THE ALKALOIDS OF DICENTRA CUCULLARIA

AND

DICENTRA CANADENSIS

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Introduction

In working on a thesis entitled "Alkaloids of Dicentra Cucullaria", submitted by O.A.Soell in 1902 for the degree of Graduate in Pharmacy, the manipulator accidentally sustained a loss during one of the more important extractions. To determine whether hereby a new base had been lost. as well as to try and corroborate the rest of Mr.Soell's results, the following work was undertaken.

Unfortunately the quantity of material available was appreciably smaller than that worked with heretofore so that the yield of alkaloids with one exception was correspondingly smaller, and experimental identification rendered difficult.

Contrary to expectation, the yield of protopine was considerably larger than that obtained before; due probably to the fact that the material was collected in a different part of the state. The method of isolating the different bases was practically the same as that pursued by my predecessor, so that a detailed account of the various methods of extraction, purification and crystallization will here be omitted.

Experimental.

The crude material consisted of the whole plant collected in the vicinity of Cedarburg, Ozaukee Co., Wis. during the month

of May. The herb after being carefully air-dried was separated from the bulbs, and each worked up separately. The quantity of the herb was 245 g. while that of the root was 272 g.

The root and herb were both extracted with dilute (2 1/2%) acetic acid, the percolate evaporated to a syrupy consistency, ammonia water added in slight excess and the resulting precipitate washed and dried. This precipitate(A) in both the herb and root was mixed with an equal weight of powdered glass and then extracted in a Soxhlet extraction apparatus, first with ether and then with chloroform.

The ethereal extracts in both cases yielded crystals, the quantity, however, being very small, especially in the case of the root. They were minute granular colorless crystals adhering firmly to the bottom of the flask. From the chloroform extracts the one from the root yielded flat colorless crystals of irregular outline, melting at 2ii C. Only enough crystals were obtained for one melting point determination.

The ammoniacal filtrate from(A) in both the herb and root were deprived of alkaloids by repeatedly passing them in a fine stream through a column of chloroform in an apparatus specially adapted for that purpose. The united chloroformic extracts yielded on evaporation a blackish residue, which on being taken up with a mixture of alcohol and chloroform deposited

crystals of two kinds; the one dense and prismatic, the other light and feathery. The first mentioned crystals were recrystallized from chloroform and alcohol. Thus purified the crystals appeared to be regular octohedrons melting at 207°. They were further identified as protopine by their color reactions.

Besides protopine there were deposited from this solution, as already stated above, a second kind of crystals. Separation of the two was accomplished by elutriation. For purposes of purification they were recrystallized from a mixture of alcohol and chloroform in which they were slightly soluble. The crystals thus obtained were fine, acicular, colorless needles, with a melting point of 230-231° C. Toward alkaloidal reagents the following color reactions were observed: Conc. sulphuric acid turned them red, then orange and gradually becoming dark yellow. With hydrochloric acid conc., they first assumed a bright yellow color, gradually becoming more intense on standing. They were almost insoluble in chloroform, acetone, alcohol and ether, but on continued boiling with a mixture of alcohol and chloroform a solution could be obtained. This was undoubtedly the alkaloid designated by Soell as alkaloid C.

In the case of the herb, crystals corresponding to the above mentioned ones were also obtained, but a different

method of purification was pursued. The impure alkaloids were dissolved in dilute acid, the solution rendered alkaline with potassium carbonate, and shaken out with chloroform. Depending upon the kind of acids used, differences in the resulting crystals were observed. Part of the crystals were dissolved in acetic acid with the result that the crystals obtained were similar to those from the root; melting at 230-231°. The rest of the same crystals were purified in a similar manner, except that hydrochloric acid was used.

While the crystals dissolved in acetic acid to form a colorless solution, the solution had a citrine color whenever hydrochloric acid was employed, and the crystals finally obtained consisted of lemon yellow needles of irregular outline.

During the deposition of the above mentioned yellow crystals, another kind, differing vastly from the former, were obtained. They were larger, more regular and colorless, with a melting point of 220-221°. Behavior toward alkaloidal color reagents: Concentrated sulphuric acid: red, orange, then yellow, changing to a lighter yellow.

