Indeed the water is of no importance and may be left out of the ordinary commercial analysis. From the sugar as given by the saccharimeter, the sugar tester deducts 5 times the weight of the ashes. The result is the *rendement*. If the sugar should be found to be 92 p. c. and the ashes 2.50, the *rendement* would be $92-(2.5\times5)$ $=$ 79 p. c. It is on this number, 79, that the sale of beet sugar is based in all European markets, which is a fact of itself more extraordinary to me than the $\frac{4}{5}$ process. The "coefficient 5," which is generally accepted, is based on nothing but assumptions which have no foundations. Those who are willing to buy and sell by the "coefficient 5" need find no fault with the $\frac{4}{5}$ process.

My attention has been called to a description of the $\frac{4}{5}$ process in Wurtz, *Dictionnaire de Chimie*, III., p. 67. After describing Clerget's process, the author of the article says: "Depuis un certain "temps, pour éviter un dosage aussi long, on employe, dans les "laboratoires, un procédé beaucoup plus simple et qui donne des "résultats à peu près exacts." * * * Then follows a brief description of the $\frac{4}{5}$ process.

THE ESTIMATION OF MORPHINE IN OPIUM.

By J. Howard Wainwright, Ph. B.

As one of the chemists connected with the United States Laboratory at the port of New York, my attention has been in a large measure directed to the assaying of opium, samples of which, from every case entered here, are sent to this laboratory for the estimation of morphine.

The literature upon this subject is very voluminous, probably more so than that relating to the assay of any other drug, and comprises the descriptions of many methods.

The requirements of a method adapted to the work of this Laboratory are, rapidity of manipulation, simplicity of the apparatus and, most important of all, accuracy of results. I have, therefore, undertaken an investigation of this very interesting subject, the purpose of which has been, not to test all of the methods published, but simply to try some of the most general and to compare them in order to find one, or the essential features of one, which best meets the above demands.

There are not many different varieties of opium imported at this port, by far the largest amount being Smyrna or Turkish, occasion-

ally some Persian, and very rarely small amounts of Egyptian and Indian—these latter usually in sample lots. The total number of samples assayed during the year ending December 30th, 1884, was 401, the percentage of morphine being generally between 9 and 15, some few samples of Persian opium yielding as high as 18 per cent, and two or three samples of Symrna yielding less than 9 per cent. As the law prohibits the importation of the drug showing less than this proportion of morphine, such cases as the latter are rare. Assays are made upon samples as they are received from the official drug examiner. When the percentage is over 15 per cent. or under 9, duplicate determinations are invariably made.

The sampling of opium for the morphiometric assay is a matter of great importance, especially when the drug is in the moist commercial condition.

The best method, and the one usually employed for sampling a case, is described by Dr. Squibb in his "Ephemeris," Vol. I., No. 1, as follows :—"About every tenth lump of a case should be sampled by cutting out a cone-shaped piece from the middle of the lump with an ordinary pocket knife. Then, from the side of each cone, a small strip is taken from point to base, not exceeding half a gramme from cones which would average 10 to 15 grammes, and the cone is then returned to its place in the lump. The little strips are then worked into a homogeneous mass by the fingers, and the mass is wrapped in tin foil, moist cloth or paper to prevent drying, until it can be weighed off for assay." This sample obtained from the case should not be less than 100 grammes, and should be sampled down to the convenient weight to be taken for assay. This is quite important, as I have found that the morphine contained in pieces taken from different parts of the same sample lump frequently varies as much as one or more per cent. Also, whilst some opiums may be "worked into a homogeneous mass by the the fingers," as above, in others this will be found very difficult if not impossible, as they may be either too moist and sticky or too hard and dry. I am, therefore, in the habit of sampling the large sample lumps in one of three ways, according to the condition of the drug. If quite moist the ball is flattened out and small portions are taken from every part on the end of a pen knife until the required weight is obtained ; or, whenever possible, a thin section is cut through the middle of the ball, and

from this the sample is taken from around the edges and from the centre, and when the opium is hard and dry, or where great accuracy is required, the ball is broken up in a mortar as finely as possible, weighed and dried, the moisture being determined from the loss in weight. It is then powdered and thoroughly mixed, and the proper quantity weighed off.

