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CLX.—*Contributions to our Knowledge of the Aconite Alkaloids. Part XVII. Bikhaconitine, the Alkaloid of Aconitum Spicatum.*

By Wyndham Rowland Dunstan, F.R.S., and Albert Edward Andrews, Salters' Company's Research Fellow.

This new and highly toxic alkaloid has been obtained from the roots of a supposed variety of *Aconitum ferox* known as "spicatum," and also from another variety of *Aconitum ferox* provisionally named "flavidiflorum," which were collected for the Imperial Institute in Darjeeling under the supervision of Sir George Watt, who has provided the following description of the supposed variety for which Brühl proposed the name "spicatum."

"This aconite is very possibly the true Nepal aconite or Bikh of European pharmacy. It is the plant alluded to by Sir Walter Elliot as the *atívisha* (very poisonous) of Sanskrit authors. In most languages of India it is simply denoted by *bish* or *bikh* (poison).

"Bikh is the most plentiful and extensively used aconite in India, although it would appear to be employed more as a poison than as a drug. Its poisonous property is universally recognised, although the root is derived almost exclusively from Garhwal, Nepal, Sikkim, and Bhutan. The roots are large, thick, when fresh soft, flexible, and pale greenish-white, but when quite dry they become hard and of a dark brown or black colour externally. The half dry root, when cut, resembles horn in consistence, but as it matures and dries it becomes hard and has darker portions developed as imbedded irregular patches within the tissue. These patches somewhat resemble resin in cleavage. The fibro-vascular bundles are seen to form an irregular, sharply-pointed, star-shaped structure, which encloses a small central core surrounded by a second circular ring of fibro-vascular bundles."

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A further examination of this plant by Dr. Otto Stapf, of Kew, has led to the conclusion that it is not a variety of *Aconitum ferox*, but a new species of aconite for which he proposes the name *Aconitum spicatum*.

We believe that Sir George Watt is mistaken in stating that this plant furnishes the Nepal aconite of European pharmacy, since various specimens of roots purchased in Europe have been shown to furnish a distinct alkaloid, pseudaconitine.

The alkaloid contained in the roots of *Aconitum spicatum* has been isolated and examined both as regards its chemical composition and its physiological action. The results now recorded show that, whilst it differs in composition and properties from the other known aconitines, it is closely related to pseudaconitine (Trans., 1897, **71**, 350) both in its chemical properties and physiological action. For this alkaloid we propose the name bikhaconitine, from the vernacular name for the plant, "bikh."

Extraction of the Alkaloid.

The method employed for the separation of the alkaloid from the roots was the same, with slight modification, as previously described in the paper on indaconitine obtained from *Aconitum chasmanthum*.

The roots were finely ground and extracted at the ordinary temperature with a mixture of methyl and amyl alcohols. The methyl alcohol was completely separated from the percolate by distillation under reduced pressure, and the alkaloid removed from the residual portion (consisting of the extractive matter in amyl alcohol) by repeatedly shaking with water and separating the aqueous liquid. It was unnecessary to use dilute acid for this purpose as the aqueous extract had a decided acid reaction. It was found to facilitate greatly the separation of the alkaloid if, before shaking with water, the amyl alcohol was mixed with about an equal volume of ether.

The aqueous liquid containing the alkaloid was shaken with ether to remove any ether soluble substances, then made alkaline with dilute ammonia and the alkaloid extracted with ether, each successive portion being washed with water and then dried over a few pieces of fused calcium chloride before distilling the solvent. The relatively small portion of alkaloid not extracted by ether was removed from the aqueous liquid with chloroform.

The weight of the ether-soluble alkaloid represented approximately 0·6 per cent. of the undried roots taken, and of this about two-thirds was obtained as crystalline bikhaconitine. The remaining third could not be crystallised, but by hydrolysing it and crystallising the alkaloid thus obtained, it was proved that the original material must have consisted largely of bikhaconitine with probably some of its

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hydrolytic product, veratroylbikhaconine, the presence of which would interfere with its crystallisation.

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Properties of Bikhaconitine.

Bikhaconitine does not crystallise with the readiness usually so characteristic of the "aconitines."

Its purification was accomplished by fractional precipitation and then crystallisation of the least coloured portions by adding water to the solution in alcohol. The base thus obtained was finally purified by preparing a pure salt, preferably the hydrobromide, and regenerating the base from this salt.

A peculiar property of bikhaconitine and one which distinguishes it from all other aconitines is the manner in which it crystallises, especially from ether. From this solvent, it separates as white, semi-spherical or button-shaped masses, which as a rule do not appear distinctly crystalline, but are composed of concentric rings of the substance. The gradual addition of water to an alcoholic solution affords the most ready means of crystallisation, when the alkaloid is obtained in white granules consisting of a hydrate which loses its molecule of water at 100°.

0·6143 gram dried at 100° lost 0·0165 gram. Loss = 2·68.

$C_{36}H_{51}O_{11}N,H_2O$ requires $H_2O = 2{\cdot}60$ per cent.

The melting point of bikhaconitine is indefinite and somewhat variable, as the water it contains cannot be removed without the alkaloid undergoing fusion. Crystallised from alcohol and water and dried at 85°, it softens and melts at 113—116°. When crystallised from ether, it melts at a rather higher temperature, namely, 118—123°. The fusion is unaccompanied by decomposition. Bikhaconitine is readily dissolved by ether, alcohol, or chloroform, but is practically insoluble in water or light petroleum.

Specific Rotation of Bikhaconitine.

The following results were obtained with Laurent's half shadow polarimeter, using an alcoholic solution of the alkaloid dried at 100°.

(i) observed angle (a) = +39·5′ at 20°; length of tube (l) = 2 dcm.; concentration (c) = 2·6472; whence $[\alpha]_D^{20°} + 12{\cdot}43°$.

(ii) a = +37′ at 20°, l = 2 dcm., c = 2·572; whence $[\alpha]_D^{20°} = 11{\cdot}99°$.

Mean $[\alpha]_D^{20°} = +12{\cdot}21°$.

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Composition of Bikhaconitine.

The base, crystallised from alcohol and water and dried at 100° was burnt in oxygen, the tube being packed with cupric oxide and a silver spiral.

(i) 0·1695 gave 0·3976 CO_2 and 0·1167 H_2O. C = 63·97 ; H = 7·65.
(ii) 0·1883 ,, 0·4414 CO_2 ,, 0·1288 H_2O. C = 63·93 ; H = 7·60.
$C_{36}H_{51}O_{11}N$ requires C = 64·14 ; H = 7·65 per cent.

These two results were obtained with specimens of pure bikhaconitine, each of which had been separately extracted from the roots and purified. It is therefore clear that the material thus prepared is pure.

The nitrogen in bikhaconitine was determined by Dumas' method. In the hydrated base :

(i) 0·3378 gram gave 9·46 milligrams of nitrogen. N = 2·8.
(ii) 0·2550 ,, ,, 6·86 ,, ,, N = 2·69.
$C_{36}H_{51}O_{11}N,H_2O$ requires nitrogen = 2·03 per cent.

The number of methoxyl groups in the alkaloid, dried at 100°, was determined by Zeisel's method slightly modified.

(i) 0·2225 gave 0·4565 AgI. CH_3O = 27·1.
(ii) 0·1897 ,, 0·3909 AgI. CH_3O = 27·21.
$C_{30}H_{33}O_5N(CH_3O)_6$ requires CH_3O = 27·64 per cent.

Salts of Bikhaconitine.

The salts of bikhaconitine crystallise well. The haloid salts are soluble in water or alcohol, but insoluble in ether and light petroleum.

Bikhaconitine hydrobromide, prepared by dissolving the base in dilute hydrobromic acid to neutrality, crystallises from water if the aqueous solution is evaporated to a syrup and then well stirred. By allowing a warm saturated alcoholic solution to cool, crystals are readily deposited, or the salt may be fractionally crystallised by the addition of ether to an alcoholic solution.

Bikhaconitine hydrobromide melts at 173—175° if dried at 100° and introduced into the bath previously heated to 120°.

When heated at 100°, the crystalline salt loses weight equivalent to five molecules of water or two of alcohol.

0·5872 heated at 100° lost 0·0603. Loss = 10·27.
$C_{36}H_{51}O_{11}N,HBr,5H_2O$ requires $5H_2O$ = 10·66 per cent.
$C_{36}H_{51}O_{11}N,HBr,2C_2H_6O$ requires $2C_2H_6O$ = 10·87 per cent.

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An aqueous solution of bikhaconitine hydrobromide is lævorotatory. The following results were obtained with independently prepared specimens of the anhydrous salt.

1. $\alpha^{16°} = -0{\cdot}75°$, $l = 2$ dcm., $c = 3{\cdot}0291$; whence $[\alpha]_D^{16°} = -12{\cdot}38°$.
2. $\alpha^{15°} = -52{\cdot}3'$, $l = 2$ dcm., $c = 3{\cdot}4928$; whence $[\alpha]_D^{15°} = -12{\cdot}46°$.

Mean $[\alpha]_D = -12{\cdot}42°$.

The bromine in the anhydrous salt was estimated by precipitating and weighing as silver bromide.

1. 0·5961 gave 0·1466 AgBr. Br = 10·46.
2. 0·7305 ,, 0·180 AgBr. Br = 10·48.

$C_{36}H_{51}O_{11}N,HBr$ requires Br = 10·59 per cent.

Bikhaconitine hydrochloride is prepared in the same manner as the hydrobromide. It has not been crystallised from water, but only from alcohol and ether. The fact of this salt being crystalline sharply distinguishes it from the corresponding salt of pseudaconitine, which has not been crystallised (Trans., 1897, 71, 354).

Bikhaconitine hydrochloride, like the hydrobromide, crystallises with five molecules of water or two of alcohol.

0·8207 dried at 100—105° lost 0·0922. Loss = 11·23.

$C_{36}H_{51}O_{11}N,HCl,5H_2O$ requires $5H_2O = 11{\cdot}26$ per cent.

$C_{36}H_{51}O_{11}N,HCl,2C_2H_6O$ requires $5C_2H_6O = 11{\cdot}47$ per cent.

The chlorine in the hydrated salt was estimated volumetrically.

0·3211 required 4·05 c.c. of standard silver nitrate solution (1 c.c. = 0·00351 Cl); whence Cl = 4·42.

$C_{36}H_{51}O_{11}N,HCl,5H_2O$ requires Cl = 4·43 per cent.

Bikhaconitine hydrochloride (anhydrous) melts at 159—161°.

An aqueous solution of the salt is lævorotatory. The anhydrous salt in water gave the following results :

$\alpha^{20°} = -0{\cdot}37'$, $l = 2$ dcm., $c = 3{\cdot}48$; whence $[\alpha]_D^{20°} = -8{\cdot}86°$.

Bikhaconitine hydriodide is prepared by adding potassium iodide solution to an aqueous solution of bikhaconitine hydrobromide. Unless the solutions are dilute, the hydriodide separates at once in a crystalline condition.

The crystalline salt dissolves with difficulty in alcohol or water, but may be recrystallised from either solvent by allowing a hot saturated solution to cool, when it separates as a mass of fine needles. The salt gradually decomposes in presence of organic solvents; for this reason it is preferable to crystallise it from water.

Bikhaconitine hydriodide crystallised from water loses weight when dried at 105°, thus :

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1. 0·6267 dried at 105° lost 0·0363. Loss = 5·79.
2. 0·2955 ,, 105° ,, 0·0171. Loss = 5·78.

$C_{36}H_{51}O_{11}N,HI,2\frac{1}{2}H_2O$ requires $2\frac{1}{2}H_2O = 5·31$ per cent.

The salt, when dried at 105°, melts at 193—194°.

Bikhaconitine nitrate is an easily crystallisable salt. It separates from alcohol as needles which, after drying at 100°, melt at 178—180°.

Bikhaconitine aurichloride is prepared by adding an aqueous solution of auric chloride to bikhaconitine dissolved in slight excess of dilute hydrochloric acid. The salt, which separates as a bright yellow, granular precipitate, is filtered, washed with water, and dried in a vacuum. The aurichloride thus obtained is easily soluble in chloroform, slightly in alcohol, but practically insoluble in water, ether, or light petroleum. It crystallises readily by adding either alcohol, ether, or light petroleum to its solution in chloroform, and is thus obtained as small, canary-yellow needles uncombined with any solvent. It melts sharply at 232—233°.

