

case. However, the amount of conversion was too small to permit any closer identification.

The oily precipitate was found to be non-volatile in a vacuum, even at high temperatures. It reacted readily with water or alcohol to produce a white, amorphous solid, which possessed no characteristic melting point and contained no nitrogen or chlorine. It was probably a polymerized aldehyde, but it was not examined further.

SUMMARY.

1. All aliphatic alcohols tried give nitrites by treatment with nitrosyl chloride. With increase in molecular weight, pyridine as a condensation agent is necessary. When nitrites of tertiary alcohols are being prepared, pyridine should be used. The nitrites of diethyl propyl carbinol, triethyl carbinol and methyl diethyl carbinol were also made. The nitrite of diethyl propyl carbinol was made by others, as noted, but the product was not vacuum distilled and physical data were not determined.

2. Benzyl alcohol, glycerin, ethylene glycol, trimethylene chlorhydrin, menthol and chloretone gave no nitrites under the experimental conditions used.

3. Thymol and antipyrine are converted to the corresponding nitroso compounds.

4. Benzaldehyde is converted to benzoyl chloride and benzoic acid. Acetaldehyde apparently behaves in a somewhat similar manner.

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SUGGESTED ASSAYS FOR SOME N. F. PREPARATIONS.*

1. ANTISEPTIC SOLUTION.

BY S. W. GOLDSTEIN.

The most important ingredient of Antiseptic Solution, N. F. V, from the standpoint of therapeutic value, is probably boric acid. A method for the determination of the latter, therefore, appears to be desirable. The procedure suggested on page 129 is one for the direct titration of boric acid and has been found to give concordant results.

- Reagents.*—1. Glycerin
2. 0.1 N Sodium hydroxide solution
3. Phenolphthalein test solution.

* From the laboratory of A. G. DuMez, Professor of Pharmacy, School of Pharmacy, University of Maryland.

Procedure.—Add 5 cc. of Antiseptic Solution to a mixture of 10 cc. of glycerin and 5 cc. of distilled water contained in an Erlenmeyer flask. Add 3 drops of phenolphthalein test solution, and titrate with 0.1 *N* sodium hydroxide solution until a faint pink color persists.

Each cc. 0.1 *N* sodium hydroxide = 0.006192 Gm. boric acid.

A control should be run with the glycerin and water used in the assay.

Suggested Standard.—Antiseptic Solution contains in each 100 cc., not less than 2.45 Gm. and not more than 2.55 Gm. of H_3BO_3 .

DISCUSSION.

A solution was prepared according to the directions in the N. F. V, with the exception that the boric acid was omitted. This solution was found to be neutral to phenolphthalein test solution.

A series of assays was then run on the official solution containing the required amount of boric acid with the following results:

TABLE I.—TITRATION OF BORIC ACID.

Cc. Antiseptic Solution.	Glycerin.	Distilled Water.	Cc. 0.1 <i>N</i> NaOH.	Gm. H_3BO_3 .
5	20	20	20.18	0.1249
5	20	20	20.28	0.1255
5	20	10	20.14	0.1247
5	20	10	20.28	0.1255
5	10	5	20.20	0.1250

The Antiseptic Solution, glycerin and distilled water may all be added by means of pipettes; only the alkali requires a burette.

The accuracy of the method was still maintained when the glycerin content of the titration mixture was as low as 30 p. c. v/v.

2. ALKALINE AROMATIC SOLUTION.

BY S. W. GOLDSTEIN.

The alkali content of Alkaline Aromatic Solution, N. F. V, is largely responsible for its efficacy. A method for the determination of total alkalinity has, therefore, been devised. The procedure is simple and was found to give satisfactory results.

- Reagents.*—1. 0.1 *N* Sulphuric acid solution
 2. 0.1 *N* Sodium hydroxide solution
 3. Phenol red test solution, U. S. P.

Procedure.—To 50 cc. of distilled water contained in a 250-cc. Erlenmeyer flask or a beaker add 1 cc. of the Alkaline Aromatic Solution, 2 drops of phenol red test solution, and 4 cc. of 0.1 *N* sulphuric acid solution, accurately measured from a burette. Titrate the excess sulphuric acid with 0.1 *N* sodium hydroxide solution until a salmon color appears and persists for one minute.

