THE "SHAKING-OUT" METHOD FOR THE QUANTITATIVE ESTIMATION OF ALKALOIDS. II.*

EFFECT OF CLARIFICATION AND "SALTING-OUT."

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The standard method for the estimation of alkaloids in drugs and preparations thereof is based upon an extraction of the alkaloid usually as a salt, by an appropriate solvent, replacing any other solvent used by water, freeing the alkaloid from its salt combination with alkali and extracting the freed alkaloid with an immiscible solvent. The completeness of extraction and purification of the alkaloid depends upon the usually greater solubility of the alkaloidal salts in water than in the so-called immiscible solvents, and the greater solvent power of the immiscible solvents for the free bases. The rate of extraction of alkaloids by means of the immiscible solvents depends upon the coefficient of distribution for the alkaloid between the two immiscible liquids, a constant to which in this case Beal and Lewis[1] have given the name "extraction factor."

When an alkaloid is extracted directly, free or as a salt, from a drug or preparation thereof, it will be accompanied by many other extractives, among these being proteins, fats, volatile oils, organic acids, gums, resins, colors and carbohydrates. Of these, the carbohydrates will not interfere in subsequent extractions. It is customary to remove the other compounds soluble in the immiscible solvents, *e. g.*, fats, volatile oils, organic acids, and acid resins, by shaking an acid aqueous solution of the extract with the immiscible solvent, which will extract these non-basic compounds but in which the alkaloidal salts theoretically are insoluble. Beal and Lewis[2] have pointed out several sources of error at this point. Chief among these are, first, the solubility of the alkaloid salt in the always slightly hydrous solvent, and, second, the possibility of hydrolysis of the salt in aqueous solution with accompanying extraction of the free alkaloid by the immiscible solvent.

The effect of the gums, neutral resins, proteins and coloring matters in the extract is to cause, unless great care is taken, the formation of emulsions with the immiscible solvents which are difficultly broken up. In addition, the extraction of the coloring matters and neutral resins by the immiscible solvent leads to the final formation of an impure alkaloidal residue. The stability of many of the emulsions formed suggests the desirability of preventing their formation rather than the perfection of methods for their later removal.

The object of this investigation was to determine what advantages, if any, lay in the clarification of the aqueous alkaloidal solution before extraction with an immiscible solvent. Two secondary propositions were also considered, the effect upon the rate of extraction of the alkaloid by the "salting-out" effect of sodium chloride, and the amount of alkaloid removed by one extraction with the immiscible solvent.

Lead acetate and subacetate have been largely used in organic analysis as clarifying agents, particularly for the removal of coloring matters and organic

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[1] THIS JOURNAL, 5, 812–837, 1916.

[2] *Loc. cit.*

acids from raw sugar solutions and for the removal of tannins from vegetable extracts generally. Their general use as clarifying agents in general alkaloidal analysis has been suggested by Henry[3]. Henry[4] recommends lead acetate for detannating coffee extracts in the determination of caffeine and in the Stahlschmidt-Allen method for determining caffeine[5] both lead acetate and subacetate are used for the same purpose. Henry[6] suggests its use in the estimation of morphine and Barger uses lead acetate in determining the alkaloids of gelsemium.[7] Henry[8] states that lead acetate may be used in the extraction of caffeine, emetine, lycopodine, pilijanine, cytisine and several other alkaloids. In addition to these, Lyons has used it[9] in extracting digitalein and pilocarpine, Dragendorff[10] in determining coniine, and Prescott[11] in extracting morphine and in a few other instances.

The present authors took up the study with a view to determining, first, the quantitative effect of lead acetate on the extraction of certain selected alkaloids from solutions of their pure salts, and, second, its efficiency in determining certain of these same alkaloids in their parent drugs.

EXPERIMENTAL.

The alkaloids used were caffeine, quinine, strychnine and morphine.

Caffeine.—Pure anhydrous caffeine was dissolved in 4 percent acetic acid and a 10 percent solution of lead acetate added, without a perceptible reaction. The lead was removed from the solution by hydrogen sulphide and this solution, after removal of the hydrogen sulphide, was made alkaline with ammonium hydroxide and extracted with five 10 Cc. portions of chloroform. After the fifth extraction, the solution gave no positive reaction for caffeine by the murexide test. The caffeine in the chloroform extract was estimated by evaporation, dehydration and weighing.