The method of assay formerly in use here is, perhaps, the most simple, being little more than a rough estimation of morphine yielding results which are at best only approximate, and not in any way to be relied upon where great accuracy is required. However, as it is extremely simple, and with a little practice, easy of manipulation, it may be worthy of a brief description. Ten grammes of the sample are weighed off into a porcelain mortar and allowed to macerate about twelve hours or over night with 50 c. c. of hot water. It is then thoroughly mixed with the pestle and the mass transferred to a linen or flannel filter of convenient size with as little hot water as possible. The filtrate is allowed to run into a flask, accurately marked at 100 c. c., and when all that will has run through the filter and contents are squeezed between the fingers until most of the extract is expressed, it is then moistened with a little hot water and again expressed as above. This moistening and expressing is repeated until exactly 100 c. c. of extract and washings are obtained. If the extract comes through cloudy, which is sometimes the case, it will have to be refiltered through paper. The paper is then washed, and the extract, then more than 100 c. c. must be concentrated to that volume, or exactly one-half taken. If the extract in the flask is exactly 100 c. c., as it should be, it is well shaken to insure thorough mixture and allowed to stand and settle for about one hour; 50 c. c., representing five grammes, are drawn off with a pipette and transferred to a small beaker, a very slight excess of a solution of equal parts of ammonia and alcohol is added, and the liquid well stirred and allowed to stand over night, when the impure morphine will crystallize out. These crystals (which it will often be found necessary to detach from the sides of the beaker with a small steel spatula) are collected upon a tared filter and washed with a little cold water, applied drop by drop around the edges of the filter, until it runs through almost colorless. The filter and contents are now dried at a temperature not exceeding 100° C, and washed with about 25 c. c.

of ether to remove the narcotine, again dried and then weighed. From repeated experiments 85 per cent. of this weight was found to represent approximately the weight of the morphine.

The only advantage of this method is its extreme simplicity and economy of time. It was originally adopted because of the very great number of samples which then required daily examination. In ordinary cases its disadvantages however were found to be many. It is only applicable to a moist opium, as this is the only one which will yield an extract running clear through the linen or flannel filter. It is also difficult to extract the opium completely in this manner with 100 c. c. of water; at least double that amount is required. This increased volume, however, would involve the necessity of concentrating the liquid, which otherwise would be too dilute, and thus time would be lost. The precipitated morphine (it can hardly be called crystallized) is always very impure and dark colored and requires a great deal too much water to wash it, and always carries with it a large proportion of narcotine which the ether will not remove unless a large quantity is used, and then only imperfectly; the precipitate usually forming large, hard lumps. It is also difficult to remove all the precipitate from the sides of the beaker, which, however, would make no difference if the beaker were tared. The time occupied by this method is ordinarily about 48 hours, and not more than five, or at most eight samples can be conveniently run at the same time. Having used this method for upwards of six months and finding it not at all satisfactory, as something more than a rough assay was desired, I concluded to try some of the various methods published and compare the results obtained.

The method which I have been using for some time past and which leaves little to be desired, is essentially that published in the "*Ephemeris*," by Dr. Squibbs, whose kind permission I have to describe it briefly, with a few comments which may not be amiss.

I have compared this method with the official one of the Pharmacopœia and also with others, upon a specially prepared sample of opium made up from selected specimens which were dried, powdered and thoroughly mixed. In four different parts of this sample the morphine was determined by Dr. Squibbs' method, and the

average of the results obtained was taken as the percentage of morphine.

The following is a brief description of this method of assay, as used in my own practice. It consists of three distinct operations, viz.: 1st. The preparation of the extract. 2d. Separating the morphine therefrom, and 3d. The treatment of the seperated alkaloid.