Deduct the number of cc. of 0.1 *N* alkali consumed from the 4 cc. of 0.1 *N* acid used to find the alkalinity of 1 cc. of the solution.

Suggested Standard.—Each cc. of Alkaline Aromatic Solution requires for neutralization not less than 2.9 cc. and not more than 3.2 cc. of 0.1 *N* sulphuric acid solution.

DISCUSSION.

Choice of Indicator.—Phenol red was chosen as the indicator rather than the more common indicators because it gives the sharpest end-point, under the conditions, and its p_H range is nearest the field of exact neutrality. The indicator is red in alkaline medium at a p_H of 8.6, and it is yellow in acid medium at a p_H of 6.8.

Determination of Best End-Point.—A solution was prepared according to the formula for Alkaline Aromatic Solution with the exception that the cudbear was omitted. The above assay was carried out, using this solution, with the following modification: Instead of back-titrating with alkali to the appearance of a red tint, the solution was back-titrated to the disappearance of the yellow color which is present at a p_H of 6.8. This brought the end-point nearer to a p_H of 7.0, or exact neutrality. The end-point or color change that occurs at that point in the titration of the official solution was then noted and introduced into the assay.

Accuracy of the Method.—A series of assays was run on different samples of the official solution by this method, and the following results were obtained:

TABLE II.—TITRATION OF TOTAL ALKALINITY.

Cc. Alkaline Aromatic Solution.	Cc. 0.1 N H_2SO_4 Added.	Cc. 0.1 N NaOH Added.	Cc. 0.1 N H_2SO_4 Consumed.
1	4.0	0.829	3.171
1	4.0	0.829	3.171
1	4.0	0.879	3.121
1	4.0	0.838	3.162
1	4.0	0.921	3.079
1	4.0	0.916	3.084

Some difficulty in determining the end-point may be experienced due to the variation of the color of the orchil present in the cudbear, but this interference is of small importance and should not exist after a few trial assays.

3. SPIRIT OF FORMIC ACID.

BY EMANUEL V. SHULMAN.

Formic acid is the therapeutically active ingredient of Spirit of Formic Acid, N. F. V. The formic acid, however, is not all present in the free state as a portion of it combines with the alcohol-forming ethyl formate. A method has, therefore, been devised for the determination of total formic acid. The method is simple and gives satisfactory results.

- Reagents.*—1. 0.1 N Sodium hydroxide solution
 2. 0.1 N Sulphuric acid solution
 3. Phenolphthalein test solution

Procedure.—To 40 cc. of 0.1 N sodium hydroxide solution contained in a 250-cc. glass-stoppered flask, add 10 cc. of the spirit, accurately measured; warm the flask to 50° C. and set aside for about ten minutes. Titrate the excess alkali using 0.1 N sulphuric acid and phenolphthalein T.S. as indicator. Each cc. of 0.1 N sodium hydroxide corresponds to 0.0046 Gm. of formic acid.

Suggested Standard.—Spirit of Formic Acid contains not less than 1.0 Gm. and not more than 1.1 Gm. of total formic acid, free and as ester, in each 100 cc.

DISCUSSION.

The speed of the equilibrium reaction between the formic acid and the alcohol is slow as can be determined by the direct titration of the free acid present in the spirit. This reaction is reversed by the presence of free alkali and may be hastened by raising the temperature of the solution. Titrations were made with boiling solutions which in some cases gave slightly higher results than expected. This may have been due to the use of unneutralized alcohol in making the spirit.

Choice of Indicator.—Phenolphthalein was selected as the indicator for titration because the p_H values of dilute solutions of sodium formate were found to fall well within its range.

The following are typical results obtained with this method:

TABLE III.—TITRATION OF FORMIC ACID.

Cc. of Spirit.	Cc. of 0.1 N NaOH Required for Neutralization.	Equivalent Weight of HCOOH.	Theoretical Weight of HCOOH.
10	23.0	0.1058	0.1083
10	23.63	0.1087	0.1083
10	23.68	0.1089	0.1083
10	23.33	0.1073	0.1083

Calculation of Theoretical Weight of Formic Acid.—The formic acid used in the preparation of the spirit assayed 25.51 p. c. with a specific gravity of 1.0615, which is equal to 27.07 Gm. of pure formic acid in 100 cc. Spirit of formic acid contains 4 p. c. of formic acid by volume or 1.083 Gm. in 100 cc. or 0.1083 in 10 cc. The standard proposed was similarly calculated, using the percentage strength limits and specific gravity value for formic acid given in the National Formulary.