Table I shows in Column 9 the weight of caffeine taken, in Column ten, the weight obtained on complete extraction, and in Column 11, the percentage recovery of caffeine. Other details of the treatment are also given in the tables. Table II shows the percentage of caffeine extracted by a single 10 Cc. portion of chloroform. In determinations 5, 6, 7, 8, 17, 18, 19 and 20, the solutions were half saturated with sodium chloride before extraction with chloroform. Two of the results with this treatment, 6 and 8, are, respectively, 10 and 5 percent over the theoretical amount of caffeine present. In neither instance did the alkaloid as weighed give a positive test for chlorides. In the four instances in Table II, where salting-out was attempted, the percentage of alkaloid removed by a single extraction is 10 percent greater than where salting-out is not practiced.

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[3] Allen, "Comm. Org. Anal.," 4th Ed., VI, 174, 1912.
[4] *Ibid.*, p. 606.
[5] *Ibid.*, p. 607.
[6] *Ibid.*, p. 435.
[7] *Ibid.*, 7, p. 31.
[8] "Plant Alkaloids," p. 427.
[9] "Manual of Proximate Pharmaceutical Assaying," p. 40, 1886.
[10] "Plant Analysis," 1884.
[11] "Organic Analysis," p. 370, 1892.

TABLE I.

1. No.	2. Cc. of 4% acetic acid for solution.	3. Cc. of PbAc added.	4. Ppt.	5. Alkaloid freed with 10% NH_4OH. Cc.	6. Extracted with $CHCl_3$. Cc.	7. Gramme of pure caffeine taken.	8. Gramme of caffeine recovered.	9. % recovered.
1.....	25	2	No	0.2	5–50	0.1000	0.1033	103.3
2.....	25	1	No	0.4	5–50	0.1000	0.1015	101.5
3.....	25	2	No	1.0	5–50	0.1000	0.1009	100.9
4.....	25	3	No	0.3	5–50	0.1000	0.1012	101.2
5.....	25	2	No	0.3	5–50[1]	0.1000	0.1023	102.3
6.....	25	2	No	0.3	5–50[1]	0.1000	0.1101	110.1
7.....	25	2	No	0.3	5–50[1]	0.1000	0.1037	103.7
8.....	25	2	No	0.3	5–50[1]	0.1000	0.1051	105.1
9.....	25	2	No	0.3	5–50	0.1000	0.0993	99.3
10.....	25	2	No	0.3	5–50	0.1000	0.0995	99.5
11.....	25	2	No	0.3	5–50	0.1000	0.1011	101.1
12.....	25	2	No	0.3	5–50	0.1000	0.1006	100.6

TABLE II.

13.....	25	0	No	0.3	1–10	0.1000	0.0785	78.5
14.....	25	0	No	0.3	1–10	0.1000	0.0777	77.7
15.....	25	0	No	0.3	1–10	0.1000	0.0779	77.9
16.....	25	0	No	0.3	1–10	0.1000	0.0791	79.1
17.....	25	0	No	0.3	1–10[1]	0.1000	0.0892	89.2
18.....	25	0	No	0.3	1–10[1]	0.1000	0.0877	87.7
19.....	25	0	No	0.3	1–10[1]	0.1000	0.0883	88.3
20.....	25	0	No	0.3	1–10[1]	0.1000	0.0886	88.6

[1] Aqueous solution half saturated with NaCl.

Quinine.—In determining the effect of the addition of lead acetate on the extraction of quinine the same procedure is followed as with caffeine, except that the use of quinine sulphate necessitated a filtration to remove lead sulphate. The point of complete extraction of the alkaloid was determined by tests with Mayer's reagent. The results obtained are shown in Tables III and IV and are comparable with those obtained with caffeine. Addition of lead acetate causes no loss of alkaloid, and the effect of salting out is to increase the percentage recovery. No test for chlorides was obtained from the residue where salting-out was practiced.

TABLE III.

