XXXV.—*Contributions to our Knowledge of the Aconite Alkaloids.*
 Part IV. *The Composition of some Commercial Specimens of Aconitine.*

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IN our search for the most readily available source from which to obtain pure aconitine, we examined a number of commercial specimens of this alkaloid, English and foreign. For eleven of these specimens (1—11) we are indebted to Dr. J. W. L. Thudichum, who collected them some years ago, and kindly offered them to us for examination. Dr. Thudichum found that these specimens varied enormously in toxic power, many being inert, others more or less poisonous, whilst only one or two were highly toxic. The remainder of the specimens have been purchased during the past two years.

The process employed in examining them was essentially that described in connection with the separation of isaconitine from the total alkaloids of *Aconitum Napellus* (this vol., p. 444), by means of which it was possible to ascertain the presence of aconitine and isaconitine, and also of aconine and homisaconitine (homonapelline), as well as to form an approximate estimate of the proportion of crystalline aconitine to that of the amorphous alkaloids. In several instances the amount of aconitine present was too small to allow of its isolation either as crystalline base or crystalline salt. When this was the case, the presence or absence of aconitine was ascertained by observing whether a dilute solution of the mixed salts produced the characteristic tingling sensation on the tongue. The difficulty of separating the alkaloids has often been great, owing to the small amount of some of the specimens.

The results are as follows.

1. "Aconitine, Pure" (German). A yellowish-white, amorphous powder which melted indefinitely near 107°. When dissolved in

dilute hydrobromic acid, it furnished a highly coloured solution. From this liquid, pure isaconitine salt was eventually obtained, in amount corresponding with the presence of about 20 per cent. of the alkaloid in the original substance. Aconitine was present only in relatively small quantity, and it was not found possible to isolate it. Aconine, and apparently homisaconitine, were also present.

2. "Aconitine, Crystallised" (French). A white, crystalline powder melting near 187° . It completely dissolved in cold water, and proved to be the nitrate of an alkaloid, not the base itself. The alkaloid was regenerated and dealt with in the usual manner. A considerable quantity of pure aconitine hydrobromide was obtained, and from this, pure crystalline aconitine (m. p. $188-189^{\circ}$) was prepared. A smaller quantity of isaconitine hydrochloride was isolated, whilst other amorphous bases (aconine, homisaconitine, &c.) were observed in small quantity. The nitrate, of which the original substance was composed, contained about 70 per cent. of aconitine salt.

3. "Aconitine, Pure" (English). A yellowish-white, amorphous substance melting indistinctly near 88° . Its solution in dilute hydrobromic acid was highly coloured. A considerable quantity of alkaloid soluble in ether was isolated; this was chiefly isaconitine. No crystalline aconitine salt could be isolated from the small quantity of material at our disposal. The physiological action of the acid solution indicated that a small quantity of this alkaloid was present, but the specimen was chiefly composed of amorphous bases.

4. "Aconitine, Pure" (German). A dirty white, amorphous powder melting at 111° . The solution in dilute acid was yellow. No crystalline aconitine salt could be isolated, although a small quantity of the alkaloid was detected by its physiological action. Some isaconitine was obtained in addition to other amorphous alkaloids, including aconine.

5. "Aconitine, Crystallised" (German). A collection of small white crystals melting at 170° . It yielded a considerable quantity of crystalline aconitine hydrobromide, from which the pure crystalline base melting at $188-189^{\circ}$ was regenerated. Isaconitine was also obtained. Rather more than two-thirds of the original material was aconitine.

6. "Napelline" (German). Napelline was the name given by Hübschmann to what seems to have been a mixture of the amorphous alkaloids of *Aconitum Napellus*. A brown, amorphous powder melting near 120° , and not completely soluble in dilute acid. The highly coloured solution furnished some isaconitine. It also contained aconitine and considerable quantities of amorphous alkaloid, partly aconine. The original substance was probably the

total alkaloids of *A. Napellus*, from which some of the aconitine had been removed.

7. "Aconitine, Pure" (English). A yellowish, amorphous powder melting at 85°. It partially dissolved in dilute acids, forming a coloured solution, from which no crystalline aconitine salt could be isolated, although the presence of a small quantity of this alkaloid was detected by its physiological action. About two-thirds of the alkaloid consisted of amorphous alkaloids, the remainder being resinous substances, apparently non-alkaloidal, and a little aconine.

8. "Aconitine from *A. Napellus*" (German). A yellow, amorphous powder melting between 105° and 110°. Its solution in dilute acid was coloured. A considerable quantity of crystalline isaconitine salt was separated, but the amount of aconitine was too small to admit of isolation. More than one-fifth of the original substance turned out to be isaconitine, the remainder being other amorphous bases, a small quantity of aconitine, and some non-alkaloidal substance.

9. "Aconitine" (English). A nearly white, amorphous powder, dissolving in dilute acid, forming a dark coloured solution. The substance was chiefly composed of amorphous bases with very little aconitine.

10. "Aconitine Muriate" (German). A yellow, uncrystalline powder melting indistinctly at 86°. Its solution in water was highly coloured, and produced only a feeble tingling sensation on the tongue. It was chiefly isaconitine hydrochloride contaminated with the hydrochlorides of other amorphous alkaloids, and with a trace of aconitine hydrochloride.

11. "Aconitine Sulphate" (German). A reddish, crystalline powder melting indefinitely below 128°. Its aqueous solution was red. The alkaloid was regenerated, and was proved to be chiefly isaconitine with a little aconitine.

12. "Aconitine Nitrate" (German). A dark yellow, amorphous substance melting near 62°. The aqueous solution was yellow. It furnished no crystalline alkaloid, but the existence in it of a small quantity of aconitine was revealed by its physiological action. Some isaconitine was isolated, but it was contaminated with other amorphous alkaloids.

13. "Aconitine, Pure, from *Aconitum Napellus*" (English). A yellowish-white, crystalline powder melting at 186—187°. It dissolved completely in dilute acid, forming a yellow solution. A large quantity of pure aconitine was isolated, together with a small quantity (about 3 per cent.) of isaconitine.

14. "Aconitine, Pure, Crystallised, from *Aconitum Napellus*" (German). A collection of small, nearly white, distinct crystals melting at 187.5°. It dissolved in dilute acid, forming an almost

colourless solution, which furnished a large quantity of pure aconitine salt. The regenerated alkaloid melted at 188.5° . This specimen consisted of almost pure aconitine.

15—17. "Aconitine, Amorphous, from *Aconitum Napellus*" (German). Three separate specimens of this material were examined. It is a yellow, amorphous powder, dissolving in dilute acid with the production of a coloured solution. In each case aconitine, isaconitine, homisaconitine, and aconine were isolated, but the amount of aconitine obtained varied greatly; in one instance as much as 20 per cent. of the substance was found to be aconitine, whilst in another as little as 5 per cent. was present. These products appear to represent the total alkaloids of *A. Napellus*.

In the light of these results, it is not surprising to learn that great variations have been observed in the toxic power of commercial specimens of aconitine.

For medicinal purposes, nothing should in future be employed as aconitine but the pure crystalline alkaloid melting at $188-189^{\circ}$, and having the other characteristic properties recorded in Part I (Trans., 1891, 59, 271) of this enquiry (see also on this point, *Pharm. J.*, 3, 23, 765).

Of the specimens now examined, only two (13, 14) approach this standard, and are entitled to be called aconitine. It is clear from the results which are here recorded that the fact that a specimen of this alkaloid is crystalline cannot alone be accepted as sufficient evidence of purity, as some physiologists have assumed. In the case of the salts, the crystalline nature of the specimen is no criterion that the substance is an aconitine compound, since the salts of isaconitine are also crystalline.

It has already been remarked that most of the specimens described in this paper were collected some years ago, and since then, especially during the last two years, a marked improvement has occurred in the quality of commercial aconitine. It is now possible to purchase in commerce a nearly pure crystalline aconitine, represented by specimens 13 and 14, although the crude, amorphous alkaloid is still largely prepared and sold, because this satisfies the present requirements of the British Pharmacopœia!

Until now, it has not been possible to make anything approaching to a chemical examination of commercial aconitine, since the nature and properties of its chief constituents were either unknown or open to doubt. Even now it is not possible to make a complete examination, as there is certainly one, probably two alkaloids which still require investigation, making in all four, or possibly five, distinct natural alkaloidal products from *A. Napellus*.

No method is at present known for the quantitative determina-

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tion of the highly toxic alkaloid aconitine. Now that isaconitine is known to be a constituent of the plant, and since it, like aconitine, furnishes benzoic acid when hydrolysed, the method suggested by Wright for the estimation of aconitine in the crude alkaloid, by calculating from the weight of benzoic acid obtained on hydrolysis, can no longer be accepted as valid.

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