tion to the sand; again, water, sand and Fuller's earth—but all of these gave inactive precipitates. Only one experiment need be given to show the type of results obtained.

EXPERIMENT 12.

7.0 grams of precipitate; 33.9 grams of oil; 29.9 grams of 0.4 per cent. sulphuric acid; 0.35 gram of chloral.

At once.	One day.	Three days.	Five days.	Seven days.
0.8	1.4	2.7	3.9	3.1

In conclusion, we wish to return to the question of the retrogression in the acid value, several examples of which occur in the experiments cited in this paper. We have met with this phenomenon a number of times, and the following experiment, which we have selected especially for this purpose, shows this admirably.

EXPERIMENT 13.

	At once.	Two days.	Four days.	Five days.	Six days.	Seven days.
Mineral acid present in terms of N H_2SO_4	0.41	0.33	0.37	0.38	0.48	0.38
Fatty acid in the oil in terms of N acid	0.21	0.17	0.19	0.19	0.24	0.19
Total acid	0.62	0.50	0.56	0.57	0.72	0.57
N KOH to neutralize the sample	0.45	0.49	0.45	0.49	0.69	1.38

UNIVERSITY OF MICHIGAN,
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MECONIC ACID IN THE U. S. P. 1890 ASSAY OF OPIUM AND CERTAIN MECONATES.

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THE work outlined in the following pages has to do with the identification and properties of an impurity which usually contaminates, to a greater or less degree, the precipitated morphine which is obtained as the "form" to be weighed in the present (1890) U. S. P. method for the assay of opium. Incidentally, some of the salts of meconic acid with barium and calcium were prepared and examined. It should be stated at the outset that these salts seem to have a somewhat variable composition and offer considerable difficulty in their analysis. They are insoluble in all ordinary solvents and could not be purified by crystallization. The agreement between the theory and our analyses is therefore not very close.

The U. S. P. 1890 assay process consists in a thorough extraction of the opium with water and precipitation of the morphine as alkaloid by addition of dilute ammonia water to the concentrated aqueous extract. A certain amount of alcohol and ether are added to the flask containing the concentrated aqueous extract before the ammonia; this yields a purer morphine. The formation of a thin layer of a white or yellowish-white substance adhering to the bottom of the flask containing the precipitated morphine was observed with many varieties of opium, notably the "Yerli" and "Boghaditch" from Smyrna. The precipitated morphine, on the other hand, does not adhere to the flask and by using alcohol saturated with morphine it may oftentimes be washed out of the flask (a small Erlenmeyer), leaving the coating of the yellowish-white substance on the bottom. If water is used instead of alcohol saturated with morphine, the yellowish-white substance is loosened, being partially soluble. If the contents of the assay flask are transferred to the filters in the regular manner by means of a rubber-tipped rod, the yellowish-white body appears in small flakes or scales scattered through the crystalline precipitate of morphine and is weighed as such. It is generally known that the precipitated morphine produced by the U. S. P. 1890 assay is not of sufficient purity to weigh as morphine and many methods of determining the amount of impurity have been proposed. In order to obtain a purer precipitate of morphine Lamar[1] devised a modification of the U. S. P. 1890 process in which alcohol was added to the concentrated aqueous extract of the opium just before the precipitation of the morphine. The alcohol produces a precipitate, containing no morphine, which can be filtered off and the filtrate is evaporated again and the morphine precipitated as usual with dilute ammonia. This process has been used in our laboratory and the resulting morphine is nearly, if not quite, free from scales of the white body. We thought that the precipitate produced by alcohol in the Lamar modification was probably identical with the yellowish-white substance which we had observed in the precipitated morphine obtained in the regular process, but investigation proved this not to be the

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[1] Lamar: *Am. J. Pharm.*, **72**, 36 (1900).

case. The precipitate produced by alcohol was found to be chiefly calcium sulphate and some gummy substances of dark color.

The yellowish-white coating is not calcium sulphate; some scales of it were washed free of morphine on a copper sieve and tests showed calcium and meconic acid present. As it was customary to determine the purity of the weighed morphine by titration with N/10 H_2SO_4, it became important to ascertain whether the white body influenced the titre. Experiments with small amounts showed that it consumed nearly one-fourth as much acid as the same weight of morphine. Its acid-consuming power was also indicated by the fact that titrations of assay morphine containing much of the yellowish-white substance (which we shall call simply "scale" hereafter) were far too high, as was proved by subjecting the morphine to another assay, thus determining its true purity. The following figures show the magnitude of the error:

	Average purity by titration Per cent.	Average purity by re-assay. Per cent.
Assay morphine from 14 assays of Salonica opium *poor in "scale"*	96.5	94.5
Assay morphine from 3 assays of Smyrna opium *rich in "scale"*	95.1	87.9