1. No.	2. Cc. of 4% acetic acid for solution.	3. Cc. of PbAc added	4. Ppt.	5. Alkaloid freed with 10% NH_4OH. Cc.	6. Extracted with $CHCl_3$. Cc.	7. Gramme of sulphate taken.	8. Gramme taken based on free alkaloid.	9. Gramme recovered, estim. as anhydrous quinine.	10. % recovered.
1....	25	2	Yes	5.0	5–50	0.1000	0.0868	0.0890	102.2
2....	25	2	Yes	3.0	5–50	0.1000	0.0868	0.0893	102.8
3....	25	1	Yes	1.0	4–40	0.1000	0.0868	0.0880	101.2
4....	25	4	Yes	0.1	4–40[1]	0.1000	0.0868	0.0872	100.4
5....	25	3	Yes	0.3	4–40[1]	0.1058	0.0918	0.0945	103.4
6....	25	3	Yes	0.3	4–40[1]	0.1105	0.0959	0.1027	107.1
7....	25	3	Yes	0.3	4–40[1]	0.0991	0.0860	0.0840	97.7
8....	25	3	Yes	0.3	4–40	0.1086	0.0943	0.1057	111.2
9....	25	3	Yes	0.3	4–40	0.1213	0.1054	0.1062	100.8
10....	25	3	Yes	0.3	4–40	0.1108	0.0962	0.0977	101.3
11....	25	3	Yes	0.3	4–40	0.1007	0.0873	0.0864	98.9
12....	25	3	Yes	0.3	4–40	0.0988	0.0856	0.0878	102.7

[1] Aqueous solution half saturated with NaCl.

TABLE IV.

1. No.	2. Cc. of 4% acetic acid for solution.	3. Cc. of PbAc added.	4. Ppt.	5. Alkaloid freed with 10% NH_4OH. Cc.	6. Extracted with $CHCl_3$. Cc.	7. Gramme of sulphate taken.	8. Gramme taken based on free alkaloid.	9. Gramme recovered estim. as anhydrous quinine.	10. % recovered.
13....	25	0	No	0.3	1–10	0.1043	0.0908	0.0746	82.3
14....	25	0	No	0.3	1–10	0.1176	0.1020	0.0833	81.6
15....	25	0	No	0.3	1–10	0.1080	0.0938	0.0781	83.2
16....	25	0	No	0.3	1–10	0.1121	0.0974	0.0804	82.6
17....	25	0	No	0.3	1–10[1]	0.1236	0.1072	0.0928	86.7
18....	25	0	No	0.3	1–10[1]	0.1071	0.0930	0.0802	86.3
19....	25	0	No	0.3	1–10[1]	0.1155	0.1002	0.0854	85.1
20....	25	0	No	0.3	1–10[1]	0.1097	0.0952	0.0830	87.2

[1] Aqueous solution half saturated with NaCl.

Strychnine.—The series of experiments were repeated, using pure anhydrous strychnine, with results of the same general order as before. In addition, an attempt was made to simplify the analysis of nux vomica by the use of lead acetate as a clarifying agent on the aqueous extract of the drug. The procedure used follows:

Fifty grammes of powdered nux vomica were macerated with 500 Cc. of approximately half-normal sulphuric acid. This gave a thick, slimy extract which was difficult to filter. It was filtered successively through an increasing number of layers of cheese-cloth and finally through filter paper. The residue was again macerated with 500 Cc. of acid and filtered in the same manner as previously. The filtrates were combined and heated to 75° for thirty minutes to coagulate colloids, again filtered and two portions of exactly 300 Cc. each taken. To one portion was added 0.6000 Gm. of pure strychnine and both solutions clarified and deleaded in the usual manner. Extraction of the alkaloid was then carried out, with and without "salting-out," and the results obtained are given in Table VII. After clarifying the drug extract with lead acetate only a slight emulsion was obtained between the two liquids, while the unclarified extract yielded an emulsion which could not be handled in any way.

TABLE V.