4. ANISATED SPIRIT OF AMMONIA.

BY EMANUEL V. SHULMAN.

A method has been devised for the determination of total ammonia in Anisated Spirit of Ammonia, N. F. V. The following procedure which is simple was found to give satisfactory results.

- Reagents.*—1. Alcohol, neutral to phenolphthalein
 2. 0.1 N Sulphuric acid solution
 3. Methyl red test solution.

Procedure.—Pour 20 cc. of alcohol, made neutral to phenolphthalein into a 100-cc. Erlenmeyer flask, add exactly 2 cc. of the spirit and titrate with 0.1 N sulphuric acid using methyl red T.S. as indicator. Each cc. of 0.1 N sulphuric acid corresponds to 0.0017 Gm. of ammonia.

Suggested Standard.—Anisated Spirit of Ammonia contains not less than 1.8 Gm. and not more than 2 Gm. of NH_3 in each 100 cc.

DISCUSSION.

Alcohol is used in the assay to prevent the precipitation of the anethol present in the spirit during titration. The quantity of alcohol specified will keep the solution clear regardless of the condition of the spirit; usually 10 to 15 cc. of alcohol are sufficient for the official preparation.

Choice of Indicator.—Of the commonly used indicators, methyl red was found to give the most sharp and definite end-point, hence its selection.

Typical results obtained with the use of this method are given in the following table:

TABLE IV.—TITRATION OF TOTAL AMMONIA.

Cc. of Spirit.	Cc. of Alcohol Used.	Cc. of 0.1 H ₂ SO ₄ Required.	Equivalent Weight of NH ₃ Gm.	Theoretical Weight of NH ₃ Gm.
2	15	22.57	0.0384	0.0386
2	15	22.55	0.0383	0.0386
2	20	22.65	0.0385	0.0386
2	20	22.22	0.0380	0.0386

Calculation of Theoretical Weight of Ammonia.—The ammonia water used in the preparation of the spirit assayed 10.06 p. c. of ammonia with a specific gravity of 0.9593, which is equal to 9.65 Gm. of ammonia in 100 cc. of ammonia water. Anisated Spirit of Ammonia contains 20 p. c. by volume of ammonia water or 1.93 Gm. of ammonia in 100 cc. of the spirit or 0.0386 in 2 cc. The standard proposed was similarly calculated using the percentage strength variations and specific gravity value stated for ammonia water in the U. S. P. X.

A PHYSICOCHEMICAL STUDY OF SOLUTION OF MAGNESIUM CITRATE.*

BY MARGARETHE OAKLEY AND JOHN C. KRANTZ, JR.

INTRODUCTION.

The recognition of a solution of magnesium citrate in the United States Pharmacopœia of 1850 heralded the appearance of scores of papers concerned with various ramifications of this galenical over the last eight decades. An interesting bibliography of this work has been compiled by Professor Langenhan (1). The increasing of the quantity of citric acid per bottle (350 cc.) from 33 Gm. to 35 Gm. precipitated anew the discussion of this product. The pivots around which most of the discussion revolved were the increased acidic taste of the solution and the relative therapeutic efficacy of acid magnesium citrate and the normal salt. Among other writers the new formula for solution of magnesium citrate was defended ardently by Seltzer (2) in 1927 and vehemently maligned by Neimeth (3) in 1929.

It is not the purpose of this investigation to promulgate the adoption of either formula, but to study certain interesting physicochemical aspects involved in the preparation.

ACIDITY AND ACID TASTE.

Much work has been conducted to determine the relationship existing between acid taste, hydrogen-ion concentration and titratable acidity. In 1898 Kastle (4) found a relationship existing between the acid taste and the affinity constants of nineteen different acids in *N*/50 concentration. The threshold concentrations at which various acids exhibited an acidic taste has been studied by Schreiber (5). For citric acid the threshold concentration was found to be about 0.0025 per cent. Harvy (6) made a comprehensive study of the subject and found that total acid concentration and hydrogen-ion concentration were factors in determining acid taste. Through these investigations the influence of buffer salts

* Scientific Section and Section on Practical Pharmacy, Miami meeting, 1931.