphate. Lead nitrate, soluble magnesium salts and barium nitrate have all been found unsatisfactory by previous investigators. Of all the precipitants suggested, to completely precipitate the phosphate as the tertiary salt, calcium chloride was given by the greatest number of workers.

After the phosphate has been precipitated, the next problem is that of finding a suitable indicator to titrate the acid formed. Many have been tested, among which are methyl red, rosolic acid, lacmoid, litmus and phenolphthalein. If calcium chloride is the precipitant, phenolphthalein is satisfactory. It is an indicator which is familiar to all analysts and I think that is a desirable, though not an absolutely essential quality of an indicator for pharmacopœial testing.

I did most of my work with phenolphthalein and calcium chloride, because in every way this method seemed most promising. In none of the literature on this method did I find reference to variation in the results of complete titration because of temperature changes. My experiments show that this is the controlling factor in the titration, and if the requirement of the optimum temperature is fulfilled, concordant results will be obtained with any weight of sample unless there is an unreasonable excess of calcium chloride present.

The second method, in which sodium chloride is added seems inferior to the above method for several reasons. The complicated mixed indicator of methyl orange and indigo carmine is the only satisfactory one and the reading of its endpoint is difficult. In addition, Na_2HPO_4 cannot be titrated directly, but must first be combined with hydrochloric acid, because indigo carmine's blue color is destroyed in an alkaline solution. Moerk and Hughes, who originated the method, state that the results are influenced by weight of sample, normality of standard solutions and the amount of sodium chloride present. These factors are very important ones in assaying unknown samples and are sufficient to bar the method from the Pharmacopœia.

If the temperature is controlled, I believe there is no doubt of the superiority of the calcium chloride-phenolphthalein method over all the others studied and I think it would be suitable for use in the Pharmacopœia.

CONCLUSIONS.

1. The U. S. P. IX method of phosphate assay is unsatisfactory because it gives high results, which do not check on different samples of the same specimen. When modified according to Stearn, Farr and Knowlton, the results are no better. Both methods are long and tedious.

2. Rosolic acid cannot be used as an indicator because the results are too low.

3. Trinitrobenzene, although it will titrate the third hydrogen, cannot be used as the color change is too gradual. A combination of this indicator with phenolphthalein gives the color change of the latter and titrates only the second hydrogen. Calcium chloride added causes an abnormal rise of the end-point accompanied by an abnormal percentage. Combination of the indicator with indigo carmine gave an end-point in the neighborhood of the theoretical, but it was too difficult to distinguish to be of any value.

4. The mixed indicator of methyl orange and indigo carmine is fairly satisfactory. It gives good results with the acid, but low results with disodium phosphate.

5. The best method for the complete titration of phosphoric acid and mono- and disodium phosphates is the use of phenolphthalein at the temperature of 55-70° C., after calcium chloride has been added to the phosphate solution. The determination is not tedious nor long, the end-point of phenolphthalein is well-known, and the percentages check well with the gravimetric. The proportion of phosphate to calcium chloride should be 1:2-1:5.

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