Determine arsenic from this point by the U. S. P. method. The difference between the percent of As_2O_3 by the U. S. P. method and "total arsenic" calculated as As_2O_3 represents the amount of arsenic in oxidized form.

DISCUSSION.

Philip Asher, of New Orleans, referring to the method proposed by Mr. Brown of using both the gravimetric and the volumetric processes, asked, "Why not stop at the volumetric, and get the morphine content?" Referring to the author's method of determining the alcohol in iodine, he said he had used that method himself, and it was approximately correct, sufficiently so for all practical purposes, and it could be carried out in two minutes. He placed some alcohol in a graduated cylinder and added potassium carbonate. This was shaken thoroughly, and in a short while the alcohol was found lying out above the potassium carbonate, upon which he was making the determination.

Continuing, Mr. Asher said, referring to the author's determination of free acids by distillation, that, in the early '90s, he had carried on a series of experiments of this kind, and had gotten his free acids by determining the free iodine by the potassium iodate method. He started by adding sodium thiosulphate until all the free iodine was taken up, and then added a small amount of potassium iodate. The iodate, in the presence of hydriodic acid was split up into iodine. The number of cubic centimeters found, multiplied by five-sixths, and by the iodine coefficient gave the iodine that was converted into hydriodic acid. This gave an exact determination. The desired result was had, without going through the process of distillation.

Mr. Brown responded that in the determination of morphine by precipitation, and extraction of the residual morphine left in the "mother liquor," he got around the disadvantage of having to use a large amount of solvent, which would be necessary if *all* the morphine was extracted by means of an immiscible solvent.

He did not determine the "free acid" by distillation as had been suggested. If the titration method was used, all that was necessary to do was to add a little phenolphthalein indicator to the solution, after decolorizing with thiosulphate, and titrate with tenth normal alkali to get the free acid, the product of the reaction between the thiosulphate and the iodine being neutral.

THE STABILITY OF OUABAIN IN AQUEOUS SOLUTION.

CHAS. C. HASKELL AND W. A. DOEPPERS.

Galenical preparations and isolated pure principles of digitalis are comparatively slowly absorbed when administered by mouth to normal individuals. In patients suffering from cardiac disease, a condition of acute circulatory embarrassment often occurs, rendering it of the greatest importance to secure prompt drug action; but the venous stasis dependent upon the circulatory failure gives rise to engorgement of the gastro-intestinal mucosa and consequently, further delays absorption by this route.

In the treatment of such patients, clinicians have long desired some remedy that could be introduced directly into the blood stream and bring about full and prompt action. The infusion of digitalis has been employed in this way, but it would seem that it would be desirable to study upon lower animals the effect of

introducing the number of undesirable constituents present in crude preparations of digitalis before the use of the infusion in this manner could be unqualifiedly endorsed. Then too, the experiments of Hatcher and Eggleston have shown that the commonly held opinion regarding the instability of the infusion is fully justified. Finally, it would be hard to secure an estimate of the strength of crude preparations of digitalis sufficiently accurate for use in standardizing remedies for intravenous use.

Credit is due to Hatcher for drawing attention to the possible value of Strophanthin gratus; known as crystalline Strophanthin, Thoms; or better, as Ouabain. This substance is a crystalline glucoside, isolated from Strophanthus gratus; probably a definite chemical compound; and is readily soluble in water or alcohol.

Amorphous strophanthin has been used quite extensively for intravenous administration; and the results have often been very favorable. The chief disadvantage in the use of this substance is the uncertainty concerning its composition, it being probable that it is a mixture of different glucosides and different lots are apt to vary in strength.

Ouabain in a dry condition kept under ordinary climatic conditions, exposed to air and light, undergoes no change in two years that can be detected by animal experiments. The convenience afforded by offering the physician a solution of Ouabain in ampoules, has led us to undertake a study of its keeping qualities when dissolved in solutions of different composition.

Ouabain was dissolved in distilled water, in normal salt (.09%) solution; in 5 percent alcohol; in 10 percent alcohol; in 25 percent alcohol and in 95 percent alcohol. The ouabain percentage was 1/10 to 1/100. Some of these solutions were tested upon frogs, using Cushny's one hour method; others upon guinea pigs, using a 24 hour lethal dose method; and a few upon cats, using Hatcher's method. The frog and cat methods have already been fully described elsewhere. The guinea pig method is a modification of Reed's. The dose is calculated per gram body weight and injected subcutaneously as in Reed's method. We have found it necessary, however, to take account of the alcoholic content of the solution and also advisable always to use the same volume of fluid per gram, so 0.01 cc. fluid per gram weight is always injected and 25 percent alcohol has been used in all the tests. It is also more satisfactory to observe the animal for 24 hours, because it is very common for pigs to survive more than three hours and succumb before the expiration of twenty-four hours. Occasionally, an animal succumbs only at the end of forty-eight hours, but this is unusual. Attention has already been called to the unreliability of the guinea pig method in attempting to standardize the members of the digitalis group, but in a comparative study such as this the factor of seasonal variation does not enter. The results may be tabulated as follows: "Drug strength means the strength of the original solution, which was reduced to 1:100000 for the cat assay; 1:20000 for the frog assay; and 1:10000 for the guinea pig assay whenever it was originally stronger. The figures under cat assay are fractions of a milligram per kilo; under guinea pig and frog assay are fractions of a gram per gram.

I. OUABAIN IN AMBER GLASS CONTAINERS.

Age of Solution	Solvent	Drug Strength	Container	Cat Assay	Guinea Pig Assay	Frog Assay
2 days	95% Alc.	1:1000	Flask	.0788	.00000025	.00000045
9 months	Water	1:10000	Amber Bottle	.....	.00000025	.00000045
14 months	Water	1:10000	Amber Bottle	.0800	.00000025	.00000046
28 months	Normal Salt	1:1000	Amber Bottle	.0796	.00000027	.00000046

From these results it may be assumed that Ouabain dissolved in distilled water or in normal salt solution and kept in amber bottles suffers no appreciable loss of strength in 28 months.

Two samples had been kept in glass-stoppered flint bottles and the assay of these give rather surprising results.

II. OUABAIN IN FLINT GLASS CONTAINERS.

Age of Solution	Solvent	Drug Strength	Container	Cat Assay	Guinea Pig Assay	Frog Assay
2 days	95% Alc.	1:1000	Flask	.0788	.00000025	.00000045
*22 months	Water	1:1000	Flint Bottle	.....	.00000036	.00000067
*32 months	Water	1:1000	Flint Bottle	.....	.00000055	.00000075
36 months	95% Alc.	1:1000	Flint Bottle	.....	.....	.00000052

*First and second assays on same sample.

From these tests, it seems that the nature of the container and the presence of alcohol influence the rate of deterioration. While an aqueous solution in an amber cork-stoppered bottle suffers little or no change in strength during twenty-eight months; an aqueous solution in a flint glass-stoppered bottle loses strength to a considerable degree in twenty-two months. Of course, too much weight should not be given the results obtained with such a limited number of samples.

Since the aqueous solutions of Ouabain in amber bottles show no loss in strength that could be detected in twenty-eight months, it seemed unnecessary at this time to test those containing alcohol, because other things being equal, an aqueous solution is preferable to an alcoholic solution for intramuscular or intravenous use. Frog assays with these solutions showed that those containing five percent and ten percent alcohol gave the same value at the end of fourteen months as did the aqueous solutions, the containers being amber bottles.

In conclusion it may be said that the results of our work indicate that aqueous solutions of Ouabain in amber glass containers are sufficiently stable to justify reliance being placed upon them by the physician.

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