Section on Historical Pharmacy

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THE TABLET INDUSTRY—ITS EVOLUTION AND PRESENT STATUS.

L. F. KEBLER, PH. C., M. D.

Continued from Page 958, July Issue.

Puckner and Clark, and Puckner and Hilpert restricted their observations entirely to the determination of phenol in tablets of bismuth, opium and phenol. It is conceded by all that volatile agents of the phenol type should not be compressed into tablet form and that manufacturers should prepare such commodities only on special request. They should furthermore safeguard their reputation by placing upon the label a statement of the following character: "The amount of phenol declared to be present in each tablet according to label was used in their preparation, but on account of the volatile nature of phenol it is impossible to give any assurance as to the amount present in the finished product and it is supplied with this understanding." The results obtained by these workers are given herein, but they do not form a part of any general conclusion made here relating to tablets, except in so far as it may pertain to tablets containing volatile agents.

TABLE VIII.—*Determination of Phenol in Bismuth, Opium and Phenol Tablets, by Puckner, Clark and Hilpert.*

Product.	Amount declared.	Amount found.	Variation.
	Grains.	*Grains.*	*Percent.*
Phenol[1]	0.5	0.109	—78.1
do	.5	.244	—51.2
do	.125	.066	—47.2
do	.5	.351	—29.8
do	.5	.235	—43.
do	.5	.363	—27.4
do	.5	.173	—65.4
do	.5	.132	—73.6
do	.5	.069	—86.2
do	.5	.231	—53.8
do	.5	.197	—60.6
do	.5	.063	—87.4
do [2]	.5	.1710	—65.8
do	.5	.2880	—42.4
do	.125	.0794	—36.5
do	.5	.2343	—53.1
do	.5	.2670	—46.6
do	.5	.1159	—76.8

[1]Puckner, W. A., and Clark, A. H., J. Am. Med. Asso., 1908, *51*: 881.
[2]Puckner, W. A., and Hilpert, W. S., J. Am. Med. Asso., 1910, *55*: 2169

Product.	Amount dclared.	Amount found.	Variation.
	Grains.	*Grains.*	*Percent.*
Phenol[2]	.5	.1405	—71.9
do	.5	.2688	—46.3
do	.5	.0614	—87.7
do	.5	.1725	—65.5
do	.5	.3422	—31.6
do	.125	.1035	—16.8
do	.5	.2342	—53.2
do	.5	.1907	—61.8
do	.5	.1243	—75.1
do	.5	.1412	—71.8
do	.5	.5632	+12.6
do	.5	.2073	—58.5

Seel and Friederich made the latest observations recorded in literature. They examined tablets of only three separate drugs and in one instance but two determinations were made. The results by these investigators, recorded in Table 9, are satisfactory. A large majority of the tablets examined contained less than the amount declared, but for all practical purposes they come within the 10 percent maximum variation from the amount declared upon the label.

TABLE IX.—*Results of Analyses of Tablets by Seel and Friederich.*[4]

Product.	Amount declared.	Amount found.	Variation.
	Grams.	*Grams.*	*Percent.*
Acetylsalicylic acid	0.5	0.4912	—1.7
do	.5	.4712	—5.8
do	.5	.5038	+0.8
do	.5	.4872	—2.5
do	.5	.4408	—11.8
do	.5	.498	—0.4
do	.5	.533	+6.6
do	.5	.498	—0.4
do	.5	.491	—1.8
do	.5	.4822	—3.5
do	.5	.483	—3.4
do	.5	.492	—1.6
Pyrazolphenyldimethylsalicylate	.5	.447	—10.6
do	.5	.490	—2.0
do	.5	.5	0.0
Salipyrin	.5	.452	—9.6
do	1.0	.923	—7.7

From the results recorded by Liebreich fifteen years ago, and the observations of Seel and Friederich, a 10 percent maximum variation from the declaration upon the label would be satisfactory. But the observations made by other analysts militate against such a restricted standard. In order to obtain more extended data on this point, a large number of tablets of American make were examined and the results are recorded in Table 10. These results represent the average of ten or more tablets.

[3]Puckner, W. A., and Hilpert, W. S., J. Am. Med. Asso., 1911, *56:* 1844.
[4]Seel, Eugen, and Friederich, Albert, Med. Klin., 1911, *7:* 888, 928.

TABLE X.—*Results of the Analyses of Tablets made by Various Chemists in the Bureau of Chemistry.*

Product.	Amount declared.	Amount found.	Variation.
	Grains.	*Grains.*	*Percent.*
Acetanilid	2.	1.836	—8.2
do	2.	1.52	—24.0
do	2.5	2.46	—1.6
do	4.	3.88	—3.
do	5.	4.	—20.
do	2.	1.85	—7.5
do	5.	4.35	—13.
do	3.	2.50	—17.
do	3.	1.86	—38.
do	3.	2.57	—14.3
do	3.	2.37	—21.
do	2.	1.957	—2.1
do	2.	1.90	—5.
do	2.	1.78	—11.0
do	2.	1.996	—.2
do	2.	1.605	—19.8
do	1.	0.848	—15.2
do	3.	3.02	+.6
do	5.	4.832	—3.4
Acetanilid comp.:			
Acetanilid	3.5	2.563	—26.7
Caffein, citrated	.5	.53	+6.
Acetanilid comp.:			
Acetanilid	2.	1.919	—4.1
Caffein, citrated	.5	.486	—3.
Acetanilid comp. No. 1:			
Acetanilid	2.	2.	00
Caffein, citrated	.5	.447	—10.6
Acetanilid comp. No. 2:			
Acetanilid	2.5	1.954	—21.8
Caffein, citrated	1.	.782	—21.8
Acetanilid comp. No. 6:			
Acetanilid	2.5	2.27	—9.2
Caffein, citrated	1.	.949	—5.
Acetanilid comp.:			
Acetanilid	3.	2.25	—25.
Caffein	.5	.35	—30.
Acetanilid comp. (Searle):			
Acetanilid	3.	3.008	+.3
Caffein	1.	.943	—5.7
Acetanilid comp.:			
Acetanilid	1.4	1.414	+1.
Caffein	.2	.201	+.5
Acetanilid comp.:			
Acetanilid	3.5	3.372	—3.6
Caffein, citrated	.5	.488	—2.4
Acetanilid comp.:			
Acetanilid	3.5	3.546	+1.3
Caffein	.5	.487	—2.6
Acetanilid comp.:			
Acetanilid	3.5	2.771	—20.8
Caffein	.5	.426	—15.
Acetanilid comp. (Aulde):			
Acetanilid	3.5	3.34	—4.5
Caffein	.5	.518	+3.6
Acetanilid comp:			
Acetanilid	3.5	2.998	—14.4
Caffein	.25	.422	+69.

TABLE X.—(*Continued.*)

Product.	Amount declared.	Amount found.	Variation.
	Grains.	*Grains.*	*Percent.*
Acetanilid comp:			
Acetanilid	2.5	2.54	+1.6
Caffein, citrated	.5	.62	+24.
Acetanilid comp. (Kerr):			
Acetanilid	3.	2.301	—23.3
Caffein, citrated	.5	.546	+9.
Acetanilid comp:			
Acetanilid	3.5	2.69	—23.
Caffein, citrated	.5	.474	—5.
Acetanilid comp:			
Acetanilid	3.0	3.11	+3.6
Caffein, citrated	.5	.524	+4.8
Acetanilid comp:			
Acetanilid	3.5	3.104	—11.4
Caffein	.5	.474	—5.2
Acetanilid comp:			
Acetanilid	3.5	3.428	—2.1
Caffein, citrated	.5	.505	+1.
Acetanilid comp:			
Acetanilid	3.	2.576	—14.1
Caffein, citrated	.5	.447	—10.6
Acetanilid comp:			
Acetanilid	3.5	2.7	—23.
Caffein	.5	.42	—16.
Acetanilid comp:			
Acetanilid	3.5	3.303	—5.6
Caffein	.5	.41	—18.
Acetanilid comp:			
Acetanilid	3.0	2.835	—5.5
Caffein	.5	.491	—2.
Acetanilid comp. (Aulde):			
Acetanilid	.35	.336	—4.
Caffein, citrated	.05	.054	+8.4
Acetanilid comp. (Aulde):			
Acetanilid	3.5	3.28	—6.3
Caffein, citrated	.5	.486	—3.
Acetanilid comp., powd.:			
Acetanilid	3.5	3.455	—1.3
Caffein	.5	.496	—1.
Acetanilid comp., Special:			
Acetanilid	3.	2.955	—1.5
Caffein, citrated	.5	.515	+3.
Acetanilid comp:			
Acetanilid	2.5	2.29	—8.4
Caffein, citrated	1.0	.856	—14.4
Acetanilid comp.:			
Acetanilid	2.	1.77	—11.5
Caffein, citrated	.5	.432	—13.6
Acetanilid comp.:			
Acetanilid	3.	2.659	—11.4
Caffein	1.	.874	—12.6
Acetanilid comp.:			
Acetanilid	3.	2.743	—8.6
Caffein, citrated	.5	.439	—12.
Acetanilid comp.:			
Acetanilid	3.	2.844	—5.2
Caffein, citrated	.5	.475	—5.

TABLE X.—(*Continued.*)

Product.	Amount declared.	Amount found.	Variation.
	Grains.	*Grains.*	*Percent.*
Acetanilid comp. (Aulde):			
Acetanilid	3.5	3.381	—3.4
Caffein	.5	.47	—6.
Acetanilid comp. (Hubbard):			
Acetanilid	3.5	3.235	—7.6
Caffein	1.	.92	—8.
Acetanilid comp., pow. U. S. P.:			
Acetanilid	3.5	3.49	—.3
Caffein, citrated	.5	.52	+4.
Acetanilid and codein:			
Acetanilid	3.3	3.27	—1.
Codein	.25	.24	—4.
Caffein		.46	
Acetanilid	3.5	2.56	—27.
and codein (sulphate)	.25	.17	—32.
and caffein, citrated	.5	.37	—26.
Acetanilid comp.:			
Acetanilid	3.5	2.896	—17.2
Caffein, citrated	.5	.44	—12.
Codein	.125	.065	—48.
Acetanilid comp.:			
Acetanilid	3.	3.20	+6.7
Morphin sulphate	1/22	.04	—12.
Acetanilid comp.:			
Acetanilid	2.5	1.849	—26.
Sodium salicylate	1.	.903	—9.7
Acetanilid comp. and codein:			
Codein sulphate	.25	.264	+5.6
Acetanilid	3.325	3.366	+1.2
Caffein, citrated	.475	.48	+1.
Acetanilid comp. and codein:			
Acetanilid	3.	2.734	—8.9
Caffein, citrated	.5	.462	—8.
Codein sulphate	.25	.143	—42.8
Acetanilid comp. and codein:			
Acetanilid	3.325	2.554	—23.
Caffein	.475	.342	—28.
Codein	.25	.158	—36.8
Acetanilid comp. and codein:			
Codein sulphate	.25	.227	—9.
Acetanilid	3.	2.813	—6.2
Caffein, citrated	1.	.865	—13.5
Acetanilid comp. with codein:			
Acetanilid	3.	2.98	—.7
Codein	.25	.23	—8.
Caffein, citrated	.5	.5	000.
Acetanilid comp. with codein:			
Acetanilid	3.5	3.16	—10.
Caffein, citrated	.25	.33	+32.
Codein sulphate	.25	.20	—20.
Acetanilid and quinin:			
Acetanilid	2.5	2.42	—3.
Quinin sulphate	2.5	2.4	—4.
Acetanilid and			
Sodium bromid	3.5	2.90	—17.
Caffein, citrated		.566	
Acetanilid and sodium comp.:			
Acetanilid	3.5	3.45	—1.4
Caffein, citrated	.5	.455	—9.