We thought that the "scale" was probably some basic salt of calcium and meconic acid, and accordingly attempted to reproduce it from pure material before making analyses of it. A solution of calcium nitrate was added to a solution of meconic acid made noticeably alkaline with ammonia. A voluminous, yellowish-white precipitate formed at once which settled very slowly, and owing to its gelatinous nature filtered with difficulty and dried into a lemon-yellow horn-like substance apparently without crystalline structure. It was observed that the mother-liquor no longer smelled of ammonia although previous to the addition of calcium nitrate the excess of ammonia was quite evident, and in fact the mother-liquor under these conditions was actually acid, as we found later. The lemon-yellow salt, after washing and drying at 60°, consumed only about 1.5 cc. of N/10 H_2SO_4 for 0.5 gram and after long digestion on the water-bath with 10 cc. N/10 H_2SO_4 about 2.0 cc. N/10 H_2SO_4 were consumed. Litmus paper was used as indicator. Ten cc. of N/10 H_2SO_4 digested on a water-bath similarly showed no appreciable loss of acid. The same amount of "scale" under like treatment would require about 4.0 cc. N/10 H_2SO_4. The lemon-yellow salt also lacks the physical properties of the "scale" and we concluded that they were not identical, a conclusion which subsequent experience verified. The salt loses little or no water at 100°, but attains approximate constancy at 150-160° C., the loss of weight amounting to 24.5 per cent. Calculated for $Ca_3(C_7HO_7)_2.9H_2O$, 23.9 per cent.

The determination of lime in the dried salt gave 28.5 and 28.7 per cent. of calcium oxide; calculated, 32.17 per cent. A correct determination of lime in a meconate by incineration was found to be very difficult, if not impossible. The salt ignites and burns like moist gunpowder, no matter how gradually the heat is increased. It was found best to keep the crucible tightly closed until organic matter is nearly all consumed.

The dried salt was slightly discolored superficially. The air-dried salt before drying at 160° gave a strong test .for ammonia with lime. No means of dissolving and crystallizing this salt was found. It was found later that tribarium meconate gives off small amounts of carbon dioxide when similarly heated, and an ammonium calcium meconate is also described later which gives off large amounts of ammonia and carbon dioxide. The low content of calcium, the great loss in drying, and presence of ammonia show that the yellow salt is not a pure tribasic calcium salt, but contaminated with ammonium calcium meconate.

Assay Scale.—The conditions under which "scale" is formed in the assay flasks are abundance of meconic acid and of ammonia and scarcity of calcium, for the amount of the latter naturally occurring in opium is small in comparison to the meconic acid. After several different methods had failed to yield a product anything like the assay "scale," the following procedure was successful. Four grams of crystallized meconic acid were dissolved in 100 cc. of water containing a little alcohol. This solution in a flask was now covered with a layer of ether, and ammonia water added in excess followed by 25 cc. of a solution of calcium nitrate which analyzed 1.674 grams CaO per 100 cc. At first the same yellow voluminous precipitate formed as was previously obtained in adding calcium nitrate to meconic acid saturated with ammonia, but it re-dissolved on shaking and after a few minutes a white flaky salt began to form and precipitate slowly on the bottom of the flask About 2.2 grams of the salt were obtained which had the physical appearance of the "scale" from assays, except that it was white instead of yellowish-white.

If a concentration greater than the above proportions is used or if the solution is warmed, the lemon-yellow tribasic calcium salt will not all dissolve.

Determinations of the lime content in this salt (which we shall call "artificial scale" to distinguish it from the "assay scale" obtained from actual assays on opium) and in "assay scale" were made by incinerating and weighing the calcium oxide produced. It was found that both the "artificial scale" and the "natural scale," after thorough washing, gave strong tests for ammonia with lime. Kjeldahl determinations for ammonia were therefore made.

The recrystallized assay scale was prepared by dissolving assay scale in cold dilute hydrochloric acid and reprecipitating with ammonia. It is slightly soluble in water but no solvents were found from which to crystallize it. Under the microscope, this salt and the "artificial scale" showed the same form of crystals (diamond-shaped plates, often cut off at the four points). The "natural scale" viewed under the microscope appeared as such a closely interlaced mass that its crystalline structure could not be made out. The presence of the coloring-matter in the form of a gum is probably responsible for this fact.

No accurate determinations of the crystal water in the "artificial" and "assay scales" were possible by heating. On drying at various temperatures up to 160° no constancy of weight was reached but both salts lost about equally, the losses being as high as 30 per cent. of the air-dried weight. After drying for about a week, day and night at 160° both salts were still losing weight, but it was observed that now the salts gave very weak tests for ammonia with lime, whereas at the start the air-dried salts gave strong tests. Experiment showed that both carbon dioxide and ammonia were given off. It is well known that meconic acid loses carbon dioxide easily when heated in the dry state or when boiled with water or with water containing acid, forming comenic acid by the loss of one of the two carboxyl groups[1]. Under certain conditions a second molecule of carbon dioxide may be lost and pyrocomenic acid forms. How[2] has shown that a solution of meconic acid saturated with excess of ammonia upon prolonged boiling yields, when acidified, carbon dioxide and a precipitate which upon drying turns out to be comenic acid amide, $C_5H_3O_3CONH_2$. In view of these facts, we thought that if the calcium ammonium meconate were heated

[1] *Ann. Chem.*, **7**, 237 (1833).