Owing to the slight solubility of bikhaconitine aurichloride in alcohol and water, it could not be satisfactorily decomposed by sulphuretted hydrogen when held in suspension in either of these liquids. It was therefore necessary in analysing the gold salt to dissolve it in chloroform, add water, and pass through the liquids a brisk current of sulphuretted hydrogen. The aqueous portion was then decanted through a filter and the chloroform, after being washed with water by decantation, was allowed to evaporate spontaneously. The precipitate after being finally washed was ignited and the metallic gold weighed.

The filtrate and washings were freed from sulphuretted hydrogen by a current of air and the chlorine estimated volumetrically.

0·5068 gave 0·0981 Au, and required 20·1 c.c. of silver nitrate solution (1 c.c. = 0·00351 Cl); whence Au = 19·35; Cl = 13·92.

$C_{36}H_{51}O_{11}N,HAuCl_4$ requires Au = 19·45; Cl = 13·99 per cent.

The combustions of the aurichloride were made in a tube packed with fused lead chromate and cupric oxide; a silver gauze spiral was also employed and the burning conducted in a current of oxygen.

(1) 0·2697 gave 0·418 CO_2 and 0·1219 H_2O. C = 42·27; H = 5·02.
(2) 0·2832 ,, 0·4408 CO_2 ,, 0·1305 H_2O. C = 42·45; H = 5·12.

$C_{36}H_{51}O_{11}N,HAuCl_4$ requires C = 42·62; H = 5·18 per cent.

Physiological Action of Bikhaconitine.

Like the other aconitines, bikhaconitine produces in excessively dilute solution the characteristic tingling sensation on the tongue.

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The physiological action of bikhaconitine has been described in a paper communicated to the Royal Society (Cash and Dunstan, *Proc. Roy. Society*, 1905, B, **76**, 468). The alkaloid is found to agree very closely with pseudaconitine, whilst in its general action it resembles that of the entire aconitine group.

The toxicity towards warm-blooded animals is greater than that of either aconitine or japaconitine and is referable to the greater depression of the respiratory function caused by bikhaconitine than by the other two alkaloids.

Grouping these alkaloids according to their relative toxicity, bikhaconitine occupies a position between japaconitine and pseudaconitine, the last of these being the most active of the series.

Hydrolysis of Bikhaconitine.

Bikhaconitine resembles pseudaconitine (Trans., 1897, **71**, 356) in containing both an acetyl and a veratroyl group, the separation of which may be effected in two stages according to the equations:

i. $\underset{\text{Bikhaconitine.}}{C_{36}H_{51}O_{11}N} + H_2O = \underset{\text{Veratroylbikhaconine.}}{C_{34}H_{49}O_{10}N} + \underset{\text{Acetic acid.}}{C_2H_4O_2}.$

ii. $\underset{\text{Veratroylbikhaconine.}}{C_{34}H_{49}O_{10}N} + H_2O = \underset{\text{Bikhaconine.}}{C_{25}H_{41}O_7N} + \underset{\text{Veratric acid.}}{C_9H_{10}O_4}.$

The reaction represented by the first equation is best conducted by the method usually adopted with these alkaloids. In the present case, a neutral aqueous solution of bikhaconitine sulphate was heated in a closed tube at 130° for about seven hours. The veratroylbikhaconine thus produced is precipitated with dilute ammonia and extracted with ether.

The acetic acid also formed was estimated in conjunction with the veratric acid which results from the complete hydrolysis of bikhaconitine (p. 1644). It will be seen that the veratric acid and the alkaloid (bikhaconine) were completely extracted from an aqueous liquid which then contained the acetic acid only. This was estimated by distillation into a known volume of standard alkali, the excess of which was titrated with standard acid, using phenolphthalein as indicator.

By this method the percentage of acetic acid found was 9·24 per cent. The above equation requires 8·91 per cent. acetic acid. The identity of the acid was established by its qualitative reactions and the analysis of the silver salt, which was found to contain 64·45 per cent. of metal. Silver acetate contains 64·66 per cent. of silver.

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Veratroylbikhaconine.

This alkaloid was purified by preparing the aurichloride, as this salt readily crystallises and affords the best means of separating any unaltered bikhaconitine that may be present.

The regenerated base is thus obtained in a pure condition, but all attempts to crystallise it have been unsuccessful.

Veratroylbikhaconine is soluble in ether, alcohol, and chloroform, but nearly insoluble in light petroleum or water. The amorphous base melts indefinitely between 120° and 125°.