TABLE X.—(*Continued.*)

Product.	Amount declared.	Amount found.	Variation.
	Grains.	*Grains.*	*Percent.*
Acetanilid and sodium comp.:			
Acetanilid	3.5	3.4	—3.
Caffein	.25	.235	—6.
Acetanilid and sodium comp.:			
Acetanilid	2.	1.926	—3.7
Sodium salicylate	3.	2.839	—5.4
Acetanilid and sodium comp.:			
Acetanilid	2.5	2.336	—6.5
Caffein, citrated	1.	.902	—10.
Acetanilid and sodium comp.:			
Acetanilid	2.5	2.515	+.6
Caffein, citrated	1.	.977	—2.3
Acetanilid and sodium comp.:			
Acetanilid	3.5	3.42	—2.3
Caffein	.25	.24	—4.
Acetanilid and sodium comp.:			
Acetanilid	3.5	3.02	—13.
Caffein	.5	.51	+2.
Acetanilid and sodium comp.:			
Acetanilid	3.5	3.367	—3.8
Caffein, citrated	.5	.487	—3.
Acetanilid and sodium comp.:			
Acetanilid	3.5	3.245	—7.3
Caffein, citrated	.5	.494	—1.6
Acetanilid and sodium comp.:			
Acetanilid	3.5	3.249	—7.2
Caffein, citrated	.5	.441	—12.
Acetanilid and sodium comp. with codein:			
Acetanilid	3.5	3.232	—7.6
Caffein	.25	.236	—5.6
Codein	.25	.239	—4.4
Acetanilid and sodium comp.:			
Acetanilid	3.5	3.459	—1.2
Caffein, citrated	.5	.510	+2.
Acetanilid and sodium comp.:			
Acetanilid	3.5	3.507	+.2
Caffein, citrated	.5	.53	+6.
Acetanilid and sodium comp.:			
Acetanilid	3.5	3.4	—3.
Caffein, citrated	.5	.523	+4.6
Acetanilid and sodium comp.:			
Acetanilid	3.5	3.386	—3.2
Caffein, citrated	.5	.493	—1.4
Acetanilid and sodium comp.:			
Acetanilid	2.5	1.966	—21.4
Caffein, citrated	1.	.905	—9.5
Acetanilid and sodium comp.:			
Acetanilid	3.5	3.477	—.65
Sodium bicarbonate	.9	.867	—4.
Sodium bromid	.1	.111	+11.
Caffein	.25	.238	—5.
Acetanilid and sodium comp.:			
Acetanilid	3.5	2.898	—17.2
Caffein, citrated	.5	.431	—14.
Acetphenetidin	5.	4.547	—9.
do	2.	1.97	—1.5
do	3.	2.31	—23.
do	3.	3.05	+1.6
do	3.	2.6	—13.3
do	5.	4.6	—8.

TABLE X.—(*Continued.*)

Product.	Amount declared.	Amount found.	Variation.
	Grains.	*Grains.*	*Percent.*
Acetphenetidin	3.	2.7	—10.
do	3.	2.98	—.6
do	2.	2.15	+7.5
do	5.	4.59	—8.2
do	3.	2.84	—5.33
do	3.	3.01	+.3
do	3.	2.53	—15.7
do	2.	1.56	—22.
do	5.	4.196	—16.
do	2.	1.819	—9.
do	2.	1.47	—26.
do	5.	4.16	—16.8
do	3.	2.84	—5.33
do	2.	1.80	—10.
Acid salicylic	2.5	1.87	—25.
Morphin (sulphate)	1/12	1/24	—50.
Ammonium salicylate	.166	.162	—2.4
do	2.5	2.295	—8.2
do	5.	6.28	+25.
Ammonium salicylate comp.:			
Ammonium salicylate	3.	3.25	+8.
Phenacetin	1.	1.	00.
Caffein	.5	.5	00.
Ammonium salicylate comp.:			
Phenacetin	1.	.85	—15.
Salicin	1.5	.989	—40.7
Ammonium salicylate	3.	1.685	—47.2
Caffein	.5	.465	—7.
Analgesic comp. with codein:			
Acetphenetidin	1.	1.	00.
Acetanilid	2.	1.96	—2.
Codein sulphate	.25	.225	—10.
Sodium salicylate	1.	1.1	+10.
Caffein	.5	.49	—2.
Anodyne comp.:			
Acetanilid	3.5	3.516	+.5
Caffein	.5	.494	—1.
Anodyne comp.:			
Acetanilid	3.5	3.57	+2.
Caffein	.5	.495	—1.
Antipyrin	2.	1.87	—6.5
do	3.	2.834	—5.9
do	2.	1.99	—.5
do	3.	3.	00.
Antiseptic mercuric chlorid	.82	1.37	+67.
Citric acid	.80	.63	—21.
Antiseptic mercuric chlorid	.82	1.882	+130.
Citric acid	.87	.893	+2.6
Aspirin	2.	1.93	—3.5
do	5.	5.05	+1.
do	5.	4.9	—2.
do	5.	4.77	—4.6
do	3.	1.76	—41.
do	5.	4.9	—2.
do	5.	4.4	—12.
do	5.	4.6	—8.
do	5.	4.16	—17.
do	3.	2.4	—20.
do	5.	4.9	—2.

TABLE X.—(*Continued.*)

Product.	Amount declared.	Amount found.	Variation.
	Grains.	*Grains.*	*Percent.*
Aspirin	5.	4.8	—4.
do	5.	4.4	—12.
do	5.	3.5	—30.
do	5.	3.7	—26.
do	5.	5.	00.
do	5.	5.	00.
do	5.	4.8	—4.
do	5.	4.7	—6.
do	5.	4.95	—1.
do	5.	4.7	—6.
Bismuth subnitrate	.1	.22	+120.
and calomel	.1	.19	+90.
Caffein	.5	.22	—56.
do	.5	.22	—56.
do	1.	.8269	—17.3
Caffein, citrated	1.	.80	—20.
do	1.	.47	—53.
do	2.	.69	—65.
do	1.	.92	—8.
do	.166	.145	—10.
do	1.	.87	—13.
do	1.	.955	—4.5
do	1.	.47	—53.
do	1.	.986	—1.4
do	1.	.865	—13.5
Calomel	1.	.944	—6.
and sodium bicarbonate	1.	.923	—8.
Calomel	1.	.97	—3.
and sodium bicarbonate	1.	.93	—7.
Calomel	1.	.74	—26.
and sodium bicarbonate	.5	.22	—56.
Calomel	.5	.6	+20.
and sodium bicarbonate	.5	.57	+14.
Calomel	1.	.93	—7.
and sodium bicarbonate	1.	.91	—9.
Calomel	1.	.99	—1.
and sodium bicarbonate	1.	.93	—7.
Calomel	1.	.7	—30.
and sodium bicarbonate	1.	1.01	+1.0
Calomel	1.	1.06	+6.0
and sodium bicarbonate	1.	1.05	+5.0
Calomel	1.	.89	—11.
and sodium bicarbonate	1.	.98	—2.
Calomel	1.	.9	—10.
and sodium bicarbonate	1.	.9	—10.
Calomel	1.	1.01	+1.0
and sodium bicarbonate	1.	.95	—5.
Calomel	1.	1.16	+16.
and sodium bicarbonate	1.	1.23	+23.
Calomel	1.	1.07	+7.0
and sodium bicarbonate	1.	.99	—1.
Calomel	.5	.5	0.
and sodium bicarbonate	.5	.48	—4.
Calomel	1.	1.	0.
and sodium bicarbonate	1.	1.06	+6.0
Calomel	1.	1.05	+5.0
and sodium bicarbonate	1.	.98	—2.
Calomel	1.	1.11	+11.
and sodium bicarbonate	1.	.95	—5.

TABLE X.—(*Continued.*)

Product.	Amount declared.	Amount found.	Variation.
	Grains.	*Grains.*	*Percent.*
Calomel	1.	.82	—18.
and sodium bicarbonate	1.	1.16	+16.
Calomel	1.	1.01	+1.
and sodium bicarbonate	1.	.98	—2.
Calomel	1.	1.03	+3.0
and sodium bicarbonate	1.	.85	—15.
Calomel	1.	1.015	+1.5
and sodium bicarbonate	1.	.98	—2.
Calomel	1.	.99	—1.
do	2.	.97	—51.
do	1.	1.16	+16.
do	1.	1.08	+8.0
do	.1	.096	—4.
do	1.	1.07	+7.0
do	1.	1.07	+7.0
do	1.	.89	—11.
do	.1	.125	+25.
Codein	.5	.489	—22.
do	.5	.314	—37.
do	.25	1/6	—33.
Corrosive sublimate	7.3	7.438	+1.9
do	1.8	2.047	+13.7
do	7.3	7.01	—4.0
do	1.82	1.74	—4.4
do	7.5	7.016	—6.4
do	1.75	1.553	—11.2
do	1.75	1.345	—23.1
do	7.3	8.170	+11.9
do	7.3	7.395	+1.3
do	7.3	7.396	+1.3
do	7.5	7.490	—.1
do	7.5	7.510	+.1
do	1.75	1.634	—6.6
do	7.3	6.974	—4.5
do	7.3	6.360	—12.9
do	7.0	6.897	—1.4
do	1.74	1.840	+5.7
Formin	5.	4.79	—4.2
do	5.	5.032	+.6
Grip:			
Acetanilid	2.5	2.380	—4.8
Ammonium salicylate	2.5	2.397	—4.1
Caffein, citrated	.5	.526	+5.
Heroin	.1	1/16	—37.
Heroin hydrochlorid	1/24	1/30	—20.
do	1/12	.0725	—13.
do	1/24	1/30	—20.
Hexamethylene	5.	4.9	—2.
do	5.	4.95	—1.
Hexamethyleneamin	5.	4.91	—2.
Hexamethylenetetramin	2.	2.25	+12.5
do	5.	4.51	—9.8
do	5.	4.813	—4.
do	5.	5.116	+2.3
do	5.	4.998	—.04
do	5.	5.043	+.86
do	5.	4.958	—.8
Migraine:			
Acetanilid	2.	1.85	—7.5
Caffein	.25	.27	+8.0

TABLE X.—(*Continued.*)

Product.	Amount declared.	Amount found.	Variation.
	Grains.	*Grains.*	*Percent.*
Migraine:			
Acetanilid	2.5	2.326	—7.
Sodium salicylate	1.	.914	—8.6
Migraine:			
Acetanilid	2.5	2.144	—14.2
Sodium salicylate	1.	.874	—12.8
Migraine:			
Acetanilid	2.	1.827	—8.6
Caffein, citrated	.5	.45	—10.
Migraine No. 1:			
Acetanilid	2.	1.955	—2.25
Caffein, citrated	.5	.512	+2.4
Morphin sulphate	.25	.225	—10.
do	1/6	.137	—18.
do	1/6	.199	+19.4
Myalgic (Dr. Woodward):			
Acetanilid	2.	1.843	—7.8
Sodium salicylate	2.	1.831	—8.4
Caffein	.5	.514	+3.
Nux vomica	1.	1.1	+10.
do	.25	.25	0.
do	.1	1/11	—10.
do	.25	.145	—41.
do	.25	1/6	—33
do	.25	.25	0.
do	.5	.46	—8.
do	.25	.125	—50.
Phenacetin	5.	3.90	—22.
do	3.	2.35	—21.6
do	3.	2.83	—5.6
Quinin sulphate	2.	1.76	—12.
do	2.	1.77	—11.5
do	2.	2.04	+2.0
do	2.	1.92	—4.
do	2.	1.94	—3.0
do	2.	1.92	—4.
do	2.	1.88	—6.
do	2.	1.83	—8.5
do	3.	2.92	—2.6
do	3.	2.3	—23.
do	2.	1.97	—1.5
Rheumatic (Dr. Lord):			
Sodium salicylate	5.	1.592	—68.
Codein sulphate	1/16	None	—100.
Rheumatic No. 4:			
Sodium salicylate	7.5	6.47	—13.7
Sodium bicarbonate	2.	1.48	—26.0
Rheumatic No. 6:			
Sodium salicylate	5.	3.564	—28.7
Codein sulphate	1/16	.0298	—52.
Rheumatic No. 6:			
Codein sulphate	1/16	.059	—5.6
Sodium salicylate	5.	4.779	—4.4
Salol	2.5	2.26	—9.6
do	2.5	2.32	—7.2
do	5.	4.27	—14.
do	2.5	2.32	—10.8
do	1/6	.14	—16.
do	2.5	2.23	—7.
do	5.	4.88	—2.4

TABLE X.—(*Continued.*)

Product.	Amount declared.	Amount found.	Variation.
	Grains.	*Grains.*	*Percent.*
Salol	2.5	2.41	—4.
do	2.5	1.80	—28.
do	5.	4.77	—4.6
do	5.	3.80	—24.
do	2.5	1.94	—22.4
do	2.5	2.96	+18.4
do	2.5	2.24	—10.4
do	5.	4.804	—3.9
do	5.	4.66	—6.8
do	2.5	2.288	—8.48
do	2.5	2.522	+1.
do	2.5	2.38	—4.8
do	2.5	2.05	—18.
do	2.5	2.36	—5.6
do	2.5	2.30	—8.
do	5.	4.43	—11.4
Sodium salicylate	3.	1.82	—39.
do	5.	4.59	—8.2
do	3.	3.08	+3.
do	5.	3.445	—31.
do	5.	4.88	—2.4
do	5.	4.85	—3.
do	5.	4.85	—3.
do	5.	4.78	—4.4
do	5.	4.40	—12.
do	5.	3.745	—25.
do	3.	2.91	—3.
do	5.	4.75	—5.
do	5.	4.45	—11.
do	5.	4.24	—15.2
do	5.	4.766	—4.8
do	5.	4.437	—11.2
do	3.	2.60	—13.
do	5.	4.57	—8.6
do	5.	4.855	—2.9
do	5.	3.23	—35.4
do	3.	2.82	—6.
do	5.	4.6	—8.
do	5.	4.871	—2.6
do	5.	4.91	—1.8.
Strychnin nitrate	1/50	1/48	+4.
do	1/40	1/49	—18.4
do	1/40	1/41	—2.5
do	1/40	1/47	—15.
do	1/40	1/38	+5.
Strychnin sulphate	1/40	1/28	+42.
do	1/40	1/38	+5.
do	1/40	1/53	—24.
do	1/40	1/56	—29.
do	1/40	1/43	—7.0
do	1/40	1/41	—2.5
do	1/40	1/39	+2.5
do	1/50	1/46.3	+8.
do	1/50	1/58	—14.
do	1/40	1/39	+2.5
do	1/40	1/39.5	+1.
do	1/40	1/37	+8.1
Sulphonethylmethane	5.	4.83	—3.4
Trional	5.	2.72	—45.6
Zinc phenolsulphonate	5.	3.64	—27.4

SUMMARY OF ANALYTICAL RESULTS, EXCEPTING NITROGLYCERIN TABLETS.

