SCIENTIFIC SECTION

OBSERVATIONS ON THE OPIUM ASSAY.*

BY JOSEPH ROSIN AND C. J. WILLIAMS.[1]

Opium is assayed in most of the Pharmacopœias by either the Helfenberger or by the Lime method. Among the Pharmacopœias using the Helfenberger method or some modification of it are the Austrian, Belgium and German. The British, French (Codex), The Netherlands, Danish and Swiss use the Lime method. The United States Pharmacopœia also uses the Lime assay method with some modification. The Lime assay seems to be the more favored. Some of the Pharmacopœias recently revised have changed from the Helfenberger to the Lime assay method.

Helfenberger Method.—A weighed quantity of the opium is triturated with water, then made up to a definite weight with water, and after standing for 30 minutes and mixing, it is filtered. To an aliquot portion of the filtrate, generally corresponding to about two-thirds of the original opium, 1 or 2 cc. of normal ammonia water is added with gentle mixing and the mixture filtered immediately. This treatment with ammonia precipitates the other alkaloids, such as narcotine, papaverine, etc. To an aliquot portion of the second filtrate 2 or 2.5 cc. of normal ammonia water is again added and shaken for 10 minutes, which precipitates the morphine. It is then shaken with ether or ethyl acetate, filtered, washed and the morphine weighed or titrated.

Lime Method.—A weighed quantity of the opium is triturated with water and slaked lime, then made up to definite weight or volume with water, mixed well and filtered. To an aliquot portion of the filtrate, generally corresponding to one-half or two-thirds of the original opium taken, ether and a small quantity of alcohol are added, followed by 1 or 2 Gm. of ammonium chloride, the addition of the ammonium chloride causing the liberation of the morphine from its combination with lime. After mixing, the mixture is allowed to stand over night. It is then filtered, washed and the morphine titrated.

The United States Pharmacopœia assay of opium differs from the other Lime assay methods in that the opium is first completely extracted with water, thus eliminating the use of an aliquot portion with the attendant uncertainties that may be occasioned by the variation in the proportions of water and insoluble matter in the opium.

Criticisms of an opposite character have been frequently leveled against the Lime method. On the one hand it is maintained by some investigators that it yields too high results, claiming that the precipitated morphine is contaminated with co-precipitated titratable lime compounds; others assert that the results obtained by the Lime assay are too low because no account is taken of the morphine lost in the assay process due to solubility of the morphine in the solvents used in the assay. The latter criticism of the Lime method appears to have been the more prevalent, and has been met by some of the Pharmacopœias using the Lime method by applying a "correction" frequently designated as "solubility correction." The

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[1] Merck & Co., Inc., Rahway, N. J.

correction ranges from 1 to 1.1 mg. for each cc. of lime-morphine solution used in the assay, and amounts to from 1 to 1.1% on the Opium, or to about 8% of the morphine present in the average opium. A comparison of results obtained in the assay of opium with the British Pharmacopœia—a lime assay applying a correction, with the United States Pharmacopœia assay—a lime assay but without a correction and with the German Pharmacopœia assay which typifies the Helfenberger method, is illustrated in the following tabulation:

TABLE I.—ASSAY OF OPIUM BY B. P., U. S. P. X AND PH. G. VI METHODS.

	B. P. % Anhydrous Morphine.	U. S. P. % Anhydrous Morphine.	Ph. G. VI % Anhydrous Morphine.
Opium (partially dried)	16.38	15.55	15.08
		15.61	15.22
		15.58 Av.	15.15 Av.
Opium	13.76	13.09	12.12
		12.90	12.29
		13.00 Av.	12.21 Av.
Opium powder	10.71	9.77	9.08
		9.91	8.91
		9.84 Av.	9.00 Av.
Opium granular	10.39	9.73	8.94
Opium	...	15.24	14.75

The Helfenberger method it will be noted, gives the lowest indications; also, the differences between this method and the other two methods is greatest with the lower testing opiums. This is probably due to the fact that with the lower testing opiums there is a larger excess of ammonia present in the first treatment with ammonia for the removal of the other alkaloids and, therefore, more morphine is precipitated at this stage than with the higher testing opium.