Specific Rotation of Veratroylbikhaconine.

The following determination was made with an alcoholic solution of the amorphous base dried at 80—90°.

$\alpha^{20°} = 1°40'$, $l = 2$ dcm., $c = 2{\cdot}787$; whence $[\alpha]_D^{20°} = +29{\cdot}9°$.

This result provides a striking difference between this alkaloid and its analogue, veratroylpseudaconine, which is lævorotatory (Trans., 1897, **71**, 356).

Salts of Veratroylbikhaconine.

The only haloid salt which has been obtained in a crystalline condition is the hydriodide. Both the hydrochloride and hydrobromide were prepared by dissolving the pure base in dilute acid and evaporating the neutral aqueous solutions *in vacuo*, but neither could be obtained crystalline.

Veratroylbikhaconine hydriodide was prepared by mixing aqueous solutions of potassium iodide and veratroylbikhaconine hydrobromide and concentrating *in vacuo*. The hydriodide separates as large rosettes of needles which may be recrystallised from alcohol or water. When crystallised from water and dried at 100°, the salt melts at 189—190°.

Veratroylbikhaconine nitrate was obtained by dissolving the pure base in the requisite amount of dilute nitric acid to form a neutral solution.

The pure salt may be crystallised from alcohol, or more conveniently by adding ether to an alcoholic solution, when it separates as rosettes of acicular, prismatic hexagons, which, after drying at 100°, melt somewhat indefinitely without darkening at 175—178°.

Two combustions were made of the salt dried at 100° :

(1) 0·1692 gave 0·3622 CO_2 and 0·1142 H_2O. C = 58·38 ; H = 7·49.
(2) 0·195 ,, 0·4178 CO_2 ,, 0·1326 H_2O. C = 58·43 ; H = 7·55.

$C_{34}H_{49}O_{10}N,HNO_3$ requires C = 58·75 ; H = 7·26 per cent.

Veratroylbikhaconine aurichloride is completely precipitated when

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auric chloride solution is added to an aqueous solution of veratroylbikhaconine hydrochloride acidified with hydrochloric acid. The precipitate is filtered, washed with water, and dried under reduced pressure.

The salt crystallises from alcohol or when ether or light petroleum is added to a chloroform or alcoholic solution. It separates in bright orange-yellow clusters or rosettes of prismatic crystals. Veratroylbikhaconine aurichloride loses weight when dried at 100°.

(1) 0·6462 lost 0·0519. Loss = 8·03.
(2) 1·046 „ 0·0842. Loss = 8·05.

$C_{34}H_{49}O_{10}N,HAuCl_4,2(C_2H_6O)$ requires $2C_2H_6O = 8·66$ per cent.
$C_{34}H_{49}O_{10}N,HAuCl_4,5(H_2O)$ „ $5H_2O = 8·48$ per cent.

The melting point of the salt is indefinite; after crystallisation from chloroform, alcohol, and ether and drying at 100°, it melts between 145° and 148°.

The gold and chlorine were estimated by the method described under bikhaconitine aurichloride (p. 1641), the analysis being conducted with the salt dried at 100°.

(1) 0·4912 gave 0·0995 Au and required 20·6 c.c. of silver nitrate solution (1 c.c. = 0·00351 Cl). Au = 20·25; Cl = 14·72.
(2) 0·4682 gave 0·0938 Au and required 19·9 c.c. $AgNO_3$. Au = 20·04; Cl = 14·92.

$C_{34}H_{49}O_{10}N,HAuCl_4$ requires Au = 20·29; Cl = 14·59 per cent.

Bikhaconine.

As already stated, this alkaloid is produced by the separation of a veratroyl group from veratroylbikhaconine, and is the final product of the hydrolysis of bikhaconitine.

The preparation of bikhaconine is effected by the action of alcoholic soda on bikhaconitine, or on veratroylbikhaconine, at the ordinary temperature. The acetic and veratric acids furnished by the hydrolysis of the parent base were estimated in the following manner:

1·0693 grams of bikhaconitine were dissolved in alcohol, 2 c.c. of 20 per cent. solution of pure caustic soda added, and the mixture allowed to stand for about twenty hours. The liquid, diluted with water, was then neutralised with dilute sulphuric acid and the alcohol completely evaporated, preferably in a vacuous desiccator over sulphuric acid. The veratric acid was precipitated from the aqueous liquid by dilute sulphuric acid and extracted with benzene, each successive portion of which was washed with water. By the distillation of the solvent, the veratric acid was obtained as a slightly coloured crystalline residue, which weighed 0·2859 gram.