Number of samples of tablets examined	324
Number of determinations made	449
Percenage exceeding 10 percent above or below declaration	36.7
Percentage exceeding 12 percent above or below declaration	30.9
Percentage exceeding 15 percent above or below declaration	24.5
Percentage exceeding 20 percent above or below declaration	17.8

	Number	Percentage
Variations below declaration	343	76.4
Variations above declaration	94	20.9
Products in accord with declaration	12	2.7
Variations more than 10 percent below declaration	142	31.6
Variations more than 10 percent above declaration	23	5.1
Variations more than 15 percent below declaration	94	20.9
Variations more than 15 percent above declaration	16	3.6
Variations more than 20 percent below declaration	69	15.4
Variations more than 25 percent above declaration	11	2.4

COMMENTS.

The variations are unexpectedly large both in numbers and amounts. The tablets examined are of relatively simple composition, and, for the most part, contain medicinal agents which can be readily estimated with a fair degree of accuracy. The tablets examined are fairly representative of all manufacturers In only a few factories were the finished tablets actually examined chemically. The best tablets were found in factories where competent chemical control exists. In fact, no excessive variations were found in several brands so supervised. A careful review of the tablets examined shows, with possibly a few exceptions, that all of the results should have fallen within 10 percent, either above or below, the declaration. To find over one-third exceeding this variation does not substantiate the old-time claims for accuracy and uniformity. Even on a 15 percent basis nearly one-fourth are wanting. There is no reasonable excuse for such deviations, for example, as the presence of twice as much corrosive sublimate as claimed. This simply shows gross carelessness and incompetence. It will also be observed that a much larger number of the results fall below the amounts declared than above. The methods of analyses may contribute to this in a few instances. It is claimed that this is the safest side to err on, but the factor of safety is frequently too liberal, for example, 20 percent or more below claim in simple tablets of acetanilid or acetphenetidin or aspirin savors either of gross carelessness or design. It should be noted that since this investigation was begun more competent control has been provided in a considerable number of establishments, and there are indications of general improvements.

TABLETS CONTAINING VOLATILE OR UNSTABLE AGENTS.

Although the tablets containing volatile or unstable drugs are comparatively small in number, they are sufficiently important to call for careful consideration. Agents coming under this classification are nitroglycerin, phenol, camphor, chloro-

form, ether, ammonium carbonate, various essential oils, etc. Except in a few cases the amount of work done is inadequate to warrant conclusions, but it is well known that medication of this character is difficult to prepare and keep. It is furthermore common knowledge that the fact that the tablets are right at the outset is no proof that they will long remain so. Medical men should not resort to such uncertain medication, as it reflects discredit upon the profession and tends toward drug nihilism. The writer has in his possession tablets containing camphor which is sublimed on the sides of the bottle. They are no longer suitable medicines. In the case of essential oils there is often only sufficient present to impart a flavor. The phenol variability has been pointed out by Puckner and Clark,[1] and Puckner and Hilpert.[2]

In the present investigation nitroglycerin tablets, for various reasons, received chief consideration. Nitroglycerin is one of the most powerful heart remedies, and is depended upon by physicians in cases of emergencies which are sometimes of a very serious character. It has been reported from time to time that nitroglycerin tablets are of uncertain character, and that even though they are originally made with the proper quantity of nitroglycerin, it is impossible to state or represent how long they will remain so. This uncertainty of nitroglycerin tablets has been charged to the supposed volatility[3] of nitroglycerin. With this general knowledge available, whether correct or otherwise, it seems rather strange that some manufacturers should fill orders with nitroglycerin tablets made three or more years previously. Some manufacturers of deficient goods explained the shortage on the ground that the tablets had been on hand three, four or five years at the time the orders were filled. Yet in no instance did there appear any information on the packages to the effect that they were several years old. The packages, however, did bear the declaration that each tablet contained a given quantity of nitroglycerin. If such claims appear, they should be at least approximately correct. Such potent drugs should not be made on the hit or miss basis. A goodly number of the tablets on the market were purchased and examined, with the following results:

Results of Examination of Nitroglycerin Tablets.

Amount claimed. *Grains.*	Amount found (Nitrate method.) *Grains.*	Amount found (Nitrite method.) *Grains.*	Shortage. *Percent.*
0.005	0.0010	0.0011	80
.0020	.0017	.0008	91
.010	.010	.0098	0
.020	.015	.014	25
.020	.0050	.0045	75
.010	.004	.004	60
.020	.0012	.0011	94
.020	.008	.0073	60
.020	.009	.008	55
.020	.014	.0135	30
.020	.0096	.0108	46
.020	.0121	.0123	38

[1] J. Am. Med. Asso., 1908, *51*, 881.
[2] J. Am. Med. Asso., 1910, *55*, 2169.
J. Am. Med. Asso., 1911, *56*, 1344.
[3] H. Hager, Pharm. Centrh., 1877, *18*, 89.
J. M. Merrick, Am. J. Science and Arts, 1868, *36*, 212.

Amount claimed. *Grains.*	Amount found (Nitrate method.) *Grains.*	Amount found (Nitrite method.) *Grains.*	Shortage. *Percent.*
.020	.0108	.0117	41
.020	.0115	.0141	29
.020	.006	.006	70
.010	.0006	.0007	93
.010	.0076	.0082	18
.020	.0136	.0122	32
.010	.0093	.0086	7
.010	.0065	.0066	34
.010	.007	.0074	26
.010	.0026	.0026	74
.010	.0085	.009	10
.010	.0066	.006	34
.010	.008	.0083	58
.010	.0055	.0056	44
.020	.0074	.0087	56
.010	.007	.0077	23

It will be noted that the determinations made by two separate and distinct methods gave fairly concordant results. The shortages recorded are based upon the highest results obtained by either of the methods. The deficiencies found are abnormally large. Notwithstanding the general belief (which does not appear to be well founded) that nitroglycerin tablets are prone to deteriorate with age, it is reasonable to expect that they should possess at least 75 percent of the actual value claimed for them. It is furthermore believed that a 25 percent deficiency is excessive. Even on this basis a large majority (78 percent) are wanting. Over 42 percent exceed a 50 percent deficiency. During the interviews it developed that the tablets were not generally analyzed. The 10 percent nitroglycerin alcoholic solution and 10 percent nitroglycerin milk sugar triturations used were apparently accepted as represented in most instances without question. Various experiments were made to determine how rapidly nitroglycerin tends to volatilize at room temperature in a vacuum desiccator. The results seem to indicate that nitroglycerin is not as volatile as is believed by some. Experiments made with nitroglycerin tablets thus far show that some at least are fairly stable. The subject is, however, still under investigation.

It should be stated that after this paper was read, the writer's attention was called to a report of a "Committee of Chemists appointed to investigate the possible deterioration of drug extracts," which report was said to contain useful information on the stability of nitroglycerin tablets. After some correspondence a copy of this private publication, dated December 31, 1908, was received. The results recorded are herewith submitted:

Nitro-Glycerin Tablets.[1]

"We give below four samples assayed and re-assayed, and they do not seem to indicate any deterioration to amount to anything, and we know of no case of a nitro-glycerin tablet which failed to act physiologically, no matter how old it was. This seems to point to the fact that nitro-glycerin on milk sugar (which we know to be a good preservative and prevent oxidation quite largely) as it is used by physicians almost altogether, does not deteriorate appreciably with age."

Sample of Feb. 23, '05, of nitro-glycerin tablet, 1-25 grain; assayed May 31, '07, 1-30 grain
Sample of Apr. 17, '06, of nitro-glycerin tablet, 1-100 grain; assayed May 31, '07, 1-150 grain
Sample of Nov. 15, '06, of nitro-glycerin tablet, 1-50 grain; assayed May 31, '07, 1-80 grain
Sample of May 2, '07, of nitro-glycerin tablet, 1-100 grain; assayed May 31, '07, 1-100 grain

—A. R. L. DOHME.

Nitroglycerin.[2]

		Supposed Content.	Assay.	Age.
Tablet Triturate	No. 456	.0066 grain	.00679 grain	5 years
" "	No. 122	.010 "	.00979 "	1 "
" "	No. 123	.020 "	.0139 "	11 "
" "	No. 123	.020 "	.0264 "	9 "
" "	No. 123	.020 "	.0254 "	7 "
" "	No. 618	.010 "	.007 "	8 "
C. C. Tablet	No. 108	.010 "	.0098 "	10 "
" "	No. 108	.010 "	.0084 "	10 "
" "	No. 108	.010 "	.0098 "	9 "
G. C. Pill	No. 423	.030 "	.029 "	5 "
" "	No. 423	.030 "	.010 "	8 "
" "	No. 423	.030 "	.014 "	8 "

—J. M. FRANCIS.

CONCLUSIONS.

1. Tablets are not as uniform and accurate as is generally believed.

2. There is little difference between the uniformity of the larger tablets produced by the single or multiple vertical punch or the rotary machines.

3. The vertical single punch delivers more uniform hypodermic tablets and so-called compressed tablet triturates.

4. There does not appear to have been much advancement in the manufacture of uniform tablets during the past twenty years, even though the machinery has been materially improved.

5. The number of tablets produced from a given quantity of material should not vary to exceed 5 percent from the number calculated.

6. The variation in weight of tablets should not exceed 8 percent, either above or below the average.

7. The variation from the declaration should not exceed 10 percent in the average tablet or tablets of a fairly simple composition.

8. In complex, very small and difficult tablets to manufacture the variation from the declaration may be as great as 15 percent.

9. Volatile agents should not be compressed into tablet form, excepting flavoring agents and possibly nitroglycerin under strict control.

10. The amount of talcum used should not exceed 5 percent.

11. Fillers such as fuller's earth, chalk, gypsum, terra alba, kaolin, etc., should not be used.

12. No insoluble or non-disintegrable tablets should be placed on the market.

METHODS OF ANALYSIS.

INTRODUCTION.

The methods given here have not reached the stage where improvement is impossible. They are offered as a basis for future work, and it is hoped that all interested in this line of analysis will not only assist in trying out and improving these methods but will devise new ones as time and opportunity permit.

The work in this article has been restricted to uncoated tablets. Some of the methods, however, will undoubtedly give satisfactory results not only with uncoated but with many coated tablets as well. Some skill and adaptation may be

[1] Report of Committee of Chemists, 1908, p. 4.
[2] Report of Committee of Chemists, 1908, p. 16.

necessary with the latter products. A casual review of the ingredients used medicinally and in giving form to tablets shows that extreme care must be exercised in devising analytical methods which will insure accuracy and reliability. The majority of compressed tablets containing insoluble agents usually contain starch, gummy material and some lubricant. Soluble chemicals are frequently compressed without excipient. Lubricants are, however, often employed. Molded tablets generally contain either sugar of milk or sucrose, or both, as a base. Some disturbing features are liable to creep in with the utmost circumspection. Checking and counter checking must be employed frequently. The chemical reagents used must be carefully tested. In preparing granulations the process may be such as to occlude some of the medicinal agents so that it is very difficult to remove them completely with the ordinary solvents from the powdered material. For example, if in the manufacture of caffein tablets starch paste is used, some of the caffein may be dissolved and intermixed with the starch paste which on drying, envelopes the caffein and thus makes it very difficult to remove. In fact, in some instances it is virtually impossible to remove it completely. Starch and gummy material are great handicaps in formulating simple methods of analysis.