The difference between the United States Pharmacopœia and the British Pharmacopœia assay results is approximately 0.75%. It should, however, be noted that within the last couple years the assays of a number of lots of opium by the British Pharmacopœia method gave results only about 0.2% above the United States Pharmacopœia.

There is no question but that some morphine is held in solution by the solvents in the assay, but the basis for the magnitude of the correction was somewhat obscure, at least to us. It is very much larger than could be accounted for by the solubility of morphine in the solvents. An endeavor to find the basis for the magnitude of the correction and to account for it resulted in the work recorded below.

EXPERIMENTS WITH MORPHINE.

The morphine used for the experiments was recrystallized twice from hot methanol and was in the form of well-defined, relatively large crystals. By titration it showed a purity of 99.93% as hydrated morphine. It was also free from non-phenolic alkaloids. The same morphine was used for all the subsequent experiments.

U. S. P. Assay.—1.050 Gm. of the morphine was dissolved in water and a slight excess of normal hydrochloric acid, the solution made up with water to 30 cc. and then assayed according

to the U. S. P. In a few of the tests the morphine was dissolved in meconic acid instead of hydrochloric acid.

B. P. Assay.—1.200 Gm. of the morphine was dissolved in water and a slight excess of normal hydrochloric acid, treated with lime and made up to 90 Gm.; 52 cc. of the filtered solution was then assayed according to directions of the B. P.

The results are shown in Table II.

In all the subsequent experiments with the U. S. P. or B. P. assay, the quantities of morphine just indicated were used.

TABLE II.—SERIES A—U. S. P. X METHOD.

Per Cent Morphine Recovered.		
98.2	94.4	97.5
97.4	96.9	96.3
97.6	94.5	95.8
97.9	94.4	
Average 96.44%		

Average "loss" of anhydrous morphine per assay	17.6 mg.
Average "loss" of anhydrous morphine per cc. of morphine-lime solution	0.58 mg.

TABLE III.—SERIES B—B. P. METHOD.

Per Cent Morphine Recovered.	
Uncorrected.	Corrected.
94.4	103.1
93.6	102.3
94.6	103.3
93.8	102.5
95.0	103.7
94.3 Av.	103.0 Av.

Average "loss" of anhydrous morphine per assay	37.6 mg.
Average "loss" of anhydrous morphine per cc.	0.72 mg.

(Three analysts participated in Series A, and two in Series B, C, D.)

Several of the assays in Series A are obviously too high. They are higher than would be expected even on the basis of only the theoretical solubility of morphine in the assay solvents. We attributed these high results to inclusion of titratable lime compounds with the precipitated morphine. The difference between the lowest and the highest results corresponds to only 2 mg. of calcium oxide or its equivalent of other titratable lime compounds.

TABLE IV.—SERIES C—U. S. P. X METHOD, BUT MORPHINE DISSOLVED IN HOT METHANOL.

Per Cent Morphine Recovered.		
93.8	94.3	94.7
94.3	94.4	94.3
94.2	93.8	
Average 94.2		

Average "loss" of anhydrous morphine per assay	28.6 mg.
Average "loss" of anhydrous morphine per cc.	0.95 mg.

TABLE V.—SERIES D—B. P. METHOD, BUT MORPHINE DISSOLVED IN HOT METHANOL.

Per Cent Morphine Recovered.	
Uncorrected.	Corrected.
92.2	100.9
92.4	101.1
93.0	101.7
92.6	101.3
92.4	101.1
92.6	101.3
92.5 Av.	101.2 Av.

Average "loss" of anhydrous morphine per assay	49.8 mg.
Average "loss" of anhydrous morphine per cc. of morphine-lime solution	0.96 mg.

To eliminate interference from lime we ran another series of assays of the morphine by the U. S. P. and B. P. tests, but dissolved the precipitated morphine from off the filter with several portions of hot neutral methanol. To the methanol

solutions of the morphine a measured volume of tenth-normal sulphuric acid was added, then the solution diluted with about 2–3 volumes cold water, allowed to cool and the excess acid titrated with tenth-normal sodium hydroxide, using methyl red as the indicator. In some of the assays, where a larger volume of methanol had to be used, the greater part of it was evaporated off after dilution with water. In methanol-water solution the morphine titrated 99.93 and 100.10%.

The results of Series C and D, and especially C, are more concordant among themselves than in the corresponding Series A and B. It will also be noted that by dissolving in hot methanol the yields by both the U. S. P. and B. P. assays are about 2% lower than when the morphine is directly dissolved in standard acid.

Series C and D practically substantiate the validity of the correction of 1 mg. per cc. of morphine-lime solution. The question now was how to account for the large correction.

NOTE: In all the assays of morphine from here on, where lime was used the precipitated morphine was dissolved in hot methanol.

When an excess of the finely powdered morphine was shaken with water, alcohol and ether, in the proportions of the U. S. P. assay for opium 30 cc. of the filtered aqueous layer gave upon evaporation 10 mg. of anhydrous morphine. From 15 cc. of the ether about 1.5 mg. of morphine was obtained on evaporation.

Portions of 0.50 Gm. of the morphine were dissolved in 30 cc. of water with a slight excess of normal hydrochloric or meconic acid, 3.5 to 4 cc. of normal ammonia added and allowed to stand over night. This quantity of ammonia gives approximately the same excess of alkalinity as in the U. S. P. assay. The precipitated morphine, after filtering and washing with ice-cold water, was dissolved in tenth-normal H_2SO_4 and back titrated with 0.1*N* NaOH. The recoveries of morphine were 98.2, 97.7 and 98.0 per cent. Repeating the experiments in presence of 2 cc. alcohol and 15 cc. ether, as in the U. S. P. opium assay, 96.7, 97.2 and 97.0 per cent of the morphine were precipitated. These recoveries correspond to a loss of about 14 mg. of anhydrous morphine, leaving about an equal quantity of additional loss when assayed by the U. S. P. method to be accounted for.

Adsorption of morphine on the lime suggested itself as a likely cause for the increased loss. If this assumption were valid, less morphine should be adsorbed if less lime is used and vice versa. We accordingly made one assay of the morphine by the U. S. P. method, but using 2 Gm. of lime instead of 4 Gm.; and one assay by the B. P. method, but using 4 Gm. of lime instead of 2 Gm. In the former, there was about 1% increase in the quantity of precipitated morphine, in the latter an additional loss of about 1.5% was sustained. These results do seem to indicate adsorption of some morphine on the lime, but not sufficient to account for all the loss in excess of the normal solubility in the assay solvents. Moreover, the loss per cc. of lime-morphine solution, as shown in Tables IV and V, is the same for the U. S. P. and B. P. assay methods, notwithstanding the different quantities of lime used.

Many alkaloids are known to react with ammonium salts on heating, the alkaloid being converted into the salt of the anion of the ammonium salt used and ammonia liberated. We found that with morphine the same reaction takes place in an aqueous solution of ammonium chloride at room temperature. It was shown

before that practically 98% of the morphine was precipitated from its solution by ammonia. When the same experiments were made in the presence of 0.5 Gm. and 1 Gm. of ammonium chloride, the precipitation amounted to 96.4 and 95.3 per cent, respectively. When, in addition to the ammonium chloride, the precipitation was made in the presence of alcohol and ether in the proportions of the U. S. P. assay, the corresponding recoveries were 96.0 and 94.9 per cent. A summation of the foregoing results is presented in Table VI.

TABLE VI.

