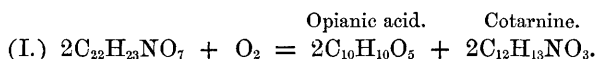


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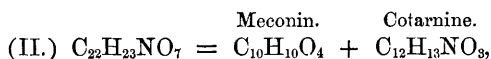
XXVII.—On Narcotine, Cotarnine, and Hydrocotarnine. Part I.

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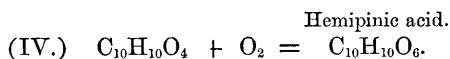
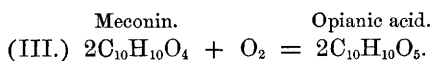
IN the course of a series of experiments on narcotine, commenced originally by the late Dr. A. Matthiessen in conjunction with Prof. G. C. Foster, and concluded conjointly with one of us (*Phil. Trans.*, 1863, 345; 1867, 657; 1869, 661 and 667; *Proc. Roy. Soc.*, xi, 55; xii, 501; xvi, 39; xvii, 337; xviii, 340), it was shown that the formulæ of narcotine and cotarnine are respectively $C_{22}H_{23}NO_7$ and $C_{12}H_{13}NO_3$, and that the production of the latter base, together with opianic acid from the former alkaloid by the action of oxidising agents, may be expressed by the equation—



It also seemed probable that this end result is brought about in two distinct stages, as it was shown that when narcotine is heated with water in a sealed tube to 150° , or even when it is simply boiled with water for a long time, meconin is formed, together with a base resembling cotarnine in its properties, and giving a platinum salt containing nearly the percentage required for cotarnine platinochloride: whence it seemed probable that narcotine first splits up into meconin and cotarnine, in accordance with the following reaction:—



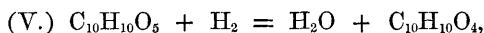
the meconin becoming partly or wholly oxidised to opianic acid (and sometimes to hemipinic acid) if oxidising agents are present, such as ferric or platinic chloride, manganese dioxide and sulphuric acid, nitric acid, &c.; thus—



Blyth and Anderson had previously shown that opianic acid and cotarnine are formed by the action of certain oxidising agents

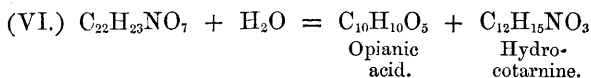
on narcotine, whilst the latter had also obtained meconin by acting on narcotine with nitric acid.

Matthiessen and Foster found, however, that meconin is not directly oxidisable either to opianic or hemipinic acid, a though nascent hydrogen readily reduces opianic acid to meconin, in accordance with the equation—



and further experiments have confirmed this, neither opianic nor hemipinic acid being obtainable from meconin by the action of platinum chloride, ferric chloride, manganese dioxide and sulphuric acid, electrolytic oxygen, permanganate of potassium (acid and alkaline), barium dioxide alone or along with sulphuric acid, potassium dichromate, &c., &c. (Matthiessen and Wright).

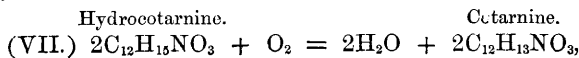
Again, Hesse has recently shown (*Ann. Chem. Pharm.*, Suppt. viii, 261) that in the mother-liquors of opium-working for extraction of alkaloids, there is contained a base called by him *hydrocotarnine*, having the formula $C_{12}H_{15}NO_3$; as he obtained a minute amount of a similar base by the action of baryta-water on narcotine, he concluded that the action of water, &c., on narcotine is probably expressed not by equation (II) but by the following:—



Hesse, however, gives absolutely no numerical values in support of this view, nor does it appear from his paper that he isolated any opianic acid from the product of any such action, nor even that he distinctly proved that the base formed was actually hydrocotarnine. On the other hand, the meconin formed by the action of water on narcotine was analysed by Matthiessen and Wright, as was also the platinum salt of the base simultaneously formed. It does not seem, however, that the details of these experiments had come under Hesse's observation, as he misquotes the names of the authors.

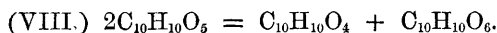
It is, however, not impossible that the base thus formed by the action of water on narcotine may be actually hydrocotarnine, this base resembling cotarnine in many respects, and the percentages of platinum in their platinum salts differing by only 0.11 per cent.