[2] Henry How: *Ann. Chem.*, 83, 350.

under proper conditions for measuring the ammonia and carbon dioxide evolved, the reaction might be shown to run as follows:

$$CaNH_4C_7HO_7 \text{ ("scale")} = NH_3 + CO_2 + CaC_6H_2O_5 \text{ (calcium comenate)}.$$

Accordingly, a slow current of air free from carbon dioxide and ammonia was passed over artificial scale heated to 160° and thence through flasks containing determinate amounts of dilute sulphuric acid and barium hydroxide. After drying for different times, samples from the absorption tube were withdrawn and the amounts of ammonia and carbon dioxide given off determined by titration; the results are as follows:

0.25 GRAM "ARTIFICIAL SCALE."

	Time of heating in days of twenty-four hours.			Theory for $CaNH_4C_7HO_7$. Gram.
	Six days. Gram.	Eleven days. Gram.	Fifteen days. Gram.	
NH_3 produced	0.01054	0.01135	0.01135	0.01380
CO_2 produced	0.02517	0.03795	0.04697	0.03558

The above experiment was made only once and the results need confirmation. It seems evident that the reaction does not run easily and that decomposition goes farther than the production of calcium comenate.

One attempt to determine the crystal water was made by heating the salt in such a manner that the ammonia and water were absorbed in sulphuric acid. From the gain in weight of the sulphuric acid tube we deducted the weight of ammonia that would have been given off according to the above equation and considered the resulting gain as due to crystal water. This method should give results approximately correct since the greater part of the ammonia is given off on prolonged heating. A test-tube containing 0.500 gram of artificial scale was placed horizontally in a drying oven and a delivery tube led out and joined to a U-tube filled with sulphuric acid and standing in cold water. The absorption of moisture from the air was prevented by a long capillary tube open at one end, sealed on to the U-tube at the other end. After several days' and nights' heating at 160-170° C., the acid gained weight—0.105 gram. If the salt has the formula $CaNH_4C_7HO_7.3H_2O$, 0.500 gram would yield 0.0276 gram NH_3; hence, the water given off $= 0.105 - 0.0276 = 0.0774$ gram.

All the analyses of the salt are grouped below:

	Calculated for $CaNH_4C_7HO_7.3H_2O$. Per cent.	Found. "Artificial scale." Per cent.	"Assay scale." Per cent.	"Assay scale" recrystallized. Per cent.
CaO	18.16	18.24	....	17.18
NH_3	5.52	5.53	5.28	5.32
H_2O	17.47	15.5	....	....

From the results of the analyses and mode of preparation of the salt, we conclude that the unknown yellowish-white "scale," which occurs in the morphine from U. S. P. assays on certain opiums, is a double salt of calcium and ammonium with meconic acid represented by the formula $CaNH_4C_7HO_7.3(?)H_2O$. The content of water we do not feel certain of. This salt or some similar double salt was known to Robiquet.[1] He states that upon treating an aqueous extract of opium with ammonia, there is precipitated along with the morphine a part of the meconic acid in the form of an insoluble double salt of lime and ammonium. After the extraction of the morphine alkaloid from the precipitate caused by the ammonia there remains this "dreifach mekonsaures Salz." The presence of alcohol and ether is the only point of difference between Robiquet's experiment and the present U. S. P. 1890 assay of opium, and these additions would, in fact, tend to produce a more complete separation of calcium ammonium meconate with the morphine, so it appears that as early as 1833 this difficulty in the precipitation of a pure morphine from an aqueous extract was known, and yet it seems to have been largely overlooked in the 1890 assay. Robiquet did not analyze his salt, and we have been unable to find any other reference to the existence of the compound.

Meconic Acid and Bases.—In the first preparation of the lemon-yellow tribasic calcium meconate, it was mentioned that the mother-liquor became acid. Liebig[2] observed the same phenomenon when silver nitrate is added to meconic acid neutralized with ammonia and recognized that the cause was the varying basicity of meconic acid towards different bases. He prepared an insoluble yellow silver salt having the formula $Ag_3C_7HO_7$ and mentions that the so-called "neutral potassium meconate" is a dibasic salt of the formula $K_2HC_7HO_7$. Stenhouse[3] found that meconic acid forms a salt with lead in which three hydrogen atoms were replaced by the metal. The generally accepted formula for

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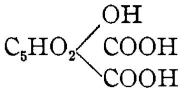
[1] *Ann. Chem.*, **5**, 82; see also Gmelin-Kraut, "Handbuch Org. Chem.," Vol. III, p. 338 (1859).

[2] *Ibid.*, **26**, 114 (1838).

[3] *Ibid.*, **51**, 231 (1844).



meconic acid is $C_5HO_2\left\langle\begin{matrix}OH\\COOH\\COOH\end{matrix}\right.$ in which the hydrogen of the hydroxyl group most probably forms the third acid hydrogen toward the above-mentioned metals. That the acid behaves quite accurately as a tribasic acid also toward calcium and barium is shown later by the preparation of the tribasic salts.