		Per Cent Morphine Recovered by Precipitation.
1.	Aqueous solution precipitated with ammonia	98.0
2.	Ditto, in presence of 0.5 Gm. ammonium chloride	96.4
3.	Ditto, in presence of 1 Gm. ammonium chloride	95.3
4.	As 1, but in presence of 2 cc. alcohol and 15 cc. ether	97.0
5.	Ditto 4, but with 0.5 Gm. ammonium chloride	96.0
6.	Ditto 4, but with 1 Gm. Ammonium chloride	94.9

The effect of ammonium chloride on the amount of morphine precipitated was corroborated by assaying the morphine by the U. S. P. method, but using 0.5 Gm. of ammonium chloride instead of 1 Gm. The following table illustrates the results.

TABLE VII.

1 Gm. NH_4Cl.	0.5 Gm. NH_4Cl.
93.6	95.3
94.2	95.0
93.8	95.1
93.9 Av.	95.1 Av.

The foregoing data clearly indicate that the ammonium chloride is responsible for holding in solution about 2%, or at least about 10 mg., of morphine in the U. S. P. assay. They also disclose that 0.5 Gm. of ammonium chloride is ample for the precipitation of the morphine from the lime solution, and that with this quantity of ammonium chloride an increased precipitation of the morphine amounting to 1% or over, is obtainable. As a matter of fact, the Netherland Pharmacopœia uses 0.2 Gm. ammonium chloride for 2 Gm. of opium, which corresponds to 0.4 Gm. NH_4Cl for 4 Gm. of opium in the U. S. P. assay.

Ammonium sulphate exerts a much smaller solvent effect than ammonium chloride. For instance, when 0.5 Gm. of morphine was dissolved in 30 cc. water with just sufficient sulphuric acid, 2 cc. alcohol and 1 Gm. of ammonium sulphate added and precipitated with 3.5 cc. of normal ammonia, 97.4% of the morphine was recovered.

The aqueous layers, exclusive of the washing, from several of the assays in Series C and D, as well as in similar experiments not reported here, were nearly saturated with sodium chloride and extracted with 4 to 6, 25-cc. portions of chloroform—alcohol mixture. The extract, after washing with a small quantity of water, was evaporated, the residue dissolved by warming with fiftieth-normal acid and the excess acid titrated with fiftieth-normal sodium hydroxide. From the mother liquor of the U. S. P. assays the alkaloid recovered ranged from 9 to 14 mg. with an average of 12 mg. corresponding to about 40% of the morphine "lost" in the assay.

From the B. P. assays the recovery ranged from 17 to 22 mg., also corresponding to about 40% of the unprecipitated morphine. From the aqueous mother liquors of the experiments summarized in Table VI, 80 to 85 per cent of the morphine held "in solution" was recovered, giving a total recovery of about 99%. We are unable yet to account for this phenomenon. The only difference between the two is the presence of some calcium chloride or possibly even some calcium hydroxide in the U. S. P. or B. P. assays.

On several occasions when the same assay of the morphine was repeated but at a different time, the results were more divergent than could be accounted for by the average error, notwithstanding that the errors in assaying pure morphine are to be expected to be greater than in many other types of quantitative determinations. It was suspected that the difference may be due to the difference in temperatures prevailing during the precipitation of morphine over night. The suspicion was corroborated, as shown in the following table, by running two sets of assays by the U. S. P. method. In one set the precipitation was allowed to take place at room temperature—about 28° C., and in the other at about 8° C.

TABLE VIII.—RESULTS SHOWING THE EFFECT OF TEMPERATURE ON RECOVERY OF MORPHINE.

Per Cent Morphine Recovered.	
Temperature during Precipitation, about 28° C.	Temperature during Precipitation, about 8° C.
93.6%	95.7%
94.5	95.5
93.4	95.8
93.8 Av.	95.7 Av.

In average laboratories such variations in temperature do not, of course, obtain, but a 10° difference between the winter and summer is not at all uncommon, and the same assay made at 20° and 30° C. may show a variation of about 1%.

We believe that the markedly lower recoveries at the higher temperature is primarily due to the greater solubility exerted by the ammonium chloride at that temperature.

It has been indicated in the literature that in the assay of opium, and especially so by the lime method, small quantities of other alkaloids, notably codeine, are co-precipitated with the morphine. We have found this to be the case in a number of samples of opium we examined. The results are recorded later on. The effect of the presence of other alkaloids on the precipitation of pure morphine was determined by assaying a "composition opium" by the U. S. P. method, after dissolving it in either hydrochloric or meconic acid. The "composition opium" for each assay was made up of 1.050 Gm. of morphine, about 0.4 Gm. of narcotine, 0.1 Gm. of codeine, about 0.08 Gm. papaverine, 0.07 Gm. of thebaine and about 0.2 Gm. of morphine free tar obtained in the process of manufacture of morphine. The proportions of the other alkaloids corresponds, approximately, to those present in average opium.

The results are on the average about 1% higher than those obtained with morphine alone (compare Table IV).

Morphine, like most other alkaloids, is "salted" out by sodium chloride or sulphate. If in the assay of morphine, in the form of hydrochloride or meconate,

TABLE IX.—SERIES E—"COMPOSITION OPIUM" ASSAYED BY U. S. P. X METHOD.

Per Cent Morphine Recovered.	
95.6	95.6
94.8	95.8
95.2	95.4

Average 95.4

by the U. S. P. method the morphine-lime solution is saturated with sodium chloride before precipitation with ammonium chloride, the amount of morphine precipitated is about 1.5% higher than without sodium chloride. We also observed, however, that saturation with sodium chloride in the assay of "Composition opium" also precipitates a somewhat greater proportion of the by-alkaloids.

EXPERIMENTS WITH OPIUM.

Effect of Methanol.—Several samples of opium were assayed by the U. S. P. method and also by the modification of dissolving the precipitated morphine in hot methanol, etc., as described under pure morphine. The results were as follows:

TABLE X.—EFFECT OF DISSOLVING THE PRECIPITATED MORPHINE IN METHANOL.

	Per Cent Anhydrous Morphine.	
	U. S. P. Assay Not Dissolved in Methanol.	U. S. P. Assay Dissolved in Methanol.
Opium No. 7	15.07	14.74
Opium No. 8	12.83	12.58
Opium No. 21	12.04	11.80

On the basis of the morphine contents the difference is about 2%, practically the same as obtained with morphine.

Effect of Ammonium Chloride.—The effect of using only 0.5 Gm. of ammonium chloride in the assay of opium instead of 1 Gm. is shown in the following tabulation. In both sets of assay the precipitated morphine was dissolved in methanol.

TABLE XI.—PER CENT MORPHINE FOUND.

	1 Gm. of Ammonium Chloride.	0.5 Gm. of Ammonium Chloride.
Opium No. 7	14.82	15.05
Opium No. 8	12.63	12.96
Opium No. 21	12.08	12.21

Effect of Temperature.—The effect of the temperature on the amount of morphine precipitated in assaying opium practically confirmed the results found with morphine. Two samples of opium precipitated at a temperature of 28–30° C. gave 15.25 and 11.85%, but when the precipitation was made at about 8° C. the percentages of morphine were 15.35 and 12.03%.

Co-precipitated Alkaloids.—In the experiments with "composition opium" described under morphine, an increased yield of about 1%, due to the precipitation of by-alkaloids, was obtained. The by-alkaloids co-precipitated with morphine in the opium assay is considerably greater. For the determination of the co-precipitated alkaloids, the morphine solution, after titration was treated with 10 cc. of 5% sodium hydroxide and shaken out with several portions of chloroform. The combined chloroform extracts were shaken with small quantities of water to remove any free alkali, filtered and evaporated nearly to dryness. A measured volume of fiftieth-normal sulphuric acid was added, warmed until the residue was dissolved and the odor of chloroform dissipated, cooled and then the excess of acid titrated with fiftieth-normal sodium hydroxide using

methyl red as the indicator. The percentages of other alkaloids thus found, calculated as morphine, are shown in the following table.

TABLE XII.—OPIUM BY-ALKALOIDS CO-PRECIPITATED WITH THE MORPHINE.

	Per Cent Anhydrous Morphine U. S. P. Assay.	Per Cent Non-phenolic Alkaloids Co-precipitated with the Morphine.	Per Cent Non-phenolic Alkaloids on the Basis of the Morphine.
Opium No. 11	15.20	0.45	2.96
Opium No. 12	12.42	0.34	2.74
Opium No. 12-A	14.76	0.53	3.59
Opium No. 13	15.06	0.45	2.99
Opium No. 16	14.64	0.39	2.67
Opium No. 18	12.58	0.35	2.78
		0.42 Av.	2.96 Av.

These determinations represent only the non-phenolic by-alkaloids. Opium contains also several phenolic alkaloids other than morphine. If they should be present in appreciable quantities they will probably be co-precipitated with the morphine, and the extraction of the sodium hydroxide solution of the alkaloids with chloroform would not eliminate them.

Shaking out of the aqueous mother liquor from several of the opium assays with chloroform-alcohol, after saturation with sodium chloride, yielded from 8 to 13 mg. of morphine, with an average of 11 mg. This recovery is practically identical with that obtained from the aqueous mother liquor in the assays of morphine.

Within the last two or three years a new type of assay for opium has been advanced, the essential features of it being the following. The aqueous or acid extract of the opium is treated with an excess of sodium hydroxide solution and shaken out with an immiscible solvent such as chloroform. Non-phenolic alkaloids are thus removed. The alkaline solution holding the morphine is acidified with HCl, then made alkaline with ammonia and shaken out with a suitable solvent. The second shaking out extracts the morphine which after evaporation of the solvent is titrated.

An assay of this type, which we would designate as "Assay by immiscible solvents" is due to Buchbinder, formerly of the Bureau of Chemistry. He uses chloroform-alcohol for the extraction of the morphine from the ammoniacal solution. Assaying morphine, in hydrochloric acid solution, by the Buchbinder method we recovered 98.4 and 97.1%. We also assayed four samples of opium by the same method. The results compared with those obtained by the regular U. S. P. method were as follows:

TABLE XIII.

	U. S. P. Method.	Buchbinder Method.
Opium No. 53	11.93	12.15
Opium No. 65	14.20	14.51
Opium No. 69	13.62	13.90
Opium granular	10.50	11.01

The Buchbinder method gives a slightly higher test than the U. S. P. method. This may be due to the fact that in the Buchbinder method an aliquot portion is taken from a solution in which there is present the insoluble matter from the opium, barium sulphate derived from barium chloride used in the assay, etc.

Another "assay by immiscible solvents" has been proposed by Eder and Stucki. They digest the opium first with normal hydrochloric acid, claiming that the acid liberates more morphine, and use a mixture of chloroform and isopropanol for both removing the non-phenolic alkaloids as well as for the extraction of the morphine.

The "assays by immiscible solvents" have, *first*, the important advantage that no correction for solubility of morphine is necessary, and *second*, the isolated morphine is not contaminated with non-phenolic alkaloids, although other phenolic alkaloids may be included as morphine. These assays have, however, one great disadvantage. On account of the limited solubility of morphine in the solvents only a small quantity of opium, 1 or 2 Gm., can be used for the assay. Such a small sample could not be well representative of the opium, especially when dealing with Gum Opium. We believe, however, that the above proposed assays for opium by immiscible solvents have laid the ground work for further investigation which we hope will result in perfecting the method and making it of practical use.

SUMMARY.

Dissolving the morphine, obtained in the lime assays, in hot methanol before titration eliminates, on the basis of the morphine contents, about 2% of foreign titratable substances calculated as morphine.

Assays of pure morphine by the U. S. P. and B. P. methods confirm the "assay-loss" of practically 1 mg. of morphine for each cc. of lime-morphine solution as indicated in the latter Pharmacopœia. This "loss," however, will fluctuate somewhat unless definite and uniform conditions are maintained in the assay.