This result was checked by dissolving the acid in standard caustic

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soda solution and titrating the excess of alkali with standard acid, using phenolphthalein as indicator.

The veratric acid estimated:

(1) Gravimetrically = 26·74 per cent.
(2) Volumetrically = 26·65 per cent.

The equation $C_{36}H_{51}O_{11}N + 2H_2O = C_{25}H_{41}O_7N + C_2H_4O_2 + C_9H_{10}O_4$ requires veratric acid = 27·04 per cent.

The identity of the acid was established by its melting point (178·5°) and the analysis of its silver salt, which was found to contain 37·32 per cent. of silver. Silver veratrate ($C_9H_9O_4Ag$) contains Ag = 37·34 per cent.

The aqueous liquid from which the veratric acid was extracted now contains the bikhaconine and acetic acid. The former was liberated by dilute caustic soda solution and extracted with ether, which, after being washed with water, was dried over a few pieces of pure fused calcium chloride and distilled. The bikhaconine was thus obtained as a colourless, transparent, gum-like residue. The acetic acid contained in the aqueous liquid and washings was estimated by distillation.

Properties of Bikhaconine.

Although it was possible to obtain bikhaconine in a pure condition by means of its crystalline nitrate, the base could not be crystallised.

Bikhaconine is soluble in ether, alcohol, chloroform, or water, but insoluble in light petroleum. The solubility in ether is interesting as this property distinguishes bikhaconine from any of its analogues, aconine, pseudaconine, and japaconine, which are insoluble, or nearly so, in this solvent.

For purposes of examination, bikhaconine may be obtained in a suitable condition by evaporating an ethereal solution to a syrupy consistency and then driving off the remaining ether in a partial vacuum. The base is thus obtained in a very fine state of division and may be easily dried and powdered. An alcoholic solution of the base has a dextrorotatory action towards polarised light. The following determinations were made with specimens of alkaloid prepared independently of each other.

1. $a^{22°} = +1°34·5'$, $l = 2$ dcm., $c = 2·3432$; whence $[\alpha]_D^{22°} = +33·6°$.
2. $a^{22°} = +1°45·5'$, $l = 2$ dcm., $c = 2·54$; whence $[\alpha]_D^{22°} = +34·1°$.

Mean $[\alpha]_D^{22°} = +33·85°$.

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Salts of Bikhaconine.

Bikhaconine forms well-defined crystalline salts, thus sharply distinguishing this alkaloid from the aconines derived from the other aconitines: aconitine, japaconitine, pseudaconitine, and indaconitine.

Bikhaconine nitrate was prepared by neutralising an aqueous solution of bikhaconine with dilute nitric acid and evaporating the liquid under reduced pressure. The salt crystallises well from alcohol or water when fairly pure, but it is most readily obtained crystalline by adding ether to an alcoholic solution, when it separates in transparent, tetragonal prisms, sometimes acicular with pyramidal ends but usually aggregated to form semi-spherical masses. The crystalline salt contains two molecules of water of crystallisation which are not expelled at 100°.

0·6726 dried at 120° lost 0·0414. Loss = 6·15.

$C_{25}H_{41}O_7N,HNO_3,2H_2O$ requires $2H_2O = 6·36$ per cent.

That this loss is due to water is further shown by the combustion figures for the hydrated and anhydrous salts.

The melting point of bikhaconine nitrate is somewhat variable, owing no doubt to its water of crystallisation, but if put into the bath at 100° it softens at 122° and melts at 125—128°.

The specific rotation of bikhaconine nitrate, using an aqueous solution of the hydrated salt, was determined.

1. $\alpha^{20°} = +40'$, $l = 2$ dcm., $c = 2·1176$; whence $[\alpha]_D^{20°} = +15·73°$.
2. $\alpha^{20°} = +35'$, $l = 2$ dcm., $c = 1·939$; whence $[\alpha]_D^{20°} = +15·03°$.

Mean $[\alpha]_D^{20°} = +15·38°$.