Froedess reagent: momentarily red, rapidly changing to green, then brown, finally violet.

Erdmann's reagent: Orange, yellow, brown to violet.

Concentrated hydrochloric acid (free from chlorine) yellow.

Dilute hydrochloric acid: slowly turns crystals bright yellow.

These reactions are similar to those of Soell's alkaloid C. Their identity, however, must be regarded as uncertain, since their melting point differs by ten degrees.

The above results indicate that there are in Dicentra Cucullaria at least four alkaloids, although it was impossible, working with such a small quantity of material, to isolate Soell's alkaloid D.

The Alkaloids of Dicentra Canadensis

Introduction.

Dicentra canadensis, Walp.

Corydalis canadensis, Goldie; (1)

Bicuculla canadensis, Goldie, Millsp.

Corydalis formasa, Pursh.

Stagger weed;

Choice Dielytra;

Turkey Corn;

Squirrel Corn;

Description. (2)

This plant flowers very early in the spring, in the north western part of the country as early as March, and the root and tuber, which is a small brown ball, should be collected only while the plant is in flower. It grows in rich soil, on hills and mountains, among rocks and old decayed timber. The root or tuber of the plant when fresh is of a dark yellow color throughout, it has a faint peculiar odor, a slight bitter taste succeeded by a somewhat penetrating persistent sensation.

The leaves are radical, somewhat triternate with incisely pinnatifed segments and very glaucous beneath. The scape is naked and rises from eight to ten inches in height with four

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1. King's Dispensatory.
2. Wenzell, Am. Journ. Pharm., 1885, p. 205

to six cymes, each with from six to ten reddish purple nodding flowers.

The only chemical work that seems to have been done on this species of Dicentra was done by W.Wenzell(1) who in 1885 reported the bulbs to contain corydaline, fumaric acid, yellow bitter extractive, acrid resin soluble in alcohol and ether, brown coloring matter, starch, albumen, bassorin, cellulose and cortical substance besides some inorganic salts.

Since the closely related species Dicentra Cucullaria was found to contain several alkaloids, it seemed highly probable that this was also the case with Dicentra canadensis. To decide this question the following investigation was undertaken.

Experimental.

The material for this work consisted of fifty pounds of the dried bulbs of Dicentra canadensis, kindly donated by Parke Davis & Co. of Detroit, Mich. The greater portion of the material was in good condition, but a considerable part consisted of accidental impurities as petals, sand and other foreign matter. After carefully removing these contaminations, the bulbs were reduced to a coarse powder and then dried at a temperature of from 45° to 50° for about 24 hours. This was found necessary to

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1. Am. Journ. Pharm., 1885, p. 205.

prevent the clogging of the mill in grinding the coarsely comminuted material to a finer powder. After thus reducing the drug to a number 60 powder it was moistened with alcohol, packed in a percolator, allowed to macerate for 48 hours, and completely exhausted with the same menstruum. To prevent all danger of decomposition incidental to the application of heat the percolate was allowed to evaporate spontaneously, leaving a thick yellowish brown extract. Upon thoroughly rubbing this up with repeated portions of acidulated (hydrochloric acid) water, most of it dissolved to form a deep yellowish brown solution, but considerable resin remained behind which no longer showed a reaction with Mayer's reagent.

A preliminary test having demonstrated that sodium carbonate would completely precipitate the alkaloids from the acid solution, while an excess of ammonia would leave some dissolved, a strong excess of the latter reagent was added to all of the solution, it being hoped that a separation of alkaloids could be accomplished in this manner. The resulting precipitate (A) was collected, dried at room temperature, mixed with powdered glass, and extracted in a Soxhlet's extraction apparatus, first with ether (B), then with chloroform (C). The different methods of obtaining the various bases will only

be discussed in brief, as it would be to complicated to outline the entire process persued.

The dark colored residue left upon evaporation of the chloroformic extract(C) was taken up with alcohol and the solution allowed to evaporate very slowly. However only a black amorphous mass resulted. This was treated with acidulated(hydrochloric acid)water, leaving considerable resinous matter undissolved, and then shaken out first with ether, secondly with chloroform. No crystals could be obtained from the ethereal extract. The residue from the chloroform extract was taken up with alcohol. Upon slow evaporation some colored crