(2) The *p*-amino benzoate of 4-(carbethoxymethyl)-1-piperazineacetate has been prepared. A 2% solution of the dihydrochloride is comparatively inactive.

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A MODIFIED ASSAY PROCESS FOR ALKALI BENZOATES AND SALICYLATES.*,†

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INTRODUCTION.

The assay processes of sodium benzoate and salicylate have been the subject of much investigation during the past three decades. In 1902, Alcock (1) called attention to the simple assay process of the British Pharmacopœia. The method consisted of simple ignition and titration of the resulting carbonate. Certain difficulties in the method were enumerated. This worker suggested the conversion to chloride and argentimetric determination of the chloride. The field was reviewed and studied comprehensively by Clark (2) in 1926. This investigator concluded that the most accurate and uniform results are obtained by either weighing the metal as chloride or extracting the liberated organic acid and weighing.

In the preparation of the official monographs for the forthcoming edition of the Pharmacopœia the method of assay recently described by Henville (3) was investigated in this laboratory.

A modification of the Henville procedure was adopted and the results obtained are set forth in this communication.

EXPERIMENTAL.

In the method suggested by Henville, a weighed quantity (about 2 Gm.) of the salt is transferred with water to a cylindrical separator. A few drops of methyl orange is added and 30 cc. of neutral ether. Half-normal hydrochloric acid is run in with careful shaking until the indicator shows a distinct red color. The aqueous layer is then transferred to another separator and the water washings of the ether are added. Neutral ether is added and upon shaking the color again becomes yellow. The titration is continued until the second end-point is reached.

In an effort to simplify the method the authors have adopted the following procedure which serves as a rapid and accurate method for Pharmacopœial purposes.

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The following procedure is applicable for sodium benzoate or salicylate.

"Transfer about 1.5 Gm. of the salt, previously dried to a constant weight at 100° C. and accurately weighed, to a tall beaker of about 300 cc. capacity and add 75 cc. of ether and 5 drops of methyl orange T.S. Titrate the mixture with half-normal hydrochloric acid, mixing intimately the aqueous and ethereal layers by vigorous stirring, until a permanent orange color is produced in the aqueous layer."

The method was tried with samples of U. S. P. sodium salicylate and benzoate which had been previously recrystallized. The results are compared in Tables I and II with those obtained by assaying the same salts by the official process.

TABLE I.—PERCENTAGE PURITY.

Sodium Benzoate.

Sample.	New Method.	U. S. P. X Method.
1	99.10	98.76
2	98.70	98.63
3	98.70	99.21
4	99.50	98.47
5	99.30	101.00
6	99.60	99.63
7	99.10	99.55
8	99.20	...
9	99.42	...
10	99.22	...
11	99.33	...
12	99.30	...
13	99.30	...
14	99.27	...
15	99.53	...
16	99.30	...
17	99.32	...
18	99.34	...
19	99.52	...
20	99.36	...
21	99.43	...
22	99.41	...
23	99.37	...
Mean	99.29	Mean 99.32
r =	0.151	r = 0.582

The statistical analysis of the raw data obtained illustrates the superiority of the new method as far as accuracy is concerned. Thus "r" the probable error of a single determination for sodium benzoate is 0.15 per cent using the new method. By the U. S. P. method r = 0.58 per cent. With sodium salicylate r = 0.07 per cent using the new method and 0.61 per cent when the U. S. P. method was employed. In these calculations

$$r = \pm 0.6745 \sqrt{\frac{\Sigma(v^2)}{n-1}}$$

The possible sources of error in the U. S. P. X method are many. During the process of ignition the salt tends to be ejected from the crucible, and, even when a small flame is used and the utmost care is taken to prevent sudden overheating, some small portion of the sample is probably lost. The Pharmacopœia directs that

TABLE II.—PERCENTAGE PURITY.

Sodium Salicylate.

Sample.	New Method.	U. S. P. X Method.
1	99.60	99.37
2	99.30	99.47
3	99.30	100.00
4	99.32	98.80
5	99.37	99.40
6	99.39	98.40
7	99.53	98.60
8	99.70	99.33
9	99.41	101.00
10	99.39	101.00
11	99.43	...
12	99.35	...
13	99.50	...
14	99.36	...
15	99.40	...
16	99.31	...
17	99.29	...
18	99.32	...
19	99.42	...
Mean	99.40	Mean 99.53
	r = 0 073	r = 0.607

the final temperature should not exceed a dull red heat, but this limitation may be variously interpreted by different operators. After ignition, the carbonized mass is to be disintegrated with a glass rod. The carbonized mass is usually very brittle, and it is very likely that during the process of disintegration small bits are thrown out of the crucible. The pulverized mass is boiled with 50 cc. of water and 50 cc. of acid; the mixture is filtered, and the residue washed free from acid. The quantity of solution thus obtained varies with different operators, but in all cases a large volume results.

CONCLUSION.

1. A rapid and more accurate method for the assay of sodium salicylate and benzoate has been devised, based upon the procedure of Henville.

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MANUFACTURE OF MEDICINAL PRODUCTS IN JAPAN.

A survey is being made of medicinal products manufactured in Japan by the Japanese Health Bureau. Among the items represented in considerable quantity are the following. The amounts are in kilograms.

Condurango Extract, 52,292; Ethyl Acetate, 366,120; Solution of Potassium Acetate, 55,318; Sodium Bicarbonate, 5,810,181; Mercuric Chloride, not including tablets, 65,154; Mercuric Dextrin, 129,595; Senega Syrup, 180,558; Paste of Tar, 20,159; Calcium Lactate, 34,830.