A preliminary titration was made to test this point. To a solution of 0.2 gram of crystallized meconic acid we added 4.17 cc. of a certain solution of calcium nitrate. To produce $Ca_3(C_7HO_7)_2$ would have required 3.94 cc. of the same solution. Decinormal sodium hydroxide solution was now run in until the mother-liquor over the precipitated salt was just alkaline to litmus; this required 23.8 cc. It was found that the calcium nitrate solution was slightly acid, 4.0 cc. requiring 0.10 cc. N/10 NaOH; hence, deducting this from 23.8 cc., we have the acidity developed in reaction 23.7 cc. N/10 acid. For the reaction $2H_3C_7HO_7 + 3Ca(NO_3)_2 + 6NaOH = Ca_3(C_7HO_7)_2 + 6NaNO_3 + 6H_2O$, the sodium hydroxide required for 0.2 gram acid is 23.62 cc. The agreement is close. On the other hand, meconic acid, if pure and free from comenic acid, titrates accurately as a dibasic acid with sodium hydroxide, using litmus paper as indicator. If the acid is sufficiently white, so that its solution is colorless, it furnishes its own indicator, so to speak, for as soon as more than two equivalents of alkali are added a very perceptible yellow color appears. This change is delicate enough to detect an excess of two or three drops of N/10 alkali. If comenic acid is present, as much as 10 or 15 cc. N/10 alkali in excess must often be added in an ordinary titration to effect a definite end-point as indicated by red litmus paper.

BARIUM AND CALCIUM SALTS OF MECONIC ACID.

In order to gain some knowledge of the behavior of meconic acid in the presence of varying amounts of calcium we attempted to replace successively one, two or three of the acid hydrogen atoms with equivalents of calcium. Barium salts were also made on account of the greater ease of handling the base quantitatively. Some of these salts have been prepared before, but the literature on the subject is not very complete. Beilstein, for example, does not give formulas of, or references to, the calcium or barium salts of meconic acid. Fehling's "Handwörterbuch," 1871 (Vol. IV, p. 294), gives formulas for the dibasic meconates of barium and calcium and for the acid calcium salt, but nothing in regard to the tribasic salts of barium and calcium. Similarly "Watts' Dictionary" (1901 edition) gives no information on these tribasic salts. Probably the best description of the early work upon the preparation of meconic acid and its salts, with many references to the original articles, is to be found in Gmelin-Kraut's "Handbuch der Organ. Chem." Vol. III, p. 332, etc. (1859). His statements must be accepted with discrimination, however, for it must be remembered that much of the early work on "meconic acid" is quite invalid because of the mode of preparation which yielded not meconic acid at all, but an impure pyromeconic acid. Although this is pointed out, it is not made clear in each description of a salt of meconic acid whether the acid was pure and properly prepared and furthermore, in some cases, the properties indicate an impure pyromeconate rather than a meconate. For example, on p. 338 under barium meconate, the statement is made on Robiquet's authority that the "pure meconic acid" does not precipitate a solution of barium hydroxide and immediately following comes a direct contradiction of this on Wackenroder's authority, to the effect that the acid gives with excess of barium hydroxide solution a slimy, heavy, yellow precipitate. The probable explanation is that the extract from Robiquet was based on work done before he knew that this acid, which was prepared by sublimation, was really an impure pyromeconic acid and not meconic acid at all. Wackenroeder[1], working about eight years after Liebig[2] had shown the true relationship of meconic, comenic and pyromeconic acids, obtained the correct reactions.

Again on p. 338 a formula is given for barium meconate which, after transforming to modern equivalents, becomes $BaHC_7HO_7.H_2O$ and the salt is described as being difficultly soluble in water but readily soluble in a solution of barium hydroxide with the production of a yellow color. Liebig is the authority for this, but we have looked up all the references to original articles by Liebig given by Gmelin-Kraut without finding any such statement. Fehling's "Handwörterbuch" gives the same information, but does not attribute it specifically to Liebig.

We have repeated Wackenroeder's experiment and find, as he did, that pure meconic acid, even with a large excess of barium hydroxide, produces a yellow flocculent precipitate which does not redissolve and cannot be made to do so by shaking or warming. We have

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[1] *Archiv. für Pharm.*, **2**, 167 (1841).

[2] *Ann. Chem.*, **7**, 257 (1833).

tried this repeatedly with small amounts of acid and large amounts of barium hydroxide and always with the same result. Comenic acid, while giving a precipitate with barium hydroxide solution of greater solubility in the excess than the corresponding one produced by meconic acid, is still far from what we would call soluble in the excess. The precipitate so produced by meconic acid, as will appear later, is the tribarium salt. If Liebig made the statement above attributed to him, it is probable that it was taken from some early experiments prior to 1833 and hence with meconic acid that was open to objection on the grounds of improper preparation.