About one-half of the assay loss is attributable to the solubility of morphine in the assay solvents. The greater part, if not all, of the balance of the "loss" is caused by the solvent action of the ammonium chloride on morphine. Adsorption on the lime may also be responsible for a small portion of the assay-loss.

It therefore follows, and it has been confirmed by experiment, that the larger the quantity of ammonium chloride used the greater will be the quantity of morphine dissolved. By using 0.5 Gm. of ammonium chloride in the U. S. P. assay, 1 to 1.5 per cent more morphine was precipitated than when 1 Gm. was used.

The temperature during precipitation of the morphine in the lime assays affects the quantity of morphine held in solution. When precipitation takes place at 28°–30° C. about 2% more of the morphine is dissolved than at 8° C. We attribute the increased solubility largely to the greater solvent action of the ammonium chloride at the higher temperature.

It is recommended: (1) that in the U. S. P. assay 0.5 Gm. of ammonium chloride be used instead of 1 Gm. This quantity, 0.5 Gm. is several times the theory for a 15% opium; and (2) that the temperature of precipitation (standing over night) be restricted to about 10° C.

Saturation or near-saturation of the lime-morphine solution with sodium chloride before adding the ammonium chloride raises 1 to 2 per cent the quantity of the morphine precipitated. In the case of opium, however, the use of sodium chloride will also increase the co-precipitation of the by-alkaloids.

The morphine precipitated in the U. S. P. and probably also in other lime assays carries about 3% non-phenolic by-alkaloids which is included in the assay as

morphine. Since opium contains also other alkali-soluble alkaloids than morphine, these, if present in appreciable quantities, may also be included with the morphine and thus show an apparent higher morphine content. Pharmacopœias applying a correction for "assay-loss" should, as a matter of scientific accuracy and of fairness to the manufacturers of morphine and its derivatives, who consume 90% or more of the total legitimately used opium, take cognizance of the occlusion of by-alkaloids in the morphine and make the necessary correction.

By coincidence of counterbalancing error factors, the U. S. P. assay of opium appears to indicate very closely the true morphine content.

The "total extraction" of the opium which has been practiced in the assay by the several revisions of the U. S. P. is an important point in its favor. It obviates errors in aliquot portions due to the variable amounts of water and insoluble matter in the opium. In the assay method under consideration by the Committee of the League of Nations, published elsewhere, these sources of "inaccuracies" are corrected for by making separate determinations of the water content of the opium, and of the total extractive matter.

Corrections, almost of any kind, are looked upon with disfavor in analytical procedures. They are most uncertain and most undesirable when the corrections involved are of appreciable magnitude.

Assays based on the isolation of the morphine, free from by-alkaloids, through the use of immiscible solvents offer a possible solution of the problem provided they can be worked with reasonably large samples. They should also strive to avoid such aliquots as may introduce any element of error, and, *ipso facto*, should not require an undue length of time.

GELATIN AS A STABILIZING COLLOID FOR OIL IN WATER EMULSION SYSTEMS.*

BY LINWOOD F. TICE.[1]

Various workers have investigated the efficiency of gelatin as an emulsifying agent. Briggs and Schmidt (1) found gelatin to be comparatively inefficient as an emulsifying agent. Clayton (2) reported drop numbers for cottonseed and peanut oils in aqueous gelatin solutions which indicated that gelatin possessed considerable ability to reduce the interfacial tension between oil and water. Holmes and Child (3) studied the effect of added electrolytes upon the emulsion system kerosene, gelatin and water and concluded that the important factor was the conferring of a favorable viscosity to the gelatin solution. Kernot and Knaggs (4) using the Donnan pipette measured the drop numbers of various oils against gelatin solutions. Limburg (5) showed that a lowered p_H favors the adsorption of gelatin around oil globules.

In reviewing the results of these workers it is very difficult for one to reach any definite conclusions as to the exact status of gelatin as a practical emulsifying agent. The following criticism may be advanced concerning these results:

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[1] Department of Research, Philadelphia College of Pharmacy and Science. Investigation conducted in behalf of the Edible Gelatin Manufacturers' Research Society of America, Inc.