1. No.	2. Cc. of 4% acetic acid for solution.	3. Cc. of $PbAc_2$ added.	4. Ppt.	5. Alkaloid freed with 2% NaOH. Cc.	6. Compound used.	7. Extracted with $CHCl_3$. Cc.	8. Gramme taken.	9. Gramme recovered as anhydrous strychnine.	10. % recovered.
7....	25	2	No	2	Pure	5–50	0.1000	0.1012	101.2
8....	25	2	No	2	Pure	5–50	0.1000	0.1107	110.7
9....	25	2	No	2	Pure	5–50	0.1000	0.0998	99.8
10....	25	1	No	1	Pure	5–50[1]	0.1115	0.1148	102.0
11....	25	1	No	1	Pure	5–50[1]	0.1235	0.1532	124.0
12....	25	1	No	1	Pure	5–50[1]	0.1157	0.1194	103.0
13....	25	1	No	1	Pure	5–50[1]	0.1271	0.1500	118.0

TABLE VI.

14....	25	0	No	1	Pure	1–10	0.1386	0.1055	76.1
15....	25	0	No	1	Pure	1–10	0.1074	0.0822	76.5
16....	25	0	No	1	Pure	1–10	0.1431	0.1085	75.8
17....	25	0	No	1	Pure	1–10[1]	0.1116	0.0973	87.1
18....	25	0	No	1	Pure	1–10[1]	0.1231	0.1038	84.3
19....	25	0	No	1	Pure	1–10[1]	0.1371	0.1161	84.7

[1] Aqueous solution half saturated with NaCl.

TABLE VII.

1. No.	2. Cc. of 4% acetic acid for solution.	3. Cc. of $PbAc_2$ added.	4. Ppt.	5. Alkaloid freed with 2% NaOH Cc.	6. Compound used.	7. Exracted with $CHCl_3$. Cc.	8. Gramme taken	9 Gramme recovered as anhydrous strychnine.	10. Average.
20....	50	15	Yes	1	Extract	5–50	.....	0.0455	.....
21....	50	15	Yes	1	Extract	5–50	.....	0.0537	0.0492
22....	50	15	Yes	1	Extract	5–50[1]	.....	0.0473	.....
23....	50	15	Yes	1	Extract	5–50[1]	0.1000	0.1491	.....
24....	50	15	Yes	1	Extract	5–50	0.1000	0.1486	.....
25....	50	15	Yes	1	plus pure	5–50	0.1000	0.1497	0.1491
26....	50	15	Yes	1	alkaloid	5–50[1]	0.1000	0.1492	.....

[1] Aqueous solution half saturated with NaCl.

Morphine.—Supposedly pure morphine and morphine sulphate U. S. P. VIII were used with less satisfactory results than with the other alkaloids. Morphine sulphate U. S. P. VIII is supposed to contain five molecules of water of crystallization, but determination of nitrogen by the Kjeldahl method showed the salt to be anhydrous. A recalculation based on this data gave much better results.

In order to determine more accurately, if possible, the amount of alkaloid extracted, the residue on evaporation of the solvent, after weighing, was dissolved in a measured amount of standard acid, and the excess of acid determined by titration with standard alkali.

On solution of the alkaloidal residue in acid a small amount of resinous matter was left, which was determined quantitatively whenever possible. Evidence favoring the view that this represents oxidation products of the morphine is strengthened by the fact that the quantity of this residue was greatly diminished by evaporation of the solvent in an atmosphere of carbon dioxide.

The solvent most suitable for the extraction of morphine was found to be amyl alcohol. Puckner[12] suggested the use of a mixture of chloroform 80 percent and alcohol 20 percent, claiming that on evaporation and drying at a temperature not over 60° the alkaloid retained one molecule of water. Taylor,[13] when using amyl alcohol as solvent, obtained anhydrous morphine at 100° C. Prescott[14] found the alkaloid crystallized with one molecule of water to be stable at 100°, becoming anhydrous at 120°. The authors, using amyl alcohol as solvent, have found that if the solvent was evaporated at a temperature not exceeding 40° and the dish then heated on the steam bath at 100° for two hours, there was no further loss in weight on heating at 120°. The alkaloid thus obtained was found to be anhydrous.

The best procedure for extraction involved the use of six portions of hot amyl alcohol, 30, 20, 10, 10, 5 and 5 Cc., the first portion being added just before making the solution very slightly ammoniacal. If the solvent was evaporated in air at 100° the resinous matter formed averaged 7.5 percent. When evaporated at 100° in CO_2, practically no resin was formed. Evaporating in air at 40° left about 3 percent of resin. Aside from these discrepancies, the results both from the use of lead acetate as a clarifier and sodium chloride for "salting-out" are satisfactory and of an order similar to those obtained with the other alkaloids used. The results obtained are given in Table VIII.

[12] *J. Am. Chem. Soc.* 23, p. 470.
[13] *Pharm. Jour.*, [3] 18, pp. 161, 273.
[14] "Organic Analysis," p. 363.

TABLE VIII.

1. No.	2. Cc. of 4% acetic acid for solution.	3. Cc. of PbAc added.	4. Ppt.	5. Alkaloid freed with 10% NH_4OH. Cc.	6. Compound used.	7. Extracted with.	8. Gramme taken.
3.....	25	2	No	1.0	Pure		
4...	25	2	No	1.0	Pure		
9...	25	4	Yes	0.1	Sulphate		
10...	25	4	Yes	0.1	Sulphate	6–70 Cc. Hot Amyl Al[1]	0.1000
11...	25	3	Yes	0.1	Sulphate	6–70 Cc. Hot Amyl Al[1]	0.1000
12...	25	3	Yes	0.1	Sulphate	6–80 Cc. Cold Amyl Al	0.0980
13...	25	4	Yes	0.1	Sulphate	6–80 Cc. Cold Amyl Al	0.1093
14...	25	0	No	0.1	Sulphate	6–70 Cc. 80% $CHCl_3$: 20% Al[3]	0.1084
23...	25	4	Yes	0.1	Sulphate	6–70 Cc. 80% $CHCl_3$: 20% Al[3]	0.1675
24...	25	4	Yes	0.1	Sulphate	5–70 Cc. Cold Amyl Al	0.1177
26...	25	4	Yes	0.1	Sulphate	5–70 Cc. Cold Amyl Al	0.1357
27...	25	4	Yes	0.3	Sulphate	5–70 Cc. Hot Amyl Al[1]	0.1135
28...	25	4	Yes	0.3	Sulphate	5–70 Cc. Hot Amyl Al[1]	0.0936
29...	25	4	Yes	0.3	Sulphate	5–70 Cc. Hot Amyl Al[1]	0.1148
30...	25	4	Yes	0.3	Sulphate	6–70 Cc. Cold Amyl Al	0.1253
32...	25	4	Yes	0.3	Sulphate	6–70 Cc. Cold Amyl Al	0.1190
33...	25	4	Yes	0.3	Sulphate	6–70 Cc. Cold Amyl Al	0.1107
34...	25	4	Yes	0.3	Sulphate	6–70 Cc. Hot Amyl Al	0.1370
35...	25	4	Yes	0.3	Sulphate	6–70 Cc. Hot Amyl Al	0.0773
36...	25	4	Yes	0.3	Sulphate	6–70 Cc. Hot Amyl Al	0.1119
37...	25	0	No	0.3	Sulphate	6–70 Cc. Hot Amyl Al[1]	0.1126
38...	25	0	No	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1]	0.1905
39...	25	4	Yes	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1]	0.1962
40...	25	4	Yes	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1]	0.2242
41...	25	4	Yes	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1]	0.2091
42...	25	4	Yes	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1]	0.2011
43...	25	0	No	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1]	0.2146
44...	25	0	No	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1]	0.2204
45...	25	0	No	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1]	0.2009
46...	25	0	No	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1 2]	0.1000
47...	25	0	No	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1 2]	0.1295
48...	25	0	No	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1 2]	0.1106
49...	25	0	No	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1 2]	0.1214
50...	25	0	No	0.3	Sulphate	6–80 Cc. Hot Amyl Al[1 2]	0.1086
						6–80 Cc. Hot Amyl Al[1 2]	0.1132
						6–80 Cc. Hot Amyl Al[1 2]	0.0997
						6–80 Cc. Hot Amyl Al[1 2]	0.1206

[1] Solvent added before freeing alkaloid.

[2] Solvent evaporated in current of CO_2.

[3] Solution half saturated with NaCl.

9. No.	Gramme taken estimated as anhydrous morphine.	10. Gramme recovered gravimetrically estimated as anhydrous morphine.	11. % recovered gravimetrically.	12. Gramme recovered volumetrically.	13. % recovered volumetrically.	14. Gramme resinous substance.	15. % resinous substance.	16. Total % recovered 14 and 15 or 12.
3..	0.1000	0.0943	94.3	....	...	....	....	94.3
4..	0.1000	0.0938	93.8	....	...	....	....	93.8
9..	0.0837	0.0742	88.5	....	...	....	....	88.5
10..	0.0935	0.0835	89.4	....	...	....	....	89.4
11..	0.0926	0.0868	93.8	....	...	....	....	93.8

TABLE VIII.—(*Continued*).

9. No.	10. Gramme taken estimated as anhydrous morphine.	11. Gramme recovered gravimetrically estimated as anhydrous morphine.	% recovered gravimetrically.	12. Gramme recovered volumetrically.	13. % recovered volumetrically.	14. Gramme resinous substance.	15. % resinous substance.	16. Total % recovered 14 and 15 or 12.
12	0.1430	0.0420	29.3	....	...	....	....	29.3
13	0.1003	0.0894	89.0	....	...	....	....	89.0
14	0.1158	0.1021	88.2	....	...	....	....	88.2
23	0.0968	0.0890	92.0	0.0886	91.5	....	....	91.5
24	0.0799	0.0757	94.9	0.0764	95.5	....	....	95.5
26	0.0980	0.0927	94.6	0.0898	91.7	....	....	91.7
27	0.1070	0.1105	103.2	0.0870	81.3	....	....	81.3
28	0.0938	0.0774	82.5	0.0846	90.2	....	....	90.2
29	0.1013	0.0690	68.2	0.0743	73.3	....	....	73.3
30	0.0944	0.0809	85.7	0.0798	84.6	....	....	84.6
32	0.0658	....	...	0.0586	89.0	0.0049	7.0	96.0
33	0.0995	....	...	0.0801	88.8	0.0091	8.95	97.9
34	0.0962	....	...	0.0659	68.6	0.0060	5.94	74.5
35	0.1621	0.1591	98.4	0.1478	91.0	0.0123	7.13	98.2
36	0.1672	0.1628	97.6	0.1518	90.8	0.0112	6.31	97.1
37	0.1748	0.1730	99.0	0.1570	89.96	0.0177	8.74	98.7
38	0.1721	0.1702	98.8	0.1561	90.7	0.0148	7.8	98.5
39	0.1715	0.1689	98.4	0.1577	91.9	0.0117	6.4	98.3
40	0.1718	0.1690	98.3	0.1542	89.93	0.0150	8.21	98.14
41	0.1724	0.1687	97.7	0.1550	89.58	0.0144	7.87	97.45
42	0.1708	0.1661	97.4	0.1552	91.15	0.0109	6.02	97.17
43	0.0853	0.0842	98.61	0.0841	98.50	0.0003	0.3	98.80
44	0.1105	0.1097	99.12	0.1096	99.10	Trace	....	99.10
45	0.0944	0.0940	99.50	0.0938	99.46	0.0005	0.5	99.51
46	0.1037	0.1025	98.85	0.1023	98.83	Trace	....	98.83
47	0.0926	0.0902	97.46	0.0876	94.56	0.0028	3.06	97.5
48	0.0967	0.0955	98.6	0.0917	94.9	0.0030	3.1	98.0
49	0.0852	0.0843	98.84	0.0814	95.7	0.0029	3.4	99.1
50	0.1029	0.1021	99.1	0.0984	95.5	0.0033	3.2	98.7

SUMMARY.

It is shown that lead acetate when used as a clarifier for alkaloidal extracts has no harmful effect upon the extraction of the alkaloid by immiscible solvents.

The addition of sodium chloride to such extracts after clarification increases the quantity of alkaloid removed at a single extraction.

The assay of powdered nux vomica was greatly facilitated by the use of lead acetate as a clarifying agent upon a dilute acid extract of the drug, which was then immediately made alkaline and shaken out with the solvent.

The conditions for obtaining a residue of anhydrous morphine have been determined.

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PARTIAL ANALYSES OF 330 AMERICAN CRUDE DRUGS.

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BY JOSEPH F. CLEVENGER AND CLARE OLIN EWING.