1st. A convenient weight of the sample (preferably about 10 grammes) is introduced into an ordinary salt mouth vial of about 4 to 6 ounces capacity, fitted with a good cork. About 100 c. c. of *boiling* water is added and the bottle is tightly corked and allowed to stand, after frequent hard shaking, for from 12 to 24 hours. The magma is allowed to settle and the dark extract is decanted upon a filter of convenient size. When most of this extract has run through into a medium sized beaker, from 30 to 50 c. c. of boiling water is added, the bottle is well agitated, and the contents are then transferred to the filter with as little hot water as possible. When all the liquid has drained through the filter it is carefully washed down with a very little hot water, applied drop by drop around the edges, and allowed to drain as much as it will. As soon as the liquid ceases to drop the beaker is replaced by an evaporating dish of about 100 to 150 c. c. capacity, and the contents of the filter are brought back into the bottle by means of a small spatula, and again shaken up with about 50 c. c. of hot water. They are then thrown upon the same filter and are washed completely upon the filter from the bottle, this washing being continued until about 100 c. c. have run through into the dish, or until the washings come through colorless. The dish is now placed upon a water bath and the weak extract evaporated, adding to it from time to time the stronger portion from the beaker, until the whole is concentrated to a volume of about 20 to 25 c. c. The concentrated extract is transferred with as little water as possible, to a 2 ounce Erlenmyer flask, accurately tared and provided with a tight fitting cork, and allowed to cool. It is now ready to be submitted to the second part of the process, viz., the separation of the morphine.

2d. After adding 10 c. c. of 95 per cent. alcohol, the flask is agitated and a volume of ether equal to that of the contents is added, the cork is tightly fitted and the flask well shaken. The cork is now removed, and, before the ether has had time to separate, a

slight excess (about 4 c. c.) of a 10 per cent. solution of ammonia is added. The cork is again replaced and the flask well shaken until crystals of morphine begin to separate. The flask is now set aside in a cool place and the separation of the alkaloid allowed to continue for about 12 hours, when it will be complete. This complete separation may also be accomplished in from half an hour to two or three hours by continuous or frequent agitation.

The alcohol is added in order to permit of the ether mixing readily with the aqueous extract and thereby prevent the separation of narcotine which is readily soluble in this menstruum.

3d. When the separation of morphine is complete the cork is removed from the flask and the upper stratum of ethereal fluid carrying most of the narcotine, etc., is carefully decanted through a tared filter of 9 cm. diameter, without disturbing the dark, watery liquid in the bottom of the flask. Upon this dark liquid is now poured about 20 c. c. more ether which is rinsed around the sides of the flask and the surface of the liquid and is decanted carefully through the filter as before, that remaining being absorbed by means of a strip of blotting paper. The filter is washed down with a little more ether, applied drop by drop around the edges and allowed to dry so that the heavy liquid which is now thrown upon it, together with the morphine, will pass through readily. The crystals remaining in the flask are then washed upon the filter with cold water and the washing continued until the water comes through colorless.

The filter and contents are removed from the funnel, and the edges, having been carefully folded together, are pressed between folds of blotting paper until most of the moisture is absorbed. It is then dried in an air bath (together with the tared flask, if any of the crystals remain adhering to its sides) at a temperature of 100° C., and weighed, the result obtained, after subtracting the tare of the filter (and flask, if it has been found necessary to dry and weigh it), will be the weight of morphine in the sample taken.

Dr. Squibb directs that 1 gramme of these crystals, finely powdered, should be weighed off and treated in a large test tube fitted with a cork, with 10 c. c. of officinal lime water; upon occasional shaking the whole should dissolve, thereby showing the absence of narcotine.

He also says that the filter should be tared both before and after weighing the crystals. This, I think, hardly necessary, as the coloring matter and gumming substances can be washed quite free from the paper and crystals without danger of loss of morphine if the water used is quite cold. I have tried this repeatedly and find that 50 c. c. of water used in washing will not make any great difference in the weight of the morphine.

It is also my experience that the use of *hot* water in making the extract seems to work much better than cold; the final results of the assay, if carefully conducted, being about the same in either case, but the opium can be completely extracted with much less water in the former case, the resulting liquid filters much more readily, and the magma is much easier to wash.

I hope to continue this subject in a future paper describing some results with other methods upon the sample already referred to.