If Hesse's view be correct, the production of opianic acid and cotarnine from narcotine by the action of oxidising agents must take place in the two stages indicated by equation (VI) and the following reaction:—



the sum of these two reactions being that expressed by equation (I), which also expresses the sum of equations (II) and (III).

The production of meconin from narcotine must therefore be brought about either by the reduction of opianic acid to meconin by the decomposition-products of the hydrocotarnine which is mostly destroyed during the action, or by the splitting up of the opianic acid into meconin and hemipinic acid, according to the reaction shown by Matthiessen and Foster to take place when opianic acid is heated with very concentrated potash solution, viz. :—



In order to throw some light on the question as to whether the first action of water and aqueous solutions on narcotine is that indicated by equation (II) as originally supposed by Matthiessen and Wright, or that represented by reaction (VI) as considered probable (but in no way proved) by Hesse, the following experiments were made. Their general result is to show that the latter view is the only one tenable in the present state of our knowledge.

The narcotine employed for these experiments was obligingly presented for the purpose by Messrs. Macfarlan, of Edinburgh, to whom we have already been so much indebted for similar kindnesses.

Conversion of Cotarnine into Hydrocotarnine.

Pure cotarnine was prepared by the process recommended by Matthiessen and Foster, viz., adding gradually and quickly to a boiling solution of 2 parts narcotine in 30 of water and 3 of sulphuric acid, 3 parts of manganese dioxide at 60 per cent. After cooling and standing for some hours, the liquid is filtered from opianic acid that has crystallised out, nearly neutralised with lime-paste, and rendered alkaline with sodium carbonate. The filtrate contains the whole of the cotarnine. Matthiessen and Foster recommend to evaporate this liquid, and after separating from crystals of sodium sulphate, to precipitate the cotarnine by strong caustic potash. We have found, however, that a larger and purer yield is obtained if the alkaline solution be simply precipitated by very strong caustic soda solution without evaporation, as this seems to decompose a portion of the cotarnine. The strongly alkaline liquid thus obtained, after filtering off from the cotarnine, can be neutralised with sulphuric acid, evaporated, allowed to stand for sulphate of sodium to crystallise out, treated again in the same way, and finally again precipitated by caustic soda. A little more cotarnine is thus regained, but it is less trouble to work up this alkaline filtrate into hydrocotarnine by the

method described below. In any case but little substance is thus obtained.

The cotarnine thus precipitated is washed with water, dried, and boiled with benzene; the solution, filtered hot, deposits slightly yellow crystals of cotarnine on cooling, retaining in solution a reddish brown resinous substance and other bye-products. Care should be taken to use benzene of as low boiling-point as possible, as cotarnine readily decomposes when heated to 100° for some time. In this way 100 grams of narcotine yield upwards of 20 grams of recrystallised cotarnine, with from 2 to 5 grams retained along with other substances in the benzene solution, together with some 2 or 3 grams more retained in the potash liquor. The theoretical yield of crystallised cotarnine is 57 grams, wherefore it is evident that much is destroyed by secondary actions. The benzene mother-liquors are best worked up into hydrocotarnine by agitating with hydrochloric acid and treating the impure cotarnine hydrochloride solution thus obtained as described below.

The crystals of cotarnine thus obtained from benzene are almost chemically pure, saving that a trace of colouring matter is present. This can be removed by solution in hydrochloric acid, fractional precipitation by caustic potash, solution in ether, and spontaneous evaporation. Perfectly white crystals are thus obtainable if the original cotarnine has not been overheated; but if a very impure cotarnine be obtained in the first instance, it is excessively difficult to separate all traces of colouring matter.

Whether crystallised from boiling benzene or from ether at 15° , the crystals have the same composition, viz., $C_{12}H_{13}NO_3 \cdot H_2O$. The water of crystallisation cannot be removed without inducing a perceptible amount of decomposition. The pure crystals do not melt in a capillary tube below about 120° (unless kept for some minutes in the hot-bath), but if exposed to a temperature of only 100° for some time they soften and become a viscid fluid, much colour being simultaneously developed. It would thus seem rather as though the water were not merely water of crystallisation, especially as it is not removed by crystallisation from boiling benzene; but this water is not present in the platinum salt dried at 15° over sulphuric acid.