The analyst in the factory has a distinct advantage over the chemist not so connected. The former knows or can ascertain what breakers are ahead and may thus avoid them. Not so fortunate, however, is the chemist who simply has the tablets placed before him for analysis. For example, the factory chemist examines a sample of tablets and finds the results abnormal. He is unable to explain the difficulty, but the perplexity is readily solved when he calls for and receives the working formula. The analyst who has only the tablets to work from must depend upon his own ingenuity to solve and overcome various difficulties and it must be admitted that some of them may never be solved.

GENERAL METHODS.

WEIGHT OF TABLETS.

Weigh separately from ten to twenty-five tablets in order to ascertain the average weight and the variation from the average.

PREPARATION OF SAMPLE.

In a mortar, or other suitable apparatus, finely powder from ten to twenty-five or more tablets, mix thoroughly and introduce the powder into a weighing tube for future use. This procedure is not applicable to tablets containing volatile agents. It is of the utmost importance to powder finely and prepare a uniform sample.

DETERMINATION OF MOISTURE.

The amount of moisture may be determined in tablets containing non-volatile drugs by drying the powder in a vacuum (not less than 25 inches) at a temperature not exceeding 75° C. or in a hot water heated oven, to constant weight. These methods do not always give the same identical results, but they are sufficiently concordant for practical purposes.

DETERMINATION OF ASH.

Ignite a small portion at a dull red heat until the residue is white or gray, cool in a desiccator and weigh. Best results are secured in a well regulated muffled furnace. Flat platinum dishes are frequently used for this purpose The analyst should, however, never employ a platinum dish for ashing drugs unless he knows there is nothing present which will injure the platinum. It is always safest to use porcelain or silica dishes. Hoskin's electric furnace is well suited for ashing.

ATOMIC WEIGHTS.

The international atomic weights for 1914[1] (oxygen, 16) are used in all calculations excepting methods of analysis in Bulletin No. 107 (revised). For Pharmacopœial articles (Eighth Decennial Revision) the atomic weights recognized by that authority (hydrogen, 1) must be used.

SPECIAL METHODS.[2]

The methods given below are designed chiefly for determining the active medicinal ingredients. No claims for complete analysis are made, but in some cases the examinations are made as complete as practicable with present experience.

ACETANILID TABLETS.

Acetanilid, Method A: Place from ½ to 1 gram of the finely powdered material on small, double counterpoised filters, one within the other, in a funnel, and treat with successive portions of chloroform until all of the acetanilid is removed. From 40 to 60 cc. are generally sufficient. The solvent must be carefully applied, best from a pipette, not only to the powder directly, but to the sides and upper edges of the filters. Each addition should be allowed to drain before more solvent is used. When exhausted, wash the stem of the funnel with chloroform, collect the filtrate and washings in a tared Jena or non-sol beaker,[3] evaporate carefully at a slightly elevated temperature or in a current of air until the solvent is apparently dissipated, add 5 cc. of ether, evaporate, then heat for 15 minutes at about 100° C., cool in a desiccator and weigh.

Comments: The chloroform will remove certain lubricants such as "white oil," cocoa butter, stearic acid, and, if present, will be found with the acetanilid residue. The amounts are, however, usually so small that they may be disregarded for practical purposes. This observation is applicable to other determinations where the same or similar conditions obtain. A Gooch crucible may be used to advantage in place of the filter papers.

Purity of acetanilid: The purity of the acetanilid can be determined by the Pharmacopœial standard for this drug. The most important single observation is the melting temperature. Pure, dry acetanilid melts at from 111° to 113° C. If there is not sufficient material, a larger amount of the powder may be extracted. Occasionally artificially colored tablets are encountered. In such cases the chloroformic residue may be correspondingly colored, but the amount of color dissolved is generally negligible.

[1] J. Am. Chem. Soc., 1913, *35:* 1809; Drug. Circ., 1914, *58:* 28.
[2] With the collaboration of W. O. Emery, E. C. Merrill, A. G. Murray and S. Palkin.
[3] These beakers should be used in all similar determinations.

Acetanilid, Method B: If the acetanilid should prove impure, proceed by method A above, except collect the filtrate into a 200 cc. Erlenmeyer flask, distill to about 10 cc., add 20 cc. dilute sulphuric acid (10 percent) and digest on steam bath until the liquid is reduced to about 15 cc. and the chloroform is removed, then add 20 cc. of water, continue digestion until solution is reduced to about 15 cc., again add 20 cc. of water, continue digestion until solution is reduced to about 10 cc., finally add 40 cc. water and 15 cc. concentrated hydrochloric acid, and titrate with standard potassium bromid-bromate solution (Koppeschar's solution) until a slight yellowish color persists.

Comments: The first part of this procedure is for the purpose of converting the acetanilid into anilin sulphate and dissipating the acetic acid. The yellowish color is due to a slight excess of bromin. While adding the reagent the flask should be repeatedly rotated to agglutinate the precipitated tribromanilin formed. Should the amount of acetanilid be large and the tribromanilin precipitate too bulky, it may be necessary to dilute the anilin sulphate solution more and even titrate an aliquot part of the solution. If there is any probability of the chloroform dissolving sufficient water to carry appreciable amounts of associated bodies, the chloroform extracts should be collected in a second separatory funnel and washed with 15 or 20 cc. of water, then transferred to the Erlenmeyer flask and proceeded with as directed above. This observation should be borne in mind while working with various mixtures.

Potassium bromid-bromate solution: Dissolve 50 grams of potassium hydroxid in 50 cc. of water, add bromin, at ordinary temperature, to slight excess, dilute to 500 cc., heat to expel excess of bromin, filter, and make up to a liter. The solution is standardized against acetanilid and should be diluted so that each cc. represents about 0.01 gram of acetanilid.

Reactions involved in preparing potassium bromid-bromate solution and in determining the acetanilid by method B:

$$6KOH + 3Br_2 = 5KBr + KBrO_3 + 3H_2O$$

$$5KBr + KBrO_3 + 6HCl = 3Br_2 + 6KCl + 3H_2O$$

$$2C_6H_5NHCH_3CO + H_2SO_4 + H_2O = (C_6H_5NH_2)_2 H_2SO_4 + 2CH_3COOH$$

$$(C_6H_5NH_2)_2 H_2SO_4 + 6Br_2 = C_6H_2Br_3NH_2 + 6HBr + H_2SO_4.$$

Residue insoluble in chloroform: The total residue can be ascertained indirectly by deducting the amount of acetanilid obtained from the original weight taken. It may also be determined as follows: (a) Expose filters and contents in a protected place to the atmosphere for 24 hours, then weigh, using outer filter as counterpoise. (b) Heat filters containing the residue at 100° C. for one-half hour, cool in desiccator, and weigh, using outer filter as counterpoise. This gives residue on a moisture-free basis. Suitable calculations must be made to reduce data to uniform basis.

Comments: The residue of compressed acetanilid tablets consists essentially of starch, adhesive matter and inorganic lubricant, but in the case of molded tablets it consists chiefly of milk sugar.

The kind of starch may be determined by means of a microscope. The amount of starch may be estimated by the official method described in Bulletin 107 (revised) Bureau of Chemistry, p. 53, beginning at the point where the insoluble

residue is introduced into the refluxing flask and heated with 200 cc. of water and 20 cc. of hydrochloric acid.

Ash: Proceed as directed by general method for ash. The inorganic matter should consist essentially of talcum, but occasionally some "filler" is met.

ACETANILID COMPOUND.

Tablets bearing this name should contain as medicinal agents, acetanilid, caffein, and sodium bicarbonate, together with the ingredients usually employed in preparing tablet medication. The caffein and acetanilid of this mixture may be extracted from a neutral, an alkaline or acid aqueous solution with chloroform.

Caffein: Place about 1 gram, accurately weighed, into a separatory funnel[1] (A), add 25 cc. chloroform, shake well, add 25 cc. water and sufficient dilute sulphuric acid to render distinctly acid, agitate thoroughly and set aside for the chloroform to separate and clear. Transfer the chloroform to a 200 cc. Erlenmeyer flask through a small, dry filter. Repeat this operation with the same amount of chloroform three or four times, or until exhaustion is complete. Distill the chloroform gradually as the extraction proceeds to about 10 cc. finally. Then add 20 cc. of dilute sulphuric acid and continue distillation until all the chloroform is removed, transfer flask to steam bath and digest mixture until contents of flask are reduced to about 10 cc., add 20 cc. water and continue digestion until liquid amounts to about 10 cc.; cool, transfer to separatory funnel (B) with sufficient water to make about 25 cc. Exhaust with successive portions of chloroform (25 cc.) until all the caffein is removed. The chloroformic extractions can be evaporated in a tared beaker at a low temperature or the chloroform may be distilled from a flask to about 10 cc., then transferred with washings to a tared beaker and evaporated spontaneously or at a low temperature in a current of air. When apparently dry, cool, add 5 cc. of ether and evaporate carefully to avoid loss of caffein by crepitation, finally dry at 80° C. for one-half hour, cool in desiccator and weigh.

Comments: Test purity by U. S. P. standard for caffein. Unless extreme care is exercised the results will be low, due to incomplete extraction, creeping, etc. In this operation the acetanilid is converted into anilin sulphate, which, like many alkaloidal salts, is insoluble in chloroform and other immiscible solvents and, therefore, remains in the solution from which the caffein has been extracted.

Acetanilid: Transfer aqueous solution in separatory funnel (B) containing the anilin sulphate to an Erlenmeyer flask, wash the separatory funnel (B) and the filter used for filtering chloroformic solution of caffein above with two successive portions (15 and 10 cc.) of water, and also introduce these washings into the flask. Heat flask containing the anilin sulphate a short time to expel the chloroform, add 15 cc. of concentrated hydrochloric acid, then introduce slowly a standard potassium bromid-bromate solution, with agitation, until a distinct yellow color persists. The amount of acetanilid can readily be determined from the number of cubic centimeters of standard solution used. See comments for acetanilid under acetanilid tablets.

Sodium Bicarbonate, Method A: Introduce into a suitable dish from ½ to 1 gram of the material, incinerate at a dull, red heat, until all organic matter is

[1]The joint should be moistened with a drop of water to prevent leakage of chloroform.

destroyed and the residue is white, or nearly so; cool, dissolve the residue in water, add sufficient but a known amount of standard sulphuric acid to decompose the carbonate, then titrate back the excess of acid with standard potassium hydroxid solution, using methyl orange as indicator. Calculate results to sodium bicarbonate.

Comments: If the mixture is heated to fusion any talcum that is present may be disintegrated and the results obtained abnormal. This procedure is applicable only in special cases.

Reactions: $2\,NaHCO_3 + Heat = Na_2CO_3 + H_2O + CO_2$

$Na_2CO_3 + H_2SO_4 = Na_2SO_4 + H_2O + CO_2$

One cubic centimeter of normal sulphuric acid is the equivalent of 0.084 gram of sodium bicarbonate.

Sodium Bicarbonate, Method B: This chemical may be accurately determined by treating the mixture with 20 percent hydrochloric acid and absorbing the carbon dioxid evolved. About 2 grams of the material should be used. A detailed method with illustrated apparatus will be found on pages 169 and 170 of Bulletin 107 (Revised), Methods of Analysis, Bureau of Chemistry.

Comments: This method may be used in all cases where no other method is given.

Talcum, etc.: Introduce into a previously heated, cooled and weighed Gooch crucible provided with an asbestos mat about 1 gram, accurately weighed, of the powder; treat with sufficient warm water at about 40° C. to remove the sodium bicarbonate, etc., wash with 25 cc. alcohol, incinerate to white ash, cool in desiccator and weigh. The powder may be disintegrated in a beaker with water at about 40° C., then transferred to crucible and finished as above.

Comments: This procedure will include not only talcum but other insoluble, inorganic, non-volatile matter which may be added in the form of a filler or otherwise.

This general procedure may be used unless some non-volatile or insoluble (in water or alcohol) inorganic medicinal agent is present and should be applied when no other method is given.

Starch: Weigh into a 200 cc. beaker a suitable quantity, 2½ to 3 grams, of the dry material, add 50 cc. of alcohol, mix thoroughly, allow to stand a short time, transfer to filter and wash with about 200 cc. of lukewarm water, puncture the bottom of the filter, wash the residue into a 500 cc. flask with water, and make the volume up to 200 cc. with water, add 20 cc. of hydrochloric acid, specific gravity 1.125, attach flask to reflux condenser and heat for two and a half hours. Cool and nearly neutralize with sodium hydroxid, make volume up to 250 cc., filter and determine the dextrose in an aliquot part of the filtrate as directed in Methods of Analysis, Bulletin 107 (revised), page 49, section (b).