The salt does not, therefore, exhibit rotatory power of the opposite sign to that of its base, as is the case with pseudaconine.

Combustions of bikhaconine nitrate furnished the following results:

(i) *With hydrated salt.*

(1) 0·1753 gave 0·3389 CO_2 and 0·131 H_2O. C = 52·73 ; H = 8·30.
(2) 0·182 „ 0·3520 CO_2 „ 0·1351 H_2O. C = 52·75 ; H = 8·25.
(3) 0·1784 „ 0·3450 CO_2 „ 0·1333 H_2O. C = 52·74 ; H = 8·30.

$C_{25}H_{41}O_7N,HNO_3,2H_2O$ requires C = 53·00 ; H = 8·13 per cent.

(ii) *With anhydrous salt.*

0·1576 gave 0·3249 CO_2 and 0·1183 H_2O. C = 56·22 ; H = 8·34.

$C_{25}H_{41}O_7N,HNO_3$ requires C = 56·56 ; H = 7·98 per cent.

Bikhaconine hydrobromide may be crystallised either from water or by adding ether to an alcoholic solution. It separates as transparent,

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tetragonal prisms, generally in rosettes which, if dried at 110°, melt without darkening between 145° and 159°.

Bikhaconine hydrochloride crystallises from water if the solution is concentrated to a syrup and then well stirred. The pure salt also separates from alcohol and ether as rosettes of prismatic crystals, which, after drying at 100°, melt indefinitely at 125—130°.

Bikhaconine aurichloride is obtained directly in a crystalline condition when auric chloride is added to a strong aqueous solution of bikhaconine hydrochloride acidified with hydrochloric acid. The salt is first precipitated apparently amorphous, and then almost immediately changes to a crystalline condition.

It may be recrystallised from water or alcohol by allowing a hot saturated solution to cool, or more conveniently by adding light petroleum to a solution of the salt in chloroform and alcohol. Bikhaconine aurichloride crystallises as glistening, rhombic plates which contain three molecules of water, which are only partially expelled at 100°.

(1) 0·5258 dried at 105° lost 0·0316. Loss = 6·01.
(2) 0·9778 ,, 110—115° lost 0·0597. Loss = 6·10.
$C_{25}H_{41}O_7N,HAuCl_4,3H_2O$ requires $3H_2O = 6·27$ per cent.

This result was confirmed by analyses of the dried and undried salts :

Anhydrous bikhaconine aurichloride melts at 187—188°.
Hydrated ,, ,, ,, 129—132°.

The gold and chlorine were determined by the method already described, but in this case the aurichloride is decomposed by sulphuretted hydrogen in the presence of water only.

(i) *With the hydrated salt.*

0·2205 gave 0·0506 Au and required 10·45 c.c. of silver nitrate solution (1 c.c. = 0·00351 Cl). Au = 22·95 ; Cl = 16·63.
$C_{25}H_{41}O_7N,HAuCl_4,3H_2O$ requires Au = 22·89 ; Cl = 16·46 per cent.

(ii) *With the anhydrous salt.*

0·3099 gave 0·0758 Au and required 15·6 c.c. of $AgNO_3$. Au = 24·46 ; Cl = 17·67.
$C_{25}H_{41}O_7N,HAuCl_4$ requires Au = 24·42 ; Cl = 17·56 per cent.

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Pyrobikhaconitine.

It appears to be a common property of the "aconitines" which contain an acetyl group to undergo decomposition when heated, with the formation of a new base, acetic acid being liberated. It was, therefore, to be expected that bikhaconitine would behave in a similar manner, and this was found to be the case.

Although bikhaconitine melts at 113—116°, it does not decompose until heated to about 180°, when acetic acid is liberated and pyrobikhaconitine is formed.

The acetic acid was estimated by heating the bikhaconitine, contained in a small Wurtz flask, at 200—210°, and so arranging the apparatus that any volatile products at this temperature were carried forward by a current of dry air into a known volume of standard caustic soda solution. It was found by this means that the acetic acid amounted to 9·09 per cent. of the bikhaconitine taken.

The equation $C_{36}H_{51}O_{11}N = C_{34}H_{47}O_9N + C_2H_4O_2$ requires 8·91 per cent. of acetic acid.