The following numbers were obtained:—

- A. First crystals from benzene, 0.3540 gram gave 0.7885 CO_2 and 0.2160 H_2O .
- B. White crystals from ether, 0.3500 gram gave 0.7815 CO_2 and 0.2100 H_2O .
- C. Ditto, again crystallised, 0.3335 gram gave 0.7430 CO_2 and 0.2020 H_2O .

		Calculated.	A.	Found. B.	C.
C ₁₂	144	60·76	60·74	60·89	60·77
H ₁₅	15	6·33	6·78	6·66	6·73
N	14	5·91			
O ₄	64	27·00			
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C ₁₂ H ₁₃ NO ₃ .H ₂ O	237	100·00			

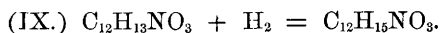
The platinum salt gave the following numbers. No appreciable loss of weight was experienced on heating in the water-oven for many hours if the substance was previously thoroughly dried over sulphuric acid at the ordinary temperature (Matthiessen and Foster could not get constant results with the platinum salt dried at 100°).

0·7575 gram gave 0·1760 Pt = 23·23 per cent.

1·0760 gram gave 0·2505 Pt = 23·28 per cent.

Calculated for (C₁₂H₁₃NO₃.HCl)₂PtCl₄ = 23·23 per cent.

The pure cotarnine thus prepared was dissolved in dilute hydrochloric acid and treated with granulated zinc, enough acid being added from time to time to keep up a just perceptible effervescence; if the liquid be too concentrated, a bulky mass of white crystals separates, consisting of the double zinc-chlorides of cotarnine and hydrocotarnine. This can be avoided by adding enough water, or by gently warming the solution. Too great heat must not be applied, as both cotarnine and hydrocotarnine are easily decomposed at 100°. After two or three days the cotarnine is wholly converted into hydrocotarnine in virtue of the reaction—



The product is poured into a large excess of ammonia, so as to dissolve all zinc hydrate, and the turbid liquid thus obtained well agitated with ether. The ethereal extract thus obtained yields after concentration, and by spontaneous evaporation, fine prisms often an inch in length. These prisms agree in all respects with the hydrocotarnine of Hesse. They are readily soluble in alcohol, ether, and benzene, and can be easily recrystallised from the latter solvents. After repeated recrystallisation they melt at 55°, but if a little impurity be present, the melting-point is lowered some degrees (Hessé found 50°). They lose their water of crystallisation at 60°, forming an oily fluid which does not solidify for a long time after cooling. They give the colour reaction with sulphuric acid described by Hesse (solution with a yellow tint, becoming carmine-red on heating; shortly violet or purple streaks become visible, and finally, by continuing to heat, the whole become a dirty reddish purple).

From 100 parts of crystallised cotarnine about 85 of crude hydrocotarnine are obtainable, 97 being the theoretical yield.

These crystals have the composition $2\text{C}_{12}\text{H}_{15}\text{NO}_3 \cdot \text{H}_2\text{O}$.

0.3015 gram gave 0.6940 CO_2 and 0.1930 H_2O .

	Calculated.		Found.
C_{24}	288	62.61	62.77
H_{32}	32	6.95	7.11
N_2	28	6.09	
O_7	112	24.35	
<hr/>		<hr/>	
$2\text{C}_{12}\text{H}_{15}\text{NO}_3 \cdot \text{H}_2\text{O}$	460	100.00	

0.8560 gram lost at 70° 0.0360 gram = 4.20 per cent.

Calculated. = 3.91 „

0.2965 gram of dried product gave 0.7095 CO_2 and 0.1930 H_2O .