Comments: This method is of general application for ordinary starch, but is not suited for estimating soluble starch. Table for calculating dextrose will be found in Bulletin 107. Starch is present in virtually all tablets containing insoluble drugs and should be determined by this method.

ACETANILID COMPOUND WITH CITRIC ACID.

Citrated caffein is sometimes used in place of the alkaloid caffein. Some manufacturers seem to forget that there is a difference between the two products and furthermore they do not appear to know that this product should consist approximately of equal parts of caffein and citric acid. All of the ingredients present in these tablets excepting citric acid may be determined by methods given under acetanilid compound.

Citric acid: If there is no disturbing factor present, the acid can be titrated directly, but usually sodium bicarbonate is present in these mixtures and frequently sufficient moisture to induce some reaction with the citric acid forming a little sodium citrate. Several methods have been tried, but the results have not been concordant. Methods tried were: Extraction with absolute alcohol and titration; precipitation as barium citrate in 50 percent alcohol; and dissolving in water, acidulating with dilute hydrochloric acid, filtering, evaporating the filtrate to dryness and eliminating all free hydrochloric acid, then titrating with a standard alkaline solution.

Comments: The amount of citric acid present as citrated caffein can be ascertained approximately from the caffein found. The latter is the basis of the caffein citrate reported in this paper.

ACETANILID COMPOUND WITH CODEIN.

The term "codein" has come through lax usage to mean either the alkaloid, sulphate or phosphate. Strictly speaking, it means the alkaloid only and not any of its derivatives. The amount of sulphate or phosphate of this alkaloid present is usually small.

Caffein and acetanilid: Proceed as directed under acetanilid compound.

Codein: The acidulated solution in the separatory funnel from which the caffein and acetanilid have been extracted is rendered alkaline with potassium hydroxid. The liberated codein is extracted with successive portions of chloroform (15 cc. each), and the chloroformic solution filtered through a dry filter into a tared dish. The chloroform is then evaporated, the residue dried on a steam bath, cooled in a desiccator and weighed.

Comments: This gives anhydrous codein, $C_{18}H_{21}NO_3$. The purity of the codein may be determined by submitting it to the Pharmacopœial test prescribed for this drug. The amount and purity may also be checked by dissolving the codein in an excess of tenth normal sulphuric acid and titrating back the excess of acid with fiftieth normal potassium hydroxid, using methyl red as indicator. One cc. of tenth normal sulphuric acid is the equivalent of 0.031719 gram of crystallized codein, 0.0393 gram codein sulphate and 0.0433 gram codein phosphate.

If the insoluble matter should cause any difficulty, the solution may be filtered, the separatory funnel and filter washed, and all collected into another separatory funnel, then extracted as before directed.

The amount of codein found, if present in the form of sulphate or phosphate, may be checked by determining the amount of sulphate or phosphate present in the mixture, provided no other sulphate or phosphate is present.

ACETANILID COMPOUND WITH QUININ.

The quinin in this mixture is usually present in the form of sulphate. The compound may be analyzed as directed for acetanilid compound with codein.

Comments: This procedure gives anhydrous quinin. One cubic centimeter of tenth normal sulphuric acid is the equivalent of 0.037826 gram of U. S. P. quinin or 0.0436 gram quinin sulphate.

ACETANILID COMPOUND WITH SODIUM BROMID.

Caffein and acetanilid: Proceed as directed under acetanilid compound for these two chemicals except that the aqueous solution is rendered alkaline with either sodium or potassium hydroxid (free from chlorid) instead of acid.

Sodium bromid: Acidulate the solution remaining after removing the caffein and acetanilid with dilute nitric acid. Dilute to about 100 cc., filter, wash separatory funnel and filter paper with water and collect filtrate and wash in suitable beaker. The volume should finally amount to about 150 cc. Add tenth normal silver nitrate solution in excess to precipitate the bromin as silver bromid. Then add 1 cc. of ferric ammonium sulphate solution (10 percent) and titrate back the excess of silver nitrate with tenth normal solution of potassium thiocyanate. From the amount of tenth normal silver nitrate solution used the quantity of sodium bromid present in the mixture can readily be calculated.

Comments: In case the mixture is of such a character as to permit titration with silver nitrate without filtering, this part of the method may be omitted. One cubic centimeter of tenth normal silver nitrate is the equivalent of 0.010292 gram sodium bromid.

Reactions: $NaBr + AgNO_3 = AgBr + NaNO_3$

$AgNO_3 + KCNS = AgCNS + KNO_3$

$6KCNS + Fe_2(NH_4)_2(SO_4)_4 = Fe_2(CNS)_6 + (NH_4)_2SO_4 + 3K_2SO_4$.

ACETANILID COMPOUND WITH SODIUM SALICYLATE.

Caffein and acetanilid: Proceed as directed under acetanilid compound with sodium bromid for determining caffein and acetanilid.

Sodium salicylate: Acidulate solution in separatory funnel, from which the caffein and acetanilid have been extracted, with dilute hydrochloric acid, remove the liberated salicylic acid with successive portions of chloroform. Transfer the chloroformic extract containing the salicylic acid into a tared beaker through a filter paper. Evaporate the chloroform at low temperature in a current of air, to avoid loss of any salicylic acid by volatilization. Finally, dry at 80° C., transfer to desiccator, cool, and weigh. From the amount of salicylic acid obtained by this operation the quantity of sodium salicylate in the mixture can be readily calculated.

Comments: The purity and the quantity of the salicylic acid can be determined by titrating the residue with tenth normal potassium hydroxid, using phenolphthalein as indicator. One cubic centimeter of tenth normal potassium hydroxid is the equivalent of 0.0138048 gram of salicylic acid or 0.0160 gram sodium salicylate.

Sodium bicarbonate: Proceed by method B under acetanilid compound.

Sodium bicarbonate and sodium salicylate: The total amounts of sodium bicarbonate and sodium salicylate in this way can be checked by incinerating a given weight of the material at a dull, red heat, dissolving the residue in water and titrating the sodium carbonate formed with standard sulphuric acid, using methyl orange as indicator. The total sodium carbonate so obtained should be equal to the amount of sodium carbonate that can be produced by incinerating the sodium bicarbonate and sodium salicylate.

Reactions: $NaHCO_3 = Na_2CO_3 + H_2O + CO_2$

$2NaC_6H_4(OH)CO_2 + 14O_2 = Na_2CO_3 + 5H_2O + 13CO_2$

$NaCO_3 + H_2SO_4 = Na_2SO_4 + H_2O + CO_2$.

One cubic centimeter of normal sulphuric acid is the equivalent of 0.084 gram sodium bicarbonate and 0.160 gram sodium salicylate.

ACETPHENETIDIN TABLETS.

Acetphenetidin: This chemical may be determined by Method A for estimating acetanilid in acetanilid tablets. The purity of the acetphenetidin is determined by the standard prescribed for this product by the Pharmacopœia. The melting temperature is from 134° to 135° C.

ACETPHENETIDIN AND CAFFEIN.

Acetphenetidin and caffein: Remove these chemicals from the mixture by the method for extracting acetanilid and caffein under acetanilid compound, transfer chloroformic solution to tared beaker, evaporate at room temperature in current of warm air, treat residue with 5 cc. of ether (which is rapidly dissipated at room temperature, heat to 80° C. for a short time, transfer to desiccator, cool and weigh. This gives the total acetphenetidin and caffein.

Caffein: Determine caffein by method for caffein under acetanilid compound.

Acetphenetidin: Deduct the amount of the caffein found from the combined weight of acetphenetidin and caffein, which gives acetphenetidin.

Comments: Acetphenetidin is not as readily hydrolyzed as acetanilid. For this reason especial care should be exercised to see that all particles of the acetphenetidin are dissolved in the acid solution by repeated rotation of the flask. If hydrolysis is incomplete the acetphenetidin will be extracted with the caffein and vitiate the results.

AMMONIUM CHLORID.

Ammonium chlorid, Method A: Dissolve a suitable amount in 50 cc. of water, acidulate with nitric acid, add an excess of tenth normal silver nitrate and titrate back with tenth normal potassium sulphocyanate, using 1 cc. of ferric ammonium sulphate solution (10 percent) as indicator.

Comments: For parallel reaction see ammonium bromid under acetanilid compound with sodium bromid. One cubic centimeter of tenth normal silver nitrate is the equivalent of 0.00535 gram of ammonium chlorid.

Ammonia gas (NH_3), Method B: Introduce about 1 gram of the material into a 500 cc. Kjeldahl flask, add 200 cc. of water and 15 cc. of a saturated solution of sodium hydroxid, and a few grains of granulated metallic zinc, No. 20, fine. Then distill the mixture until all of the ammonia gas has passed over.

Collect the distillate in a flask containing standard sulphuric acid. Sufficient liquid should be present in the flask receiving the distillate to cover the lower end of the condenser. Titrate back the excess of sulphuric acid, using cochineal as indicator. From the quantity of sulphuric acid consumed the ammonia gas can be readily calculated and from this the ammonium chlorid. The amount of ammonium chlorid obtained by this process should agree with the amount of ammonium chlorid obtained by the chlorid determination.

Comments: One cubic centimeter of normal sulphuric acid is the equivalent of 0.017034 gram of ammonia gas (NH_3) and 0.0535 of ammonium chlorid. In order to guard against any of the caustic alkali being carried over mechanically in the process of distillation, it will be necessary either to introduce a trap or incline the flask. This is a general method to be used for all ammonia compounds unless otherwise directed. The metallic zinc is added to minimize or prevent bumping.

Reactions: $NH_4Cl + KOH = NH_3 + KCl + H_2O$

$2\,NH_3 + H_2SO_4 = (NH_4)_2\,SO_4$.

Method C: Introduce 5 cc. of formaldehyde solution (37 percent) into a beaker containing 50 cc. of water, add a few drops of phenolphthalein solution and sufficient sodium hydroxid solution to render this mixture neutral, then add from ½ to 1 gram of the material to be tested, bring the mixture to boiling and titrate acid formed with semi-normal sodium hydroxid solution.

Reaction: $4NH_4Cl + 6CH_2O = 4HCl + C_6H_{12}O_4 + 6H_2O$

$HCl + NaOH = NaCl + H_2O$.

One cubic centimeter of normal sodium hydroxid is the equivalent of 0.0535 gram of ammonium chlorid.

Talcum, etc.: Incinerate a convenient quantity in a suitable crucible.

AMMONIUM CHLORID AND CODEIN.

Ammonium Chlorid: Proceed as under ammonium chlorid.

Codein: Introduce about 1 gram accurately weighed into separatory funnel, dissolve in 25 cc. of water, render alkaline and finish operation as directed for codein under acetanilid compound with codein.

AMMONIUM SALICYLATE.

Salicylic acid: Introduce from ½ to 1 gram, accurately weighed, into a separatory funnel, dissolve in about 25 cc. of water, acidulate with dilute sulphuric acid, and shake out with successive portions of 20 cc. of chloroform. Transfer chloroformic solution into tared beaker, through dry filter paper. Evaporate chloroform at slightly elevated temperature in a current of air. Finally dry the residue at 80° C., cool in desiccator and weigh.

Comments: From the amount of salicylic acid obtained, calculate the ammonium salicylate. See salicylic acid under acetanilid compound with sodium salicylate. One cubic centimeter of tenth normal potassium hydroxid is the equivalent of 0.0155 gram of ammonium salicylate.

Talcum, etc.: See Ammonium chlorid.

AMMONIUM SALICYLATE COMPOUND.

This mixture usually contains ammonium salicylate, acetphenetidin, sodium bicarbonate and caffein, together with the usual ingredients employed in the manufacture of tablets.

Acetphenetidin and caffein: Extract as directed under acetanilid compound with sodium bromid, transfer chloroformic solution to tared beaker and finish by method under acetphenetidin and caffein.

Ammonium salicylate, Method A: Follow directions for estimating sodium salicylate under acetanilid compound with sodium salicylate, substituting ammonium for sodium.

Method B, Ammonia gas (NH_3)*:* Follow directions under ammonium chlorid.

AMMONIUM SALICYLATE COMPOUND WITH SALICIN.

Contains ammonium salicylate, acetphenetidin, caffein, sodium bicarbonate, salicin, starch, etc. Exhaust about 2 grams, accurately weighed, with warm alcohol, transfer alcoholic extract to a 200 cc. tared beaker, through filter, evaporate in a current of warm air at room temperature or slightly above, heat at about 80° C. for one-half hour, cool and weigh. This gives the combined weights of ammonium salicylate, acetphenetidin, caffein and salicin.

Caffein and acetphenetidin: Transfer the residue into a separatory funnel with water and chloroform, using water first. The former should not exceed 50 cc. nor the latter 25 cc. Render the mixture alkaline and follow instructions under acetphenetidin and caffein.

Ammonium salicylate: Acidulate solution from which caffein and acetphenetidin have been removed with dilute hydrochloric acid and extract with chloroform. Proceed as directed under ammonium salicylate. This removes salicylic acid from the mixture.

Salicin: Transfer mixture from which salicylic acid has been removed to a 200 cc. beaker, wash separatory and filter paper with water, add washings to beaker, digest on steam bath until all chloroform has been dissipated, cool, dilute to about 175 cc., add 20 cc. of concentrated hydrochloric acid and finally make up to 200 cc. Mix thoroughly, transfer to 500 cc. flask, attach to reflux condenser and heat to boiling for two hours. Estimate the dextrose formed by method given in Bulletin No. 107 (Revised), Methods of Analysis, page 49.

Reactions:

$$\underset{\text{Salicin}}{C_{13}H_{18}O_7} + H_2O = \underset{\text{Dextrose}}{C_6H_{12}O_6} + \underset{\text{Saligenin}}{C_7H_8O_2}$$

or

$$\underset{\text{Salicin}}{2C_{13}H_{18}O_7} + H_2O = \underset{\text{Dextrose}}{2C_6H_{12}O_6} + \underset{\text{Saliretin}}{C_{14}H_{14}O_3}$$

Either formula may be used to calculate the salicin, from the dextrose formed, in that a given amount of salicin always produces the same quantity of dextrose.

ANALGESIC COMPOUND.

This mixture contains acetanilid, caffein, sodium bicarbonate, codein sulphate, sodium salicylate, together with the usual excipients.

Caffein and acetanilid: Place about 1 gram accurately weighed into separa-

tory funnel (A), add 25 cc. of chloroform, shake well, then add 25 cc. of water and enough dilute sulphuric acid to make acid. Agitate thoroughly, set aside to permit the chloroform to separate and clear. Transfer chloroform solution to another separatory funnel (B) through a dry filter. Repeat this operation with successive portions of chloroform until all the caffein, acetanilid and salicylic acid are removed. Add 20 cc. of water and 5 cc. of normal sodium hydroxid solution, or sufficient to make distinctly alkaline, to the chloroformic solution in separatory funnel (B), agitate well, set aside to let chloroform separate and clear. Draw off chloroform solution into separatory funnel (C). Treat chloroformic solution in separatory (C) with several successive portions of slightly alkaline water until all of the sodium salicylate is removed. Collect all of the alkaline water in separatory funnel (B), wash with 20 cc. of chloroform which is to be transferred to separatory (C). Separatory (C) contains all of the caffein and acetanilid in solution. Determine these drugs by method under acetanilid compound.

Salicylic acid: Render solution in separatory funnel (B) acid with dilute sulphuric acid, and proceed as directed under ammonium salicylate.

Codein: Render solution in separatory funnel (A) alkaline with potassium hydroxid solution, and follow directions for codein under acetanilid compound with codein.

ANODYNE COMPOUND.

The active ingredients are acetanilid, caffein and sodium bicarbonate. Analyze as directed under acetanilid compound.

ANTIPYRIN TABLETS.

Proceed as directed for acetanilid, Method A, under acetanilid tablets.

Purity of antipyrin: The purity of the antipyrin can be determined by the standard prescribed by the Pharmacopœia. It should melt between 111° and 113° C.

ANTISEPTIC TABLETS.

The chief active agent in these tablets is corrosive sublimate. The term "antiseptic" is generally applied to mercuric chlorid mixed with citric acid, or ammonium chlorid or sodium chlorid. These chemicals increase the solubility of the mercurial compound and render it more useful as an antiseptic.

Mercuric Chlorid, Method A: In a 200 cc. beaker dissolve about ½ gram, accurately weighed, in 100 cc. of water, acidulate with hydrochloric acid, heat to boiling, and precipitate with washed hydrogen sulphid gas. Transfer the precipitate to an ignited tared Gooch crucible, wash thoroughly with hot water and finally with alcohol; dissipate the alcohol from the Gooch crucible and wash the precipitate with repeated small portions of carbon bisulphid until all of the free sulphur is removed, dry at 100° C, cool and weigh as mercuric sulphid. From these data calculate the mercuric chlorid.

Comments: Methods B and C under Corrosive Sublimate tablets may also be applicable but they have not been tried.

Citric acid: Introduce 1 gram into a suitable beaker, add 25 cc. of water, an excess of neutral sodium chlorid, about 6 grams, dissolve and titrate directly with a standard potassium hydroxid solution, using phenolphthalein as indicator.

Comments: For determining ammonium chlorid or sodium chlorid see Cor-

rosive Sublimate with these ingredients. The added coloring matter frequently present in antiseptic tablets may interfere somewhat with the method. One cubic centimeter of tenth normal potassium hydroxid solution is the equivalent of 0.07003 gram of crystallized citric acid.

Arsenic trioxid: Treat a suitable amount of the powdered material with tenth normal sodium hydroxid solution to remove the arsenical compound, neutralize the solution with hydrochloric acid, add sodium bicarbonate, and treat immediately with tenth normal iodin solution.

Reactions: $As_2O_3 + 2I_2 + H_2O = 4HI + 2H_3AsO_4$

$NaHCO_3 + HI = NaI + H_2O + CO_2$.

One cubic centimeter of tenth normal iodin solution is the equivalent of 0.004948 gram of arsenic trioxid.

ASPIRIN TABLETS.

Follow directions for acetanilid (Method A) under acetanilid compound.

ATROPIN SULPHATE.

Atropin: Dissolve ½ gram in water, render alkaline with ammonium hydroxid and extract with a mixture of ether, 1 part, chloroform, 2 parts. Transfer immiscible mixture containing the atropin to a tared beaker, evaporate at room temperature in a current of warm air. Finally heat at 100° C. for a few minutes, transfer to desiccator, cool and weigh.

Comments: Atropin sulphate tablets should be freely soluble in water. The lubricant usually employed for this form of medication is boric acid.

BISMUTH SUBNITRATE.

Bismuth oxid, Method A: Ignite in a small, fused silica evaporating dish 2 grams accurately weighed of bismuth subnitrate at a dull, red temperature until all nitrous vapors cease to be evolved and all organic matter is destroyed. Cool, add a few drops of nitric acid to convert any metallic bismuth into nitrate, heat gently to evaporate excess of acid and ignite as before. Transfer evaporating dish to desiccator, cool and weigh. Deduct weight of talcum (below) which leaves amount of bismuth oxid.

Bismuth oxid, Method B: By determining the nitrogen present the amount of bismuth subnitrate can be approximately estimated. Methods for determining nitrogen in nitrate bearing substances will be found in Methods of Analysis, Bulletin 107 (Revised), pages 7 to 9, inclusive.

Talcum, etc.: Weigh 3 grams of powdered material into a suitable beaker, add 25 cc. of 20 percent nitric acid, mix thoroughly, warm to 40° C., set aside for about one hour, and during the interim agitate from time to time, then transfer to a tared previously heated Gooch crucible provided with a nitric acid treated mat of asbestos, using a little 20 percent nitric acid. Wash residue with a little nitric acid of same strength, then with dilute (10 percent) nitric acid and finish with water. Dry residue, ignite to a white or nearly white ash, cool and weigh.

Comments: Bismuth subnitrate varies somewhat in composition. It should, however, yield not less than 80 percent of pure bismuth oxid.

BISMUTH SUBNITRATE AND CALOMEL.

Bismuth subnitrate: Determine this chemical by a method given under bismuth subnitrate.

Calomel: Introduce about 2 grams accurately weighed into a 200 cc. flask, add 50 cc. of water and 25 cc. of approximately normal potassium hydroxid. Attach flask to reflux condenser and heat for about one-half hour, filter, wash residue with water and collect filtrate and washings in beaker, acidulate contents with nitric acid, add an excess of silver nitrate to precipitate the chlorid, titrate back excess of silver nitrate with tenth normal solution of potassium sulphocyanate, using about 1 cc. of ferric ammonium sulphate, 10 percent as indicator. One cubic centimeter of tenth normal silver nitrate is the equivalent of 0.023606 gram of calomel.

Comments: If there is an excessive amount of starch present the method becomes very difficult, if not impossible, of operation.

CAFFEIN ALKALOID.

Caffein: Proceed as directed for acetanilid (Method A) under acetanilid tablets.

After evaporating the chloroform solution to apparent dryness, add 5 cc. ether, evaporate carefully, finally dry at 80° C. for one-half hour, cool in desiccator and weigh.

CAFFEIN CITRATED.

Caffein: Proceed as directed under acetanilid compound for estimating caffein, except that chloroform solution is carefully evaporated to dryness and the procedure concluded as under caffein alkaloid.

Citric acid: Introduce about 2 grams, accurately weighed, into a beaker, dissolve in 25 cc. of water, and determine the amount of citric acid by means of tenth normal potassium hydroxid solution, using phenolphthalein as indicator. See citric acid antiseptic tablets.

CALOMEL AND SODIUM BICARBONATE.

Calomel, Method A: Introduce into a beaker about 1 gram, accurately weighed, disintegrate with about 50 cc. of water, add 5 grams of potassium iodid, agitate the mixture for a short time, then add an excess of standard tenth normal iodin solution. Allow the solution to stand for about 15 minutes, then determine the excess of iodin with a standard tenth normal solution of sodium thiosulphate, using starch paste as indicator.

Comments: In order to insure against possible error, run a control, using the same amount of potassium iodid and iodin solution as in the procedure above. The iodin solution and the potassium iodid may be added in reverse order and it is claimed by some with better results.

One cubic centimeter of tenth normal iodin solution is the equivalent of 0.023606 gram of calomel.

Reactions: $2HgCl + 6KI + I_2 = 2HgK_2I_4 + 2KCl$

$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$.

Method B: Introduce into a 200 cc. beaker about 1 gram, accurately weighed, of the mixture, treat with warm water (not above 60° C.) and assist in disin-

tegrating the tablets by means of a stirring rod, allow the mixture to stand for about one-half hour, then filter and collect the calomel on a tared, previously ignited, porcelain Gooch crucible, provided with an asbestos mat, wash with water and finally with alcohol, then dry at 100° C., cool in a desiccator and weigh. Heat the Gooch crucible in a Bunsen flame sufficiently to completely volatilize the calomel. The difference between the two weights represents the calomel.

Method C: Introduce about ½ gram, accurately weighed, into a 100 cc. beaker, add 20 cc. of water and about 10 cc. of normal sodium hydroxid solution, transfer to steam bath and heat for about one hour. This procedure will disintegrate the calomel, forming insoluble mercury compounds, chiefly mercurous oxid, and sodium chlorid. After the reaction is complete dilute to 50 cc., filter through a Gooch crucible, and wash thoroughly with hot water. Acidulate the filtrate with nitric acid, add standard tenth normal solution of silver nitrate to excess and 1 cc. of ferric ammonium sulphate solution, then titrate back the excess of silver nitrate, with tenth normal potassium thiocyanate.

Comments: If desired, the silver chlorid may be collected in a Gooch crucible and determined in the usual way. From the data above the amount of calomel can be readily calculated. If the mixture contains starch or a gummy substance this method will not work satisfactorily.

Reactions: $2HgCl + 2NaOH = Hg_2O$ (chiefly) $+ 2NaCl + H_2O$

$NaCl + AgNO_3 = AgCl + NaNO_3$

$6KCNS + Fe_2(NH_4)_2(SO_4)_4 = Fe_2(CNS)_6 + (NH_4)_2SO_4 + 3K_2SO_4$.

One cubic centimeter of tenth normal silver nitrate is the equivalent of 0.023606 gram of mercurous chlorid.

Sodium bicarbonate: Titrate a given weight with normal sulphuric acid, using methyl orange as indicator if no disturbing agents are present. One cubic centimeter of tenth normal sulphuric acid is the equivalent of 0.084 gram of sodium bicarbonate.

CALOMEL AND LACTOSE.

Calomel: Proceed as directed under calomel and sodium bicarbonate.

Lactose: Introduce about 1 gram, accurately weighed, into a 100 cc. glass-stoppered flask or cylinder, add about 50 cc. of water, agitate thoroughly to disintegrate, and finally make up to 100 cc. Mix thoroughly and filter; reject the first 20 cc. of the filtrate. Proceed from this point as directed on pages 241-2 of Methods of Analysis, Bureau of Chemistry, Bulletin No. 107 (revised).

CINCHONIDIN.