The meconic acid used throughout this work was prepared essentially after the method of Gregory[1] which consists simply in precipitating an aqueous extract of opium with calcium chloride and treating the resulting precipitate of crude calcium meconate with sufficient hydrochloric acid, somewhat diluted, to take it nearly into solution while hot. The clear filtered solution separates out crystals of meconic acid upon cooling which may contain some calcium. This can be separated by several crystallizations from warm water and a pure acid obtained. We were careful to avoid prolonged heating, as well as the use of very concentrated hydrochloric acid, both of which, as is well known, cause the acid to decompose. Our acid had a faint cast of yellow color, which is very difficult to remove, and had lost a little of its water of crystallization, otherwise we believe it quite pure. It gave no appreciable residue upon igniting it on platinum foil, which would indicate the absence of calcium. The last traces of calcium are difficult to remove, and two treatments with hydrochloric acid were required.

Attempts to Prepare Acid Barium Meconate.—This salt requires $Ba(OH)_2 + 2H_3C_7HO_7$. A solution of 24.79 grams of crystallized meconic acid (titrating 106.7 per cent. pure, owing to a loss of some of the crystal water) in about 600 cc. of warm water was added to 400 cc. of a solution of barium hydroxide which was $2.603 \times N/10$. A white crystalline precipitate formed after about one minute. After several hours, yellowish crystals of a different form made their appearance and settled out with the bulk of the precipitate. The precipitated salt, after washing with a little water and drying at 54°, weighed 21.8 grams.[2] The mother-liquor was intensely acid and, after standing, separated some of the same yellowish crystals which

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[1] *Ann. Chem.*, **24**, 43.

[2] The barium actually carried down, according to the formula $BaHC_7HO_7 3H_2O$, should yield 19.96 grams of salt.

were observed above. These crystals were found to be entirely soluble and nothing but pure meconic acid. A titration of a sample of the mother-liquor showed that if the acidity was figured as crystallized meconic acid, it would correspond to 11.07 grams for the whole of the mother-liquor or nearly one-half of the total meconic acid used. On the other hand, the barium in the mother-liquor, determined by weighing as barium sulphate, amounted to only 0.11 gram Ba; hence, the acid must have been present as uncombined acid. Moreover, some of the yellowish crystals, more or less contaminated with the white crystals which constituted the bulk of the precipitate, were picked out of the dried salt and were found to require 9.10 cc. N/10 alkali for neutralization, whereas the barium found corresponded to only 1.48 cc. N/10 $Ba(OH)_2$.

Under the microscope the yellowish and the white crystals were seen to have distinctly different forms[1], hence there is no doubt that meconic acid as such crystallized out with the salt proper and because of its sparing solubility in cold water was not removed by the washing. The salt was now subjected to thorough washing and upon analysis gave the following:

I. 0.500 gram dried at 54° gave 0.2873 gram $BaSO_4$.

II. 0.500 gram dried at 54° gave 0.2380 gram $BaCO_3$.

	Calculated for $BaHC_7HO_7.3H_2O$. Per cent.	Found. I. Per cent.	Found. II. Per cent.
Ba	35.28	33.80	33.12

These values are very close to those obtained for the *neutral* barium meconate described below.

It seems evident that under the conditions of temperature and concentration here used, the salt forming from a mixture of barium hydroxide and meconic acid in proportion of one molecule of base to two molecules of acid is the dibarium meconate represented by the formula $BaHC_7HO_7$, and not a salt containing one equivalent of barium. From a preliminary experiment it seems probable that the acid salt is easily prepared when hydrochloric acid is present[2].

Neutral Calcium Meconate and Barium Meconate.—These salts require $Ca(OH)_2$ (or $Ba(OH)_2$) + $H_3C_7HO_7$. A solution of 3.75 grams of crystallized meconic acid, which had been exactly neutralized with N/10 sodium hydroxide, was added to a solution of

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[1] It was afterwards found possible to get yellowish crystals of the same form from a solution of pure meconic acid in water by sufficiently slow cooling.

[2] We made a similar experiment with calcium and meconic acid. These results we have rejected because of a neglected precaution which negatives their value.

calcium nitrate containing calcium equivalent to 0.837 gram CaO. A finely crystalline white salt formed after about one minute which, dried at about 60°, weighed 4.05 grams. Theory for $CaHC_7HO_7.2H_2O = 4.04$ grams for $3H_2O = 4.31$ grams. The amount of calcium remaining undissolved in the mother-liquor was not determined, hence no correction can be made for the dissolved salt, and this fact perhaps explains the low yield. The salt agitated with cold water gives a neutral reaction with litmus paper. If, however, the water is left in contact for a long time a slight acid reaction develops, and if the salt is boiled with water it becomes yellowish and a strong acid reaction develops in the water. Similarly, if the salt is warmed with excess of decinormal caustic soda it quickly becomes yellowish and the salt loses its crystalline appearance and is converted into a voluminous light yellow precipitate, which resembles the tricalcium meconate. The salt seems to be decomposed by the action of water with the formation of a more basic salt and liberation of acid. Peratoner and Tamburello[1] obtained a salt having the formula $CaHC_7HO_7.4H_2O$, as a *yellowish* crystalline precipitate by adding calcium chloride to a solution of meconic acid exactly neutralized with ammonia. Our salt, on the other hand, was white. We can see no explanation for this other than the possibility that the salt became somewhat basic through the subsequent action of water.

To prepare neutral barium meconate we brought together 400 cc. of a solution of barium hydroxide which, as before, was $2.603 \times N/10$ and a solution of 12.39 grams of crystallized meconic acid (titrating 106.7 per cent. pure, owing to loss of some of the crystal water). These proportions correspond to one molecule of barium to one molecule of crystallized meconic acid. The volume of the solution was diluted up to 1 liter. After about one minute a nearly white crystalline salt separated which, dried at 54° C., weighed 19.77 grams. The mother-liquor reacted faintly acid and contained 0.339 gram Ba as found by precipitating as barium sulphate. The barium actually carried down in the salt is, therefore, 7.153 grams (amount of Ba in 400 cc. $Ba(OH)_2$) — 0.339 = 6.814 grams Ba, and the theoretical yield for this amount of barium based on the formula $BaHC_7HO_7.3H_2O$ is 19.32 grams. One-half gram samples of the 54° dried salt gave for $BaCO_3$ on incineration: I, 0.2396 gram; II, 0.2383 gram; III, 0.2358 gram; IV, 0.2395 gram. Similarly, the one-half gram gave 0.2878 gram $BaSO_4$.

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[1] *Chem. Centrbl.*, 1, 45 (1904).

	Calculated for $BaHC_7HO_7.3H_2O$. Per cent.	Found by weighing $BaCO_3$. I. Per cent.	II. Per cent.	III. Per cent.	IV. Per cent.	Found by weighing $BaSO_4$. I. Per cent.
Ba.........	35.28	33.34	33.16	32.82	33.34	33.86

It should be observed that the percentage of barium agrees well with that found in the washed salt of the previous preparation. In neither case, however, is the percentage of barium as high as the formula requires. The reason is not apparent; it may be that the salt contained hygroscopic moisture which the temperature of 54° failed to remove completely.

Peratoner and Tamburello obtained the salt corresponding to the formula $BaHC_7HO_7.3H_2O$ by precipitating meconic acid exactly neutralized with ammonia with barium chloride.

Neutral barium meconate behaves like the analogous calcium salt with water and sodium hydroxide, splitting off acid and coloring yellow with the formation of basic salt, but the change takes place more slowly than with the calcium salt.

Basic or Tricalcium Meconate and Basic or Tribarium Meconate.—These salts correspond to the proportion of $3Ca(OH)_2$ (or $3Ba(OH)_2$) to $2H_3C_7HO_7$. The calcium salt was prepared first from the lime and the acid and then from calcium nitrate, sodium hydroxide and the acid. Ignited calcium oxide, weighing 1.068 grams, was digested in a closed flask with a little over a liter of water and the clear solution filtered off from some undissolved oxide which, upon ignition, weighed 0.1044 gram. To the clear solution (containing $1.068 - 0.1044 = 0.9636$ gram CaO), we added a solution of 2.91 grams of crystallized meconic acid. At once, a gelatinous light yellow-colored precipitate of great volume formed. On standing, it settled easily but contracted immensely upon drying. The salt is apparently amorphous; under the microscope no crystals are to be seen and there is no effect on polarized light.

One-half gram of the air-dried salt, after drying five days at 60°, ceased to lose moisture and weighed 0.4626 gram. The temperature was raised to about 160° and after drying for three days the weight attained approximate constancy at 0.3816 gram. The salt was discolored yellowish, but only the surface, the inside remaining light yellow.

One-half gram of the air-dried salt upon incineration gave 0.1182 gram CaO.

The same salt was next made by adding a solution of 5.05

grams of crystallized meconic acid, to which three equivalents of sodium hydroxide had been added, to 100 cc. of a solution of calcium nitrate containing calcium equivalent to 1.674 grams CaO. The precipitate resembled the previous one in all respects and after drying at 60° weighed 6.4 grams. After the precipitation, the mother-liquor was slightly acid requiring 1.5 cc. N/10 NaOH[1] and contained calcium equivalent to only 0.1375 gram CaO. The salt, on the other hand, contained only a trace of sodium. It, therefore, cannot be a double salt of calcium and sodium, but must contain three equivalents of calcium.

One-half gram of the air-dried salt was dried at 60° until approximate constancy was attained; the weight was then 0.4802 gram. The same sample was now dried to constancy at about 160° when it weighed 0.3881 gram. Three determinations of the lime in this salt for 0.500-gram samples gave 0.1230 gram, 0.1219 gram, 0.1248 gram. The dried weight of 0.500 gram of the salt, as found above, was 0.3881 gram. The meconic acid was roughly determined in this salt by liberating it with oxalic acid and titrating. Allowance was made for the excess of oxalic acid present since the amount could be calculated from the acid used and the calcium present. The experiment was conducted as follows:

One-half gram of air-dried tricalcium meconate (containing by average of three determinations calcium equivalent to 0.1232 gram CaO) was triturated with 0.300 gram of crystallized oxalic acid and allowed to stand for several hours. The oxalic acid required for 0.1232 gram CaO is 0.2769 gram. The precipitate of calcium oxalate thus formed was free from meconic acid after washing, hence no meconate crystallized out with it, and it was thought that titration of the mixture, without removing the precipitate, would properly determine the meconic acid together with the excess of oxalic acid present. Two trials gave (1) 29.28 cc. and (2) 29.43 cc. N/10 NaOH.[2] The analyses on the two preparations are summarized below:

		Found.			
		Salt from base and acid.	Salt from $Ca(NO_3)_2+3NaOH$.		
	Calculated for $Ca_3(C_7HO_7)_2+6H_2O$.	Per cent.	I. Per cent.	II. Per cent.	III. Per cent.
Ca	19.33	18.27	18.31	18.15	18.58
H_2O	17.36	17.51	19.18	......	......
$H_3C_7HO_7$	64.27	......	61.0	61.3	......