	Calculated.		Found.
C_{12}	144	65.15	65.26
H_{15}	15	6.79	7.23
N	14	6.34	
O_3	48	21.72	
<hr/>		<hr/>	
$\text{C}_{12}\text{H}_{15}\text{NO}_3$	221	100.00	

When this substance was dissolved in dilute hydrochloric acid and allowed to stand over sulphuric acid, a very soluble hydrochloride was formed, having the composition $\text{C}_{12}\text{H}_{15}\text{NO}_3 \cdot \text{HCl} \cdot \text{H}_2\text{O}$. After well pressing in blotting-paper the crystals gave these numbers:—

A. 1.948 gram lost at 100° 0.1380 = 7.08 per cent.

B. Another specimen well drained in the filter-pump, exposed to the air until it ceased to lose weight, being finally triturated to a fine powder—

1.160 gram lost at 100° 0.080 gram = 6.89 per cent.

Calculated .. = 6.53 „

Hesse attributes to the air-dry crystals the formula $\text{C}_{12}\text{H}_{15}\text{NO}_3 \cdot \text{HCl} \cdot 1\frac{1}{2}\text{H}_2\text{O}$, on the strength of one determination only, when the loss of weight was 0.038 gram, representing 9.08 per cent., this formula requiring 9.49 per cent. We have found that the last quantities of interstitial moisture are given off with extreme slowness, unless the crystals be very finely powdered. Thus two specimens which had been exposed to the air for several days and finally dried for some days in a current of dry air, still retained respectively 11.17 and 10.89 per cent. of total moisture. These specimens were not in fine powder.

0.7870 gram of dry substance gave 0.4395 AgCl .

Chlorine. . . = 13.81 per cent.

Calculated .. = 13.78 „

It hence results that cotarnine is readily converted into hydrocotarnine by nascent hydrogen; hence the presence of meconin and hydrocotarnine in opium liquors can be equally well accounted for on either of the two suppositions as to the first decomposition of narcotine; for if equation (II) represent the first action, the cotarnine thereby produced would be converted into hydrocotarnine by the reducing action of organic matters, whilst this same action would cause the conversion of opianic acid into meconin if equation (VI) represented the first action.

In order to prepare pure hydrocotarnine, it is not necessary to purify the cotarnine used. Thus the caustic potash solution from which cotarnine has been thrown down, or the acid impure hydrochloride obtained as above from the benzene mother-liquors of cotarnine crystallisation can be employed, enough acid to generate hydrogen slowly with zinc being added, and the whole allowed to stand either at the ordinary temperature or at a gentle heat for two or three days, acid being added from time to time to keep up the evolution of hydrogen. Finally a large excess of ammonia is added, and the whole agitated with ether. In case only small quantities of hydrocotarnine have to be dealt with, recrystallisation from ether or benzene is difficult on account of the great solubility. In this case, or if an impure hydrocotarnine be obtained which will not crystallise readily, the base should be converted into hydrochloride by adding hydrochloric acid, leaving it to stand over sulphuric acid until it is converted to a rather thick magma of crystals. If these be well pressed in blotting-paper, dissolved in water, and treated with ammonia and ether, the hydrocotarnine crystallises readily from the ethereal solution by spontaneous evaporation. It is not even necessary to separate cotarnine at all from the product of the action of sulphuric acid and manganese dioxide on narcotine. The filtrate from the opianic acid, when treated with zinc and acid, yields a considerable quantity of nearly pure hydrocotarnine, the yield being in this case slightly increased from the circumstance that hydrocotarnine is formed in small quantities during the decomposition of the narcotine in this way, but is for the most part separated by carbonate of soda, and is therefore retained in the sulphate of calcium, &c., precipitate obtained by the above-described method of preparing cotarnine. What little is retained by the sodium carbonate is wholly separated from the cotarnine by crystallisation from benzene, the difference of solubility in the menstruum being very great.

This calcium sulphate precipitate was examined on several occasions, and *was uniformly found to contain hydrocotarnine*. This can be extracted by boiling the dried precipitate with alcohol, filtering, boiling off the alcohol, dissolving the residue in dilute hydrochloric acid,

precipitating with ammonia, and treating with ether. If sufficiently large quantities of narcotine have been dealt with in the first instance, hydrocotarnine crystallises from the ether by spontaneous evaporation; if only a syrupy residue is left, this can usually be made to crystallise by leaving a small crystal of hydrocotarnine in contact with it, or it can be converted into hydrochloride and so purified.

The crystallised hydrocotarnine thus extracted melted at 52° , and gave these numbers—

0.3145 gram gave 0.7235 CO_2 and 0.2015 H_2O .