Cinchonidin: Introduce 1 gram of the finely powdered material into a separatory funnel, add 50 cc. of water, and acidulate with dilute sulphuric acid, add 25 cc. of chloroform, render alkaline with sodium hydroxid, agitate thoroughly, set aside for the chloroform to separate and then proceed as directed for codein under "Acetanilid Compound with Codein."

Comments: If the insoluble matter interferes with the process, filter the acidulated solution, then render alkaline, add chloroform and continue as above. The purity of the cinchonidin and many other alkaloids can be determined by dissolving in a little neutral alcohol, adding a slight excess of tenth normal sul-

phuric acid and titrating back excess of acid by means of fiftieth normal potassium hydroxid, using methyl red as indicator. Tenth normal factor for cinchonidin is 0.0294196.

CINCHONIDIN SULPHATE.

Follow directions under cinchonidin.

COCAIN AND COCAIN HYDROCHLORID.

Follow directions under cinchonidin. Tenth normal factor for cocain is 0.0303178; for cocain hydrochlorid 0.03396.

CODEIN AND CODEIN SULPHATE.

Follow directions under cinchonidin. Tenth normal factor for codein, 0.031719; for codein sulphate, 0.0393.

CORROSIVE SUBLIMATE TABLETS.

This chemical is generally mixed with such ingredients as sodium chlorid, ammonium chlorid, and citric acid, but it is also put in tablet form by means of lactose. In the latter case the term "tablet triturate" is usually applied. Mercuric chlorid tablets are frequently colored artificially.

Mercuric chlorid: Estimate by Method A under antiseptic tablets, and as follows:

Method B: Introduce 1 gram accurately weighed into a 250 cc. flask, dissolve in 25 cc. water, add 2½ grams of potassium iodid (dissolved in 5 cc. of water), 30 cc. of normal caustic alkali or sufficient to make alkaline and 3 cc. of a 37 percent formaldehyde solution, mix thoroughly and set aside for 10 minutes with occasional shaking, then add 10 cc. or sufficient to make acid, 36 percent acetic acid, diluted with an equal volume of water, mix well, finally add 50 cc. of tenth normal iodin solution, stopper flask and shake vigorously for two minutes, then occasionally until the mercury is dissolved. Estimate excess of iodin with tenth normal sodium thiosulphate solution, using starch as indicator. Deduct the excess of iodin from the total amount of iodin used which gives the amount of iodin combined with the mercury.

Comments: In an alkaline medium formaldehyde reduces the mercury in the corrosive sublimate to the metallic state. The following equation shows the reaction between the metallic mercury and iodin:

$$Hg + I_2 + 2KI = K_2HgI_4.$$

Each cubic centimeter of tenth normal iodin solution is the equivalent of 0.01385 of mercuric chlorid.

Method C: Dissolve about 1 gram of the substance, equivalent to about ½ gram of mercuric chlorid, accurately weighed, in 75 cc. of water and render neutral, if not already so, to methyl orange, litmus or some other suitable indicator, add 10 cc. of 2 percent hydrocyanic acid solution, also made neutral to the indicator to be used. Estimate the amount of hydrochloric acid liberated by titrating with fifth normal sodium hydroxid solution.

Comments: The method depends upon the formation of an undissociated molecule of mercuric cyanid and the liberation of hydrochloric acid. The acidity of the hydrocyanic acid solution to the particular indicator to be used can be

determined and subtracted from subsequent operations instead of making this determination for each titration. The indicator to be used depends on the nature of the coloring matter present, if any.

Reactions: $HgCl_2 + 2HCN = Hg(CN)_2 + 2HCl$ or

$Hg^{++} + 2Cl^- + 2H^+ + 2CN^- = Hg(CN)_2 + 2H^+ + 2Cl^-$

Each cubic centimeter of fifth normal sodium hydroxid is the equivalent of 0.02715 gram of mercuric chlorid.

CORROSIVE SUBLIMATE AND AMMONIUM CHLORID.

Mercuric chlorid: Proceed as directed for determining this chemical by methods under antiseptic tablets and corrosive sublimate tablets.

Ammonia Gas (NH_3): Place about 1 gram accurately weighed into a 500 cc. Kjeldahl flask, dissolve in 200 cc. water, add 25 cc. of potassium sulphid solution (40 grams of commercial potassium sulphid dissolved in 1 liter of water)[1] or sufficient to precipitate all of the mercury. Render alkaline with sodium hydroxid and proceed from this point as directed by Method B under ammonium chlorid.

CORROSIVE SUBLIMATE AND SODIUM CHLORID.

Mercuric chlorid: Proceed by Method, A, B or C under corrosive sublimate tablets.

Method D: Into a tared porcelain evaporating dish weigh about 1 gram of the substance, previously dried at 100° C., heat in a muffle furnace at a dull, red temperature until all of the corrosive sublimate is volatilized, transfer dish to desiccator, cool and weigh. The loss represents mercuric chlorid and organic coloring matter, if present.

Sodium Chlorid, Method A: The residue left in the evaporating dish by Method D above represents the sodium chlorid.

Method B: Dissolve the residue left by Method D above in 50 cc. of water, acidulate with nitric acid and add an excess of tenth normal silver nitrate solution. Titrate back excess of silver nitrate with potassium sulphocyanid, using 1 cc. of 10 percent ferric ammonium sulphate solution as indicator.

Comments: If the amount of sodium chlorid should require too much silver nitrate solution, the residue can be dissolved in a suitable volume of water and an aliquot taken for the determination.

One cubic centimeter of tenth normal silver nitrate solution is the equivalent of 0.005846 gram of sodium chlorid.

HEROIN HYDROCHLORID.

Proceed as directed under cinchonidin.

HEROIN AND PHENACETIN.

Phenacetin: Introduce from ½ to 1 gram of the material into a separatory funnel, add 25 cc. of chloroform, agitate well, then add 25 cc. of water, and sufficient dilute sulphuric acid to acidulate, repeatedly agitate so as to bring about complete solution of the water-soluble material, then set aside to permit the chloroform to clear and separate. Transfer the chloroformic solution to tared

[1] See Methods of Analysis, Bull. 107 (revised), p. 6.

beaker. Repeat the operation until all the phenacetin is removed from the mixture. Finish by Method A under acetanilid tablets.

Heroin: Render the solution from which the phenacetin has been removed alkaline with potassium hydroxid and proceed as directed under cinchonidin. One cubic centimeter of tenth normal sulphuric acid is the equivalent of 0.03692 gram of diacetyl morphin or 0.040566 gram diacetyl morphin hydrochlorid.

HEXAMETHYLENAMIN.

This chemical is usually compressed without the addition of any foreign material, and it is therefore generally necessary only to accurately weigh the tablets in order to determine whether or not they are of proper weight.

It is desirable, however, to examine the product by the Pharmacopœial test. If it should be found that foreign material is present, such as talcum, starch, etc., the powdered material can readily be extracted with chloroform, the chloroformic extract collected in a tared beaker, evaporated, dried, cooled and weighed.

Nitrogen: By determining the percent of nitrogen the amount of hexamethylenamin and its purity can readily be ascertained. The nitrogen may be estimated by Kjeldahl or Gunning method, in Methods of Analysis, Bulletin of Bureau of Chemistry No. 107 (revised), pages 6 and 7, respectively. Hexamethylenamin contains 39.99 percent of nitrogen.

MIGRAIN TABLETS.

Under this name various mixtures are met with. A common one consists of acetanilid, caffein and sodium bicarbonate. Analyze by methods prescribed under acetanilid compound.

A second mixture encountered consists of acetanilid, caffein, sodium bicarbonate and sodium salicylate. This combination may be analyzed by procedure outlined under acetanilid compound with sodium salicylate.

MORPHIN SULPHATE.

This chemical is usually compressed with lactose. Boric acid is commonly used as lubricant. The amount of morphin may be determined either directly or indirectly as follows:

Morphin, Method A: Dissolve from ½ to 1 gram in 25 cc. of water in a suitable vessel, render alkaline with ammonium hydroxid, agitate well and allow to stand one-half hour, transfer to funnel with a small plug of cotton in throat. The precipitated morphin will be collected on the cotton. Wash the morphin sufficiently with cool water to remove all of the ammonia, then transfer the morphin and cotton to a porcelain evaporating dish, using from 25 to 50 cc. of alcohol (neutral), depending on the amount of morphin, add a slight excess of tenth normal sulphuric acid to convert the morphin into morphin sulphate, allow to stand a short time, then titrate back excess of acid with fiftieth normal potassium hydroxid, using methyl red as indicator. One cubic centimeter of tenth normal sulphuric acid is the equivalent of 0.03032 gram of morphin, or 0.0379 gram of morphin sulphate.

Method B: Estimate the amount of sulphate present in a definite quantity of morphin tablets by precipitating with barium chlorid in the usual manner. From

the amount of barium sulphate obtained, the amount of morphin sulphate can be readily calculated.

Method C: Determine nitrogen by Kjeldahl or Kjeldahl-Gunning methods, pages 5 and 7, respectively, Methods of Analysis, Bulletin No. 107. The nitrogen may also be estimated by Kjeldahl-Gunning-Arnold method. (U. S. Department of Agriculture, Bureau of Chemistry Circular 108, p. 15, 1912.)

Comments: The latter process is shorter than either of the other two. It is identical with the official Kjeldahl method except that 10 grams of crystallized potassium sulphate are added as in the Gunning method, omitting the potassium permanganate.

Lactose: Proceed as directed for this carbohydrate under calomel and lactose.

NITROGLYCERIN TABLETS.

Preparation of the sample: Crush 25 tablets under 10 cc. of ether. A 25 cc. cylindrical graduate makes a convenient container and a stout glass rod is used to crush the tablets. Rinse the rod with a little ether, allow the insoluble material to settle, and decant the solution into a 50 cc. graduated flask. No special care need be taken to prevent a little insoluble material from going into the flask. Wash the residue repeatedly with 5 cc. portions of ether and decant the washings into the flask until it has been filled to the mark. Insert stopper and mix well.

Nitrate Method: Place 20 cc. of the ethereal solution in a carefully dried and tared 50 cc. beaker. (A second aliquot of 10 cc. may be used as a check.) Evaporate the solvent in a vacuum desiccator charged with sulphuric acid. Apply the vacuum gradually, to prevent ebullition. Leave the beaker in the vacuum 30 minutes after the ether has evaporated. Weigh and calculate the ether extract per tablet. Treat the residue with 2 cc. phenoldisulphonic acid reagent, rotating the beaker in such a way that the reagent comes in contact with the entire inner surface. After 10 minutes add water and wash into a 100 cc. flask. (If a check analysis, as suggested, was made, wash this into a 50 cc. flask. Dilute to the mark and place 10 cc., representing 1 tablet, in a 100 cc. flask, add about 50 cc. water and a few drops more potassium hydroxid solution (20 percent) than is required to neutralize the acid. (Do not use sodium hydroxid.) Dilute to the mark and compare the color with that produced by a standard nitrate solution similarly treated. Use any convenient colorimeter or Nessler tubes.

Reagents and standards: Phenoldisulphonic acid reagent.—Dissolve 25 grams of pure white phenol in 150 cc. of concentrated sulphuric acid, add 75 cc. of fuming sulphuric acid (13 percent SO_3), stir well, and heat for two hours at about 100 degrees.

Standard Solution.—Dissolve 0.7217 gram potassium nitrate in 1 liter of water. Evaporate 10 cc. of this solution just to dryness on the steam bath. Cool and treat the residue with 2 cc. phenoldisulphonic acid reagent, observing the precautions noted above and using a glass rod if necessary to aid the solution of the residue. After 5 or 10 minutes dilute to 250 cc. Each cubic centimeter of this solution contains 0.004 milligram of nitrogen. Add an excess of potassium hydroxid solution to an aliquot of this solution and dilute to 100 cc. It is advisable to prepare a standard of approximately the same color as the unknown. Nitroglycerin is 5.4 times nitrate nitrogen.

Reactions:

$$C_3H_5(ONO_2)_3 + 3C_6H_3OH(SO_3H)_2 = 3C_6H_2OH(SO_3H)_2NO_2 + C_3H_5(OH)_3$$

Nitroglycerin. Phenoldisulphonic acid. Nitrophenoldisulphonic acid. Glycerol.

$$C_6H_2OH(SO_3H)_2NO_2 + 3KOH = C_6H_2OK(SO_3K)_2NO_2 + 3H_2O$$

Nitrophenoldisulphonic acid. Tripotassiumnitrophenoldisulphonate.