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[1] The calcium nitrate used was slightly acid, requiring for 100 cc. 2.4 cc. N/10 NaOH to neutralize it.

[2] These figures have been corrected for the sodium hydroxide used up by the excess of oxalic acid, 0.2769 gram.

It will be seen that the analyses fall a little short, in respect to calcium and meconic acid, of the formula $Ca_3(C_7HO_7)_2.6H_2O$. The agreement, however, between the theoretical ratio of calcium to meconic acid and the ratio found in the analyses is close, as may be seen from the following:

	Theory.	Found. (Salt from $Ca(NO_3)_2+3NaOH$.)
$\frac{3Ca}{2H_3C_7HO_7}$	0.3008	0.3001 average

Since the salt is a gelatinous, amorphous precipitate which we were unable to purify, owing to its general insolubility, it is doubtful whether any closer agreement could be expected. The remarks on p. 949 in regard to the difficulty of preventing loss in the incineration for calcium oxide should be borne in mind in judging the analyses. The salt probably carries down more than $6H_2O$, since the contraction of the precipitate is very great and the loss upon prolonged drying of the finely powdered salt in the air is considerable, even after the salt is apparently dry. Since the salt seems to have no crystalline structure, it is questionable whether the amount of water is a fixed quantity; moreover, the avidity with which the dried salt takes up moisture makes accurate weighing impossible, and the main difficulty in getting concordant analyses is in the drying of the salt because some temperature must be arbitrarily chosen below which the loss is supposed to be adhering water and not water of constitution.

To prepare basic or tribarium meconate, we brought together in solution 8.263 grams of crystallized meconic acid (titrating 106.7 per cent. purity, owing to loss of some of the crystal water) and 400 cc. barium hydroxide solution which was $2.603 \times N/10$. The reaction-mixture was diluted to 1 liter. A voluminous, flocculent, yellow precipitate fell at once and the mother-liquor was neutral. After standing in the mother-liquor for a week, the yellow precipitate had become crystalline. It should be noted that the tricalcium meconate was allowed to stand similarly but failed to become crystalline. The precipitate after drying for a week at 60° weighed 15.12 grams. A small amount was lost through the tearing of a filter; this is estimated at 0.1 gram, so the true yield was something over 15.2 grams. The mother-liquor contained 0.222 gram Ba (as determined by precipitating $BaSO_4$ and weighing) which would indicate a solubility of about 0.5 gram of tribarium meconate per liter. Calculating the theoretical yield of salt from the amount of barium actually carried down we get 15.37 grams for the formula $Ba_3(C_7HO_7)_2.6H_2O$.

That meconic acid behaves as a tribasic acid towards calcium and barium seems certain from the above work. The salts formed are light yellow, amorphous precipitates, the barium meconate becoming crystalline on long standing in contact with the mother-liquor. Both are only very sparingly soluble in water as in most ordinary solvents. Their composition is expressed approximately by the formulas $Ca_3(C_7HO_7)_2+6H_2O$ and $Ba_3(C_7HO_7)_2+6H_2O$. This, moreover, is nothing unusual, for many organic acids are known which contain, in addition to the carboxyl group, a hydroxyl group, the hydrogen atom of which may be replaced by certain metals. Salicylic acid, for example, forms a calcium salt having the formula $Ca(C_6H_4OCOO)$, analogous to the tricalcium meconate. In fact, it seems strange that we have not been able to find any analyses of the tricalcium and barium salts when the analogous compounds of meconic acid with lead and silver were studied early in the history of the acid and their nature understood. To be sure, they are not very attractive bodies to work on, being slimy precipitates of large volume and varying water content, probably also tending to become basic by the prolonged action of water. Indeed this behavior towards boiling water is one of Dott's[1] arguments in favor of his belief that meconic acid is "dibasic." He found that the percentage of silver in the silver salt increased by boiling the salt with water for several hours. Also that the lead salt prepared under various conditions contained different amounts of lead and drew the inference that these salts were only dibasic salts more or less basic. Later work has shown beyond much doubt that the acid contains two carboxyl groups and in that sense is "dibasic," but that there is also a hydroxyl group with phenolic tendencies to salt formation. We do not consider that the facts mentioned by Dott constitute the slightest objection against granting the tribasic compounds of silver, lead, calcium and barium with meconic acid the rank of true salts. In fact, if the accepted formula for the acid is correct, we should predict just such behavior.

SUMMARY.

In the assay of opium by the U. S. P. 1890 process, a yellowish scaly coating was noticed on the bottom of the flasks which evidently was not morphine. This body was isolated and analyzed.

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[1] *Chem. News*, 1880, p. 576.

It was also prepared artificially and analyzed. The results show it to be a double salt of meconic acid with calcium and ammonium, the calcium coming from the opium and the ammonia being added in the process of assay. Its composition according to our analyses is represented by the formula $CaNH_4C_7HO_7.2H_2O$ or $CaNH_4C_7HO_7.3H_2O$ and it is apparently a perfectly definite salt under the conditions of the assay procedure, namely, the presence of meconic acid, excess of ammonia, and scarcity of calcium. This salt or some similar salt was known to Robiquet, but we have not found any formula assigned to it in the literature.

The importance of the salt in the assay process, lies in the fact that if a precipitate of morphine alkaloid containing it as impurity is titrated with standard sulphuric acid to determine the purity of the morphine, the result is always too high owing to the fact that the calcium ammonium meconate consumes nearly 0.25 as much acid as morphine itself. A table is given showing the magnitude of the error in actual assays.

In this work the question arose as to whether the hydrogen of the hydroxyl group in meconic acid possesses acid properties towards barium and calcium as it does towards silver and lead and perhaps other bases forming insoluble compounds. This is shown to be the case and salts having a composition corresponding approximately to the formulas $Ca_3(C_7HO_7)_2.6H_2O$ and $Ba_3(C_7HO_7)_2.6H_2O$ have been prepared. The amount of water in these salts, however, is uncertain. The statement is made in Gmelin-Kraut's "Handbuch der Organischen Chemie" (1859) and in Fehling's "Handwörterbuch" that "barium meconate" is readily soluble in an excess of barium hydroxide and this is attributed to Liebig. We have not been able to find this statement in the original articles of Liebig on meconic acid. We find that dibarium meconate as well as tribarium meconate are nearly insoluble in a solution of barium hydroxide. We give our analyses and preliminary formulas for these tribasic salts because they are apparently not described in the literature. The dicalcium and dibarium salts have been recently prepared by Peratoner and Tamburello[1] by decomposing meconic acid exactly neutralized with ammonia with calcium and barium chlorides respectively, and are described as *yellow* precipitates having the formulas $CaC_7HO_7.4H_2O$ and $BaC_7HO_7.3H_2O$. We obtained a white calcium salt by decom-

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[1] Peritoner and Tamburello: Abst. in *Centrbl.*, 1, 45 (1904).

posing meconic acid exactly neutralized with sodium hydrate and a white barium salt by mixing solutions of barium hydroxide and meconic acid in the proportion of one molecule of barium hydroxide to one molecule of acid. The analysis of the barium salt for barium and the loss of water on drying correspond fairly well with the above formula. No analyses were made of the calcium salt.

Upon attempting to prepare monobarium meconate by mixing meconic acid and barium hydroxide we obtained a salt identical with the dibarium meconate and free meconic acid remained in the mother-liquor.

Our experience with meconic acid leads us to believe that it titrates quite accurately as a dibasic acid towards N/10 NaOH, using blue litmus paper as indicator outside of the solution.

The various salts of barium and calcium with meconic acid were studied first hand in order to throw light on the composition of the unknown "scale" of the assays. None of the combinations of calcium and meconic acid without ammonia possess the properties characteristic of the "scale," ammonium calcium meconate.

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The stars indicate the publications in which the articles were available to us. Double stars indicate articles with especial reference to salts of meconic acid or bearing upon salt formations. In general, it may be said that the literature before Liebig's discovery in 1833[1] of the true relationship between meconic, comenic and pyrocomenic (synonymous with pyromeconic) acids is of little importance except historically.

Beilstein (Vol. II, p. 2041) gives a reference[2] to an article by Liebig which is incorrect. The reference given is to an article by Blanchet and Sell on an entirely different subject and there is no other article in that volume by Liebig on meconic acid. The above list includes some references to comenic and pyrocomenic acids which were examined for information on the parent acid.

MALLINCKRODT CHEMICAL WORKS,
ST. LOUIS.

[CONTRIBUTION FROM THE DEPARTMENT OF FOOD AND DRUG INSPECTION OF THE MASSACHUSETTS STATE BOARD OF HEALTH.]

THE DETECTION AND DETERMINATION OF ETHYL AND METHYL ALCOHOLS IN MIXTURES BY THE IMMERSION REFRACTOMETER.

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THE USE of wood alcohol in various preparations which come within the domain of the public analyst for examination is apparently on the increase. It is especially to be looked for as an adulterant in medicinal preparations, liniments, tinctures, and in all varieties of flavoring and other extracts high in alcohol. In Massachusetts we have found methyl alcohol in various pharmaceutical preparations, such as tincture of iodine, and in lemon and orange extracts.

Existing methods for the detection of wood alcohol, with one or two exceptions, are extremely unsatisfactory. Most of the older methods such, for example, as the potassium permanganate

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[1] *Ann. Chem.*, **7**, 237.

[2] *Ibid.*, **5**, 286 (1833).