	Calculated.	Found.
Carbon	62.61	62.73
Hydrogen	6.95	7.12

From 100 grams of narcotine from 2 to 5 grams of crude but nearly pure hydrocotarnine are thus obtainable.

It hence appears that hydrocotarnine is a normal product of the oxidation of narcotine by manganese dioxide and sulphuric acid. Hence reactions (II) and (III) cannot express the change undergone by the narcotine: for, independently of the circumstance that reaction (III) does not take place with meconin (when not nascent), it cannot be supposed that oxidation of meconin to opianic acid and reduction of cotarnine to hydrocotarnine can go on simultaneously in the same liquid containing oxidising materials.

This production of hydrocotarnine during the oxidation of narcotine by manganese dioxide and sulphuric acid was observed by Matthiessen and one of us some years ago, but the body was then supposed to be simply cotarnine with only half the usual amount of water of crystallisation, and was described as such in *Phil. Trans.*, 1869, 667. The substance thus obtained, separated from the sodium carbonate solution of cotarnine obtained, as above described, on standing. Unfortunately the note-books containing the details of these and numerous other experiments were lost at Dr. Matthiessen's decease.

The crystals not only contained the amount of water of crystallisation appropriate to hydrocotarnine (found, 4.16 per cent.; calculated, 3.91 per cent.), but also melted below 60° , were partially volatile on continued heating at 100° , and were very readily soluble in cold alcohol and ether. As shown (*loc. cit.*), the platinum salt contained 23.08 and 23.00 per cent. of platinum, cotarnine platinochloride requiring 23.23 per cent., and hydrocotarnine platinochloride 23.12 per cent.

Action of Oxidising Agents on Hydrocotarnine.

Pure hydrocotarnine was boiled with 15 parts of water, $1\frac{1}{2}$ of sulphuric acid, and $1\frac{1}{2}$ of manganese dioxide (the proportions used in the

preparation of cotarnine from narcotine), the last ingredient being quickly added whilst boiling. A large amount of effervescence was thus occasioned, and the liquid became very dark in colour. After cooling, the acid was nearly neutralised by slacked lime, and excess of carbonate of soda added. The filtrate yielded with strong caustic soda solution a precipitate consisting of cotarnine with much tarry colouring matter: after two crystallisations from benzene nearly pure cotarnine was isolated from this substance.

0.2965 gram gave 0.6630 CO_2 and 0.1790 H_2O .

	Calculated.		Found.
C_{12}	144	60.76	60.98
H_{15}	15	6.33	6.71
N	14	5.91	
O_4	64	27.00	
$\text{C}_{12}\text{H}_{13}\text{NO}_3 \cdot \text{H}_2\text{O}$	237	100.00	

The product exhibited all the properties of cotarnine and was evidently that body: hence it is manifest that the action of sulphuric acid and manganese dioxide on narcotine is precisely that which would be anticipated if that action takes place in accordance with reactions (VI) and (VII), *i.e.*, the hydrocotarnine first formed by reaction (VI) instantly becomes almost wholly (though not altogether) converted into cotarnine and tarry decomposition-products.

Ferric chloride acts on hydrocotarnine in the same way, a much purer product being, however, obtained in the first instance. When hydrocotarnine is boiled for four or five hours with a large excess of very slightly acid ferric chloride, much ferrous chloride is formed, and almost complete dehydrogenization ensues. On adding excess of sodium carbonate to the liquid, filtering, concentrating by evaporation after slightly acidulating with sulphuric acid, and finally precipitating by strong caustic soda solution, a crystalline precipitate is obtained which furnishes almost perfectly pure cotarnine after one crystallisation from benzene.

0.2955 gram gave 0.6575 CO_2 and 0.1760 H_2O .

	Calculated.	Found.
Carbon	60.76	60.68
Hydrogen	6.33	6.62

Cotarnine can also be obtained from hydrocotarnine by treating a solution of the base in excess of dilute sulphuric acid with its own weight of potassium dichromate. In the cold no action takes place immediately, but on standing, the liquid becomes green. On adding

ammonia and filtering, an alkaline liquid is obtained from which cotarnine can be extracted by agitation with ether. If the original solution be not dilute, a precipitate of hydrocotarnine chromate is formed, which is not readily acted on. Heating the acid liquid greatly quickens the action.