Nitrite or modified Hay method: Place 5 cc. of the ethereal solution in a 50 cc. beaker, dilute with 5 or 10 cc. alcohol and add about 5 cc. of ½ percent. alcoholic potassium hydroxid. Cover with a watch glass and allow to stand 10 minutes. Place on steam bath, allow to boil, remove the watch glass, and when most of the liquid is evaporated add about 25 cc. water and leave on steam bath until about half the liquid has evaporated or until the odor of alcohol can no longer be detected. Cool and dilute to 250 cc. Each cubic centimeter of this solution represents 0.01 of a tablet. Introduce an aliquot representing 0.02 to 0.04 milligram of nitroglycerin into a 100 cc. graduated flask, dilute with sufficient water to make the volume 90 to 95 cc., add 1 drop concentrated hydrochloric acid, then 2 cc. sulphanilic acid solution and 2 cc. napthylamine hydrochlorid solution. Complete the volume with water. Prepare at the same time and in the same way standards containing known amounts of sodium nitrite. Stopper the flasks and mix well. Compare the colors after 30 minutes. Nitroglycerin is calculated by multiplying the nitrogen found by 8.

Reagents and standards: Sulphanilic acid solution.—Dissolve 1 gram in 100 cc. hot water.

Napthylamine hydrochlorid solution.—Under a hood boil 0.5 gram of the salt with 100 cc. water for 10 minutes, keeping the volume constant. Filter and keep in a glass stoppered bottle.

Standard solution of sodium nitrite.—To a cold solution of about 2 grams of sodium or potassium nitrite in 50 cc. of water, add a solution of silver nitrate as long as a precipitate appears. Decant the liquid and thoroughly wash the precipitate with cold water. Dissolve in boiling water. On cooling the silver nitrite is precipitated. Dry the crystals in the dark at the ordinary temperature (preferably in a vacuum). Weigh out 220 milligrams of the dry silver nitrite, dissolve in hot water and decompose with a slight excess of sodium chlorid. When the solution becomes clear, dilute to 1 liter. Dilute 5 cc. of this solution to 1 liter. This second dilution is the standard to be used. It contains 0.0001 milligram of nitrite nitrogen per cubic centimeter.

Essential reactions:

$$C_3H_5(ONO_2)_3 + 5KOH = KNO_3 + 2KNO_2 + HCO_2K + CH_3CO_2K + 3H_2O$$

$$C_6H_4NH_2HSO_3 + HNO_2 = C_6H_4N_2SO_3 + 12H_2O$$

Sulphanilic acid. Paradiazobenzenesulphonic acid.

$$C_6H_4N_2SO_3 + C_{10}H_7NH_2 = C_{10}H_6NH_2NNC_6H_4HSO_3$$

Alpha Naphthylamine. Azoalphamidonaphthalene-parazobenzenesulphonic acid.

Comments: Only nitrite-free water should be used in the estimation by this method.

NUX VOMICA TABLETS.

Total alkaloids: Introduce 5 grams of the material into a 200 cc. graduated cylinder, add 100 cc. of chloroform-ether mixture (1-4 by volume), agitate well and repeatedly for one-half hour, add 5 cc. of ammonia water, or sufficient to render alkaline, agitate repeatedly for 1 hour, then make up to 150 cc., agitate well, set aside for the insoluble matter to settle and the chloroform-ether mixture to clear, then decant or pipette off an aliquot part (for example, 100 cc.) and transfer to separatory funnel. Acidulate chloroform-ether solution with dilute sulphuric acid and add enough water to make about 25 cc. aqueous solution, agitate well, allow to separate and draw off the watery portion into another separatory. Repeat this operation two or three times with about 20 cc. of water and collect in separatory funnel. Render the acid solution in second separatory funnel alkaline with ammonia water, extract with three successive portions of 20 cc. of chloroform, collect chloroformic solution in another separatory, wash with 25 cc. of water, transfer the chloroform into tared beaker, evaporate on steam bath at low temperature. Rinse separatory funnel with a small portion of chloroform and transfer to beaker. When chloroform is dissipated add about 5 cc of ether, evaporate and dry at 100° C. for one-half hour, cool and weigh.

Strychnin: Destroy brucin in dried residue by adding 6 cc. of 35 percent nitric acid, mixing well and allowing the mixture to stand at ordinary temperature for 10 minutes.

Take up residue with water and transfer to separatory funnel with several small portions of water, render alkaline with ammonia water, and proceed as directed for total alkaloids.

Comments: The amount of strychnin and its purity may now be determined by taking the alkaloid up in a little (neutral) alcohol, adding a slight excess of tenth normal sulphuric acid and titrating back excess of acid with fiftieth normal potassium hydroxid, using methyl red as indicator.

One cubic centimeter of tenth normal sulphuric acid is the equivalent of 0.0334 gram of strychnin.

Brucin: Determine by subtracting strychnin from total alkaloids.

PHENACETIN TABLETS.

Analyze by methods under acetanilid tablets. Determine phenacetin by Method A.

PHENOLPHTHALEIN.

Determine by Method A under acetanilid tablets, using alcohol, however, in place of chloroform.

Comments: This chemical is now found in all forms of mixtures. A little organic acid is sometimes used to prevent the tablets from turning reddish.

POTASSIUM BICARBONATE.

Potassium bicarbonate is generally compressed without any excipient; in such cases titration may be made directly; otherwise, extract a suitable quantity of the powder with water, filter, wash and titrate the aqueous solution with standard sulphuric acid, using methyl orange as indicator.

One cubic centimeter tenth normal acid is the equivalent of 0.01001 gram of potassium bicarbonate.

POTASSIUM IODID.

Titrate direct, or, when foreign matter is present, extract a convenient quantity with water, wash residue, collect filtrate and washings in beaker, acidulate with nitric acid, add an excess of silver nitrate to precipitate the iodin, then titrate back with a tenth normal solution of potassium sulphocyanate, using about 1 cc. ferric ammonium sulphate, 10 percent solution, as indicator.

Reaction: $KI + AgNO_3 = AgI + KNO_3$.

One cubic centimeter of silver nitrate is the equivalent of 0.016602 gram of potassium iodid.

POTASSIUM PERMANGANATE.

Extract a suitable quantity with water, acidulate with sulphuric acid, warm to about 60° C., and titrate with a tenth normal oxalic acid solution.

Reactions: $2KMnO_4+5H_2C_2O_4+3H_2SO_4=K_2SO_4+2MnSO_4+10CO_2+8H_2O$.

One cubic centimeter of tenth normal oxalic acid is the equivalent of 0.00316 gram of potassium permanganate.

QUININ BISULPHATE AND QUININ SULPHATE.

Proceed as directed under cinchonidin.

One cubic centimeter of tenth normal sulphuric acid is the equivalent of 0.0378 gram of crystalline quinin, 0.0436 gram of quinin sulphate and 0.0548 gram of quinin bisulphate.

RHEUMATIC TABLETS.

One mixture was found to consist of sodium salicylate, and sodium bicarbonate, together with excipients.

Salicylic acid: Proceed as directed for salicylic acid under ammonium salicylate.

Sodium bicarbonate, talcum, etc.: Proceed as directed under acetanilid compound.

A second mixture was found to contain sodium salicylate, sodium bicarbonate and codein sulphate.

Salicylic acid: Proceed as directed for determining salicylic acid under ammonium salicylate.

Codein sulphate: Codein sulphate will be left in the solution from which the salicylic acid has been extracted. This can be removed by rendering the solution alkaline, thus liberating the codein which may now be extracted from the mixture by chloroform. The remainder of the procedure is given under Acetanilid Compound with Codein.

SALICIN TABLETS.

Exhaust a suitable quantity of the powdered material by Method A, under acetanilid tablets, substituting, however, alcohol for chloroform.

SALOL TABLETS.

This article may be analyzed by methods under acetanilid tablets. Salol is determined by Method A, using ether in place of chloroform. Considerable care must be exercised in dissipating the solvent so that none of the salol is lost. The best course to follow is to permit the ether to evaporate at room temperature in a current of warmed air, then introduce the beaker into a vacuum desiccator and allow it to remain for 24 hours before weighing.

SALOPHEN TABLETS.

Determine by Method A under acetanilid tablets.

SANTONIN AND CALOMEL.

Santonin: Determine by Method A under acetanilid tablets.

Calomel: Determine this chemical in residue left after extracting the santonin with chloroform by Method A given under calomel and sodium bicarbonate.

SODIUM SALICYLATE TABLETS.

Salicylic acid: Proceed as directed under ammonium salicylate for determining salicylic acid.

Sodium salicylate: Ignite a given weight of the material, extract the residue with water and titrate with tenth normal sulphuric acid, using methyl orange as indicator.

One cubic centimeter of tenth normal sulphuric acid is the equivalent of 0.0160 gram of sodium salicylate.

SODIUM BICARBONATE.

Determine by method given under potassium bicarbonate. The normal factor for sodium bicarbonate is 0.084.

SODIUM BROMID.

Determine by method given under potassium iodid. Tenth normal factor for sodium bromid is 0.010292.

STRONTIUM BROMID.

Determine by method given under potassium iodid. The tenth normal factor for strontium bromid is 0.01778.

STRYCHNIN SULPHATE.

Introduce about 1 gram of the powdered tablets into separatory funnel, dissolve in 25 cc. of water rendered alkaline and remove the strychnin with three or more successive portions of chloroform. The chloroform solutions are collected in a tared beaker and evaporated to dryness. The residue is allowed to cool, 5 cc. of ether added, the ether dissipated and the residue dried at 100° C. for 15 minutes.

Comments: Care should be exercised in drying so that no loss will occur by decrepitation of the strychnin. The purity and amount of strychnin present may be determined by dissolving the residue in neutral alcohol, adding an excess of tenth normal sulphuric acid, and titrating back excess of acid with fiftieth normal potassium hydroxid, using methyl red as indicator. One cubic centimeter of tenth normal sulphuric acid is the equivalent of 0.0334 gram of strychnin and 0.0428 gram strychnin sulphate.

SALOPHEN.

Exhaust from ½ to 1 gram of the powdered material with alcohol, as directed under acetanilid tablets, transfer alcoholic filtrate into tared beaker, evaporate the alcohol and heat the residue for 15 minutes at 100° C., transfer beaker to desiccator, cool and weigh.

Comments: The purity of salophen can be determined by ascertaining its melting temperature which varies from 187° to 188° C.

TRIONAL.

Proceed as directed under salophen.

Comments: The melting point of trional is 76° C.

VERONAL.

Proceed as directed under salophen, using, however, acetone as solvent.

Comment: Melting point, 188° C.

ZINC PHENOLSULPHONATE.

Zinc oxid: Exhaust from ½ to 1 gram of powdered material with alcohol, as directed under acetanilid tablets, collect filtrate in tared evaporating dish, dissipate the alcohol, incinerate the residue in a muffle at a dull, red heat until a white or nearly white residue is left. Cool dish in desiccator and weigh residue as zinc oxid.

Comments: Uneffloresced zinc phenolsulphonate leaves 14.6 percent of its weight as zinc oxid on ignition.

Reaction: $Zn(C_6H_4(OH)SO_3) + 14O_2 = ZnO + 12CO_2 + 2SO_3 + 5H_2O$.

Residue insoluble in alcohol: See residue insoluble in chloroform under acetanilid tablets. By deducting the amount of residue so obtained from the total amount of material originally taken the quantity of alcohol-soluble material (zinc phenolsulphocarbolate, chiefly), is obtained.

THE COST OF RODENTS.

Rats, mice, flies, mosquitoes, and the various form of body parasites have always been held in contempt and disgust, and always and everywhere have been regarded as vermin. Growing knowledge of the important role played by these lower forms of animal life in the transmission of disease is ample justification for this feeling. They are exceedingly expensive.

The Journal of the American Medical Association comments on a recent article in The Farm and Fireside, which discusses the amount of damage done in this country by rats, and estimates that there are in the United States at least 300,000,000 of these animals, alike destructive to property and dangerous to health. Rats are said to destroy $100,000,000 worth of grain every year in this country, or enough to feed one hen for every man, woman and child in the nation. The annual cost of rats to the nation is estimated at $360,000,000.

In addition, the rat population of the country forms a fertile field for the dissemination of bubonic plague, which only needs a starting point in any of our seaports to spread throughout the country and cause the loss of thousands of lives.

In the same issue of The Farm and Fireside, but in a different department, appears an article on the cattle tick, in which it is estimated that the difference between the market value of an animal free from this parasite and one infested with it is about $8 a cow, and that the cattle tick is today costing the stockmen of the country $1,000,000,000 each decade, or $100,000,000 each year.

The discovery and development of bacteriology showed that man had been carrying on for centuries an unconscious struggle with the lower forms of vegetable life. Recent additions to knowledge of the habits and characteristics of vermin show that an equally relentless struggle has been going on between man and the lower forms of animal life.