ON THE ESTIMATION OF MORPHINE IN OPIUM.

By Philip Schidrowitz, Ph.D.

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The number of processes for the estimation of morphine in opium is legion. The object of by far the greater number of these processes is either to set up an official standard of analysis, or to attempt the determination of the total quantity of morphine present. The recognised official methods, however unsatisfactory they may be, are obviously important from a conventional and legal point of view. Rigid processes for the estimation of *total* morphine are, in view of the varying composition and

frequent adulteration of opium and of the present state of our knowledge, almost bound to fail.

In the present paper I am not concerned with either of the above-mentioned aspects of the question of opium analysis.

Persian opium is sold and purchased almost entirely on analysis. The price varies with the morphine contents, but it must not be assumed that the value of the opium stands in direct ratio to the percentage of morphine. As a rule, contracts are made on a basis of not less than 10 per cent. of morphine.*

It is obvious, therefore, that the commercial analysis of opium is a very important matter, involving, as it does, the price and the acceptance or rejection of goods to the value of many hundreds of thousands of pounds annually.

The details of the process, according to which, apparently, the greater part of the opium imported at present is assayed, are not known. That is to say, it is an unpublished process. I wish distinctly to say that I have no desire to question or to criticise the propriety of keeping the details of a purely commercial process—a process which may be a valuable business asset—undivulged. The process which I shall describe below was devised solely with the object of ascertaining the commercial value of opium, and with immediate reference to existing commercial conditions and requirements. I think I may say that I have succeeded in attaining this object. I am not, of course, in a position to state that my process gives results identical with those obtained by the unpublished process, for the obvious reason that I have not been able to experiment with the two processes side by side ; but I can say definitely that I have the best reason for believing that my method yields results which are entirely satisfactory from a practical commercial point of view. Incidentally, however, in the course of my work, I was able to obtain a number of figures relating to the analysis of samples by the unpublished process, which are printed below in conjunction with the results obtained from the same batches of opium by my own process. I may say here that the numbers relating to results obtained by the unpublished process were put at my disposal *after* I had recorded my own figures.

The new process is to a certain extent based on the Pharmacopœia Germanica IV. method, but is simpler than the latter, and, owing to the modifications introduced, gives substantially different results. The process is as follows :

Six grammes† of opium (previously roughly powdered) are weighed into a small porcelain dish, 6 c.c. of water‡ are added, and the whole allowed to stand for about fifteen minutes. The contents of the dish are then worked up to an even creamy consistency by means of an agate pestle, and are then transferred (by means of successive small quantities of water) to a 100 c.c. Erlenmeyer flask, the latter having been previously counterpoised. The total weight of opium and water is then made up to 54 grammes. The flask, after corking, is shaken vigorously for five minutes, and is then allowed to stand for one hour, with an occasional brief shaking. The

* For Persian opium.

† No preliminary drying is, as a rule, necessary. If the opium is very wet and of low grade, it is better to dry off part of the moisture at a low temperature (30° to 40° C.), or, preferably, at the ordinary temperature, in a vacuum.

‡ Of course, *distilled* water is employed throughout.

contents are then filtered through a plain filter,* 10 centimetres in diameter, into a second previously counterpoised 100 c.c. Erlenmeyer flask. If the filtrate does not run clear at first it must be returned to the filter. When exactly 42 grammes of filtrate have been collected filtration is stopped. To the 42 grammes of filtrate are then added exactly 2 grammes of a solution of salicylate of soda in water, containing 50 grammes of salicylate per 100 c.c. The whole is then shaken for about half a minute, and thereafter immediately filtered as before. Of the filtrate 36 grammes are collected, and to these are added 15 c.c. of ether, and, after rotating the flask once or twice, 5·2 c.c. of a solution of ammonia, prepared by mixing 17 grammes of ammonia (specific gravity 0·960) with 83 grammes of water. The whole is then vigorously shaken for ten minutes,† and the flask and contents are subsequently kept for twenty-four hours at a temperature of 12° C. After this, as much of the ether as is possible is poured off through a filter 8 centimetres in diameter, 15 c.c. of fresh ether are run into the flask, the latter rotated briskly (but so as to avoid forming an emulsion), and the ether again poured off through the filter. After this the whole of the liquid is poured through the filter, the greater part (roughly two-thirds) of the crystals, however, being retained in the flask. The flask and filter are then washed with three lots of 5 c.c. each of water saturated with ether, and delivered from a pipette. Of each 5 c.c., 3 c.c. are used to rinse the flask, and 2 c.c. are run directly on to the filter. The filter with its contents is removed from the funnel, folded, and gently but firmly pressed between sheets of filter-paper. The filter is then opened, and the greater part of the crystals are returned to the flask. Filter and flask are then placed in an air oven at 55° until dry. It is then perfectly easy to transfer the small quantity of crystals still adhering to the filter to the flask. Subsequently the crystals are dissolved in 25 c.c. $\frac{N}{10}$ H_2SO_4, and the excess of acid titrated with $\frac{N}{10}$ alkali, using methyl orange as an indicator. It is preferable, prior to this titration, to dilute the liquid to roughly 50 c.c., and to fix the end-point by means of the droplet method. The percentage of morphine in the sample is then calculated as follows:

Let x = number of c.c. $\frac{N}{10}$ acid employed, then $x \times 0{\cdot}7575 + \frac{1}{13}\ (x \times 0{\cdot}7575)$ = per cent. morphine.