Action of Nascent Hydrogen on Narcotine.

20 grams of narcotine were heated to boiling with two litres of dilute hydrochloric acid and granulated zinc for four days (about eight hours' gentle boiling each day). Ammonia in excess was then added and the whole strained through coarse calico. The filtrate yielded to ether a perceptible amount of hydrocotarnine melting, at 54.5° . After drying at 60° this product gave the following numbers:—

0.3085 gram gave 0.7390 CO_2 and 0.1920 H_2O .

	Calculated.		Found.
C_{12}	144	65.15	65.31
H_{15}	15	6.79	6.91
N	14	6.34	
O_3	48	21.72	
<hr/> $\text{C}_{12}\text{H}_{15}\text{NO}_3$	<hr/> 221	<hr/> 100.00	

The ammonia precipitate was dissolved in hydrochloric acid and treated with ether. A small quantity of meconin, easily recognised by its physical characters (especially its melting under boiling water), was thus extracted, but no opianic acid. Nothing but unaltered narcotine could be obtained from the products of the reaction, whence it seems probable that narcotine, unlike cotarnine, does not take up nascent hydrogen, forming an additive compound.

The production of meconin and hydrocotarnine in this way is, as above stated, equally consistent with either reaction (II) or (VI) as the first action.

Action of Boiling Baryta-water on Narcotine.

Narcotine was boiled with enough baryta-water to give a clear solution when hot for varying periods, an inverted condenser being attached. Methylamine was evolved, and more or less barium carbonate formed according to the duration of the boiling. The product was examined for meconin, opianic acid, cotarnine, and hydrocotarnine in the following way. Sulphuric acid was added to the cooled liquid in slight excess, and the filtrate was agitated with ether. In each case meconin was dissolved out, but no trace of opianic acid. Ammonia in excess was then added, and the filtrate again treated with

ether. No trace of either cotarnine or hydrocotarnine could be detected in any of these experiments in which from 20 to 50 grams of narcotine were boiled for 8, 24, and 200 hours consecutively respectively. Hesse obtained from the product of the action of baryta-water a minute amount of a base resembling hydrocotarnine, and the experiments described below render it highly probable that hydrocotarnine is really formed thus; but apparently the baryta-water decomposes it more quickly than does ordinary water.

The meconin thus obtained presented all the physical characters of ordinary meconin, and gave the following numbers:—

0.3245 gram gave 0.7375 CO₂ and 0.155 H₂O.

	Calculated.		Found.
C ₁₀	120	61.86	61.98
H ₁₀	10	5.15	5.31
O ₄	64	32.99	
<hr/> C ₁₀ H ₁₀ O ₄	<hr/> 194	<hr/> 100.00	

In one experiment hydrochloric acid was used to neutralise the baryta-solution, and from the acid liquid crystals of narcotine hydrochloride separated on standing, containing C₂₂H₂₃NO₇.HCl.4H₂O. This lost 3½ H₂O only on drying in the water-oven till constant in weight.

2.564 grams lost at 100° 0.3140 gram = 12.25 per cent.

Calculated for loss of 3½ H₂O..... 12.08 „

0.3240 gram dried at 100° till constant gave 0.6810 CO₂ and 0.1740 H₂O.

0.6130 gram gave 0.1890 AgCl.

	Calculated.		Found.
C ₂₂	264	57.58	57.32
H ₂₅	25	5.45	5.96
Cl.....	35.5	7.74	7.63
N.....	14	3.05	
O _{7½}	120	26.18	
<hr/> C ₂₂ H ₂₃ NO ₇ .HCl.½H ₂ O	<hr/> 458.5	<hr/> 100.00	

Action of Water on Narcotine.