Pyrobikhaconitine is most advantageously prepared by heating bikhaconitine at 200° for ten minutes in a flask, the air from which has been exhausted. Under these conditions the residue which remains after the evolution of the acetic acid is only slightly coloured, and may be readily purified by dissolving in dilute acid, adding weak ammonia, and extracting the precipitated base with ether. By the distillation of the solvent, the pyrobikhaconitine was obtained as an amorphous residue, which, although perfectly colourless, could not be crystallised.

The nitrate, hydrobromide, hydrochloride, and aurichloride of pyrobikhaconitine were prepared, but all attempts to crystallise these salts have so far been unsuccessful.

The aurichloride separates as a light yellow, voluminous precipitate when auric chloride is added to a solution of the base in hydrochloric acid. The precipitated salt melts indefinitely at 115—123°.

The chief differences between bikhaconitine and pseudaconitine are shown by a comparison of their physical properties in the following tables. In composition it will be seen that pseudaconitine contains one atom more oxygen than bikhaconitine.

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Physical Properties of Bikhaconitine and Pseudaconitine.

Substance.	Melting point.	Specific rotation.	Other properties.
Bikhaconitine (base).....	113—116°	+12·21° (in alcohol)	Indefinitely crystalline hydrate.
Pseudaconitine (base)	211—212	+18·6 ,,	Well-defined crystalline.
Bikhaconitine hydrobromide	173—175	−12·43 (in water)	—
Pseudaconitine ,,	191	−19·5 ,,	Crystallises with $2H_2O$.
Bikhaconitine hydrochloride	159—161	−8·86 ,,	Crystalline.
Pseudaconitine ,,	—	—	Uncrystallised.
Bikhaconitine hydriodide ...	192—194	—	Crystallises with $2\frac{1}{2}H_2O$.
Pseudaconitine ,, ...	215—217	—	—
Bikhaconitine nitrate	178—180	—	—
Pseudaconitine ,, ...	192	—	Crystallises with $3H_2O$.
Bikhaconitine aurichloride ...	232—233	—	—
Pseudaconitine ,, ...	235—236	—	—

Veratroylbikhaconine and Veratroylpseudaconine.

Substance.	Melting point.	Specific rotation.	Other properties.
Veratroylbikhaconine (base)	—	+29·9° (in alcohol)	Uncrystallised.
Veratroylpseudaconine (base)	199°	−38·3 ,,	Crystalline monohydrate.
Veratroylbikhaconine hydrobromide	—	—	Uncrystallised.
Veratroylpseudaconine hydrobromide	—	—	Crystalline.
Veratroylbikhaconine hydriodide	189—190	—	—
Veratroylpseudaconine hydriodide	205—207	—	—
Veratroylbikhaconine nitrate	175—178	—	—
Veratroylpseudaconine ,,	222° softens 232° melts	—	—
Veratroylbikhaconine aurichloride	145—148°	—	Crystalline.
Veratroylpseudaconine aurichloride	—	—	Uncrystallised.

Bikhaconitine, $C_{36}H_{51}O_{11}N$, and pseudaconitine, $C_{36}H_{51}O_{12}N$, (i) contain six methoxyl groups.

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(ii) yield one molecular proportion of acetic acid and one of veratric acid on hydrolysis.

(iii) undergo decomposition when heated, with the liberation of acetic acid and the formation of a new base, pyrobikhaconitine and pyropseudaconitine.

Bikhaconine and Pseudaconine.

Substance.	Melting point.	Specific rotation.	Other properties.
Bikhaconine (base)	—	+33·85° (in alcohol)	Uncrystallised. Soluble in ether.
Pseudaconine (base)	94–95°(from alcohol) 86–87°(from acetone)	+39·0 (in water)	Crystallises combined with alcohol or acetone. Insoluble in ether.
Bikhaconine hydrobromide.	145—150°	—	Crystalline.
Pseudaconine ,,	—	—	Uncrystallised.
Bikhaconine hydrochloride.	125—130	—	Crystalline.
Pseudaconine ,,	—	—	Uncrystallised.
Bikhaconine nitrate	125—128	+15·38 (in water)	Crystallises combined with $2H_2O$.
Pseudaconine ,, ...	—	—	Uncrystallised.
Bikhaconine aurichloride ...	187—188	—	Rhombic plates containing $3H_2O$.
Pseudaconine ,, ...	—	—	Uncrystallised.

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