The following tables give the results obtained by the process described above and by the unpublished process respectively, and from the same lots of opium. I may add that the figures given comprise all the analyses concerning which I was able to institute a comparison between the two processes. The figures are disposed, for the sake of convenience, in four groups, as under:

A. Morphine Percentage, under Nine.

Number.	Author's Process.	Unpublished Process.
1.	7·53	8·40
2.	8·66	8·60
3.	8·90	9·10
4.	8·90	9·00

* I prefer to use C.S. and S. quantitative filters.

† It is essential that the corks with which the Erlenmeyer flasks are provided should fit perfectly. It is well to prepare these corks previously by soaking them for a few hours in water containing a little ether.

B. Morphine Percentage, Nine to Ten.

Number.	Author's Process.	Unpublished Process.
5.	9·00	9·40
6.	9·14	9·00
7.	9·30	9·45
8.	9·32	8·75
9.	9·50	9·50
10.	9·65	10·40
11.	9·68	9·70
12.	9·70	10·10
13.	9·70	9·70

C. Morphine Percentage, Ten to Eleven.

Number.	Author's Process.	Unpublished Process.
14.	10·00	10·10
15.	10·09	10·50
16.	10·27	10·20
17.	10·65	10·10
18.	10·87	11·20
19.	10·90	12·50

D. Morphine Percentage, Eleven to Twelve.

Number.	Author's Process.	Unpublished Process.
20.	11·30	12·00
21.	11·50	11·50
22.	11·63	11·80
23.	11·66	10·75
24.	11·80	12·00
25.	11·82	11·90

The following figures (E) were obtained by the analysis of a group of samples received from a different quarter than those under A to D, and I have the best reason to believe that the agreement of the figures with those yielded by the unpublished process was very good :

E. Author's Process.

Number.	Morphine. Per Cent.
26.	8·10
27.	9·35
28.	9·65
29.	10·24
30.	11·00
31.	11·82

I think it will be admitted that the results obtained by the two processes are in excellent accord. In a very few instances (*e.g.*, Nos. 1, 19, and 23) there are apparently serious differences, but these, I think, are very possibly due to errors in sampling, such errors, as is well known in the trade, being very likely to occur, especially in high-percentage opiums, unless the very greatest care is taken in drawing the sample.

It will be noticed that only in two instances do samples which show more than 10 per cent. by one method yield less than 10 per cent. by the other. In both cases the lower figures were obtained by my process. The average difference between the two methods is as nearly as possible 0·2 per cent., the new process showing the lower result.

I may add that results obtained by another operator using my process were in very good accord with my own, the mean difference being 0·1 to 0·2 per cent. The analyses recorded above only represent a small part of the work which finally led me to the process described. I think it will not be without interest to add a short table recording a few comparative results obtained with different methods at the commencement of my investigation :

F. Results obtained for Same Samples by Different Processes.

Number of Sample.	United States Pharmacopœia.	British Pharmacopœia.	Dietrich.	Loof.	Unpublished Process.
1.	12·51	11·67	10·25	6·98	10·20
2.	10·01	8·75	8·75	5·77	9·35
3.	8·23	7·56	6·75	4·50	8·50
4.	12·35	11·55	10·26	9·41	11·10
5.	10·92	11·66	10·06	7·78	11·35
6.	12·42	11·80	10·27	8·91	9·70

Discussion.

The President (Mr. Fairley) inquired whether the working of the process was affected by the other alkaloids present in opium, and whether it was possible that their influence might account for the large differences between the results given by different methods.

Dr. Schidrowitz replied that he could not say to what extent those differences might be due to the influence of other alkaloids. The various processes, of course, differed very greatly in regard to the media employed, the degree of concentration, and so on, which were known to affect the solubility of the various alkaloids. The question of temperature was also important, and he believed that the satisfactory nature of his results from a practical commercial point of view was partly due to the fact that he advocated a rigid temperature for the crystallization of the morphine. He did not know any other process in which that was done. He had at first thought the Dietrich process to be a good one, but in some cases very large differences had been found (to the extent of nearly 2 per cent. in one case) between its results and those considered to be commercially satisfactory.

Mr. Bevan asked how the results of Dr. Schidrowitz's process agreed among themselves.

Dr. Schidrowitz said that the agreement between duplicate determinations was very satisfactory. The average difference between the results of his own determinations and some he had had made by another operator was only about 0·1 to 0·2 per cent.