The former experiments of Matthiessen and Wright were repeated, careful search being made in the products of the action for meconin, opianic acid, hemipinic acid, cotarnine, and hydrocotarnine. Narcotine was heated in sealed tubes to 140°—150° for several hours, with as much water as would well cover it, the tubes being cooled

every seven hours or so, and well shaken up before heating again. After 21 to 28 hours' heating almost all the narcotine was converted into other products. The quantity of meconin formed amounted in one experiment to rather over 20 per cent. of the narcotine used, whilst the theoretical yield for equation (II) would be 47 per cent. With less heating, smaller percentages only were formed. No trace of either opianic acid or hemipinic acid could be detected, which seems to indicate at any rate that the meconin did not result from the decomposition of the opianic acid formed in virtue of reaction (VI), in accordance with the reaction of Matthiessen and Foster (VIII).

If the action be prolonged so far that all the narcotine is converted, it is impossible to extract any appreciable quantity of either cotarnine or hydrocotarnine from the product of the action; but if only six or seven hours at 140° have been allowed, a minute amount of the base formed escapes further change; by dissolving the contents of three tubes (representing altogether about 15 grams of narcotine) in dilute hydrochloric acid, agitating with ether to remove meconin, rendering alkaline with ammonia, straining, and treating the filtrate with ether again, a few centigrams of *hydrocotarnine* were dissolved out. This was purified by dissolving in acid and treating a second time with ammonia and ether. Finally crystals were obtained identical in form and properties with hydrocotarnine, melting at a little above 50° , and yielding a platinum salt of which

0.1050 gram gave 0.0245 platinum = 23.33 per cent.

Calculated for hydrocotarnine platino-chloride, 23.11 per cent.

It hence appears that Matthiessen and Wright were incorrect in supposing that the base formed during this reaction is cotarnine; but the mistake is easily understood when it is remembered that hydrocotarnine was unknown when their experiments were carried out, and that the two bases are similar in many respects, whilst their platinochlorides differ only by 0.11 per cent. in percentage of platinum.

The meconin formed during the action gave the following numbers:—

0.2640 gram gave 0.5985 CO_2 and 0.1270 H_2O .

	Calculated.	Found.
Carbon	61.86	61.83
Hydrogen	5.15	5.34

These experiments, therefore, like some of the preceding ones, show that when narcotine splits up under the influence of water at a high temperature, nothing but meconin and hydrocotarnine can be isolated from the products. As above shown, this result is equally compatible

with reactions (II) and (III) or (VI) and (VII) as expressions of the changes that take place, the bye-products in either case acting as reducing agents.

On the whole, therefore, the foregoing experiments show that whilst some of the reactions and decompositions of narcotine are not inconsistent with reactions (II) and (III), others are not at all in harmony with these equations; whilst, on the other hand, reactions (VI) and (VII) are perfectly in accordance with all the facts known as yet. The only circumstance which even appears to contradict this view is Anderson's production of meconin from narcotine by means of nitric acid. Although this meconin cannot be supposed to be formed from opianic acid by a reducing action in this case, yet it may readily be supposed to be formed from opianic acid in virtue of reaction (VIII) (splitting up into meconin and hemipinic acid), since Matthiessen and Foster have shown that this reaction can take place under certain circumstances, whilst hemipinic acid was found by Anderson to be one of the products of the action.

APPENDIX.—*On the Physiological Action of Cotarnine and Hydrocotarnine.*

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As the result of a few preliminary experiments on this subject, a well-marked difference has been established in the action of these two bases on different animals. Cotarnine was given (by subcutaneous injection of known weights of a base dissolved in just sufficient hydrochloric acid) to several kittens and rabbits, without producing the slightest noticeable effect, even in doses up to 5 decigrams. On the other hand, equivalent quantities of hydrocotarnine given similarly to animals of the same sizes and ages, produced marked results. Doses of $2\frac{1}{2}$ to 5 decigrams produced in kittens, rabbits, and guinea-pigs rapid and well-marked tremors, passing into severe epileptiform convulsions, accompanied apparently by more or less affection of the sensory organs. Great muscular prostration and salivation ensued. With kittens a dose of 0.5 gram proved fatal in ten minutes; with a guinea-pig the same result ensued with half that dose. 0.5 gram, however, did not kill a full-grown rabbit, the symptoms being somewhat less severe (though identical in kind) than those in the other cases (owing to the larger size of the animal?).

It hence results that the addition of hydrogen to cotarnine converts a base which is apparently inert into a very active substance, the change in physiological action being far more striking even than the alteration brought about in the physical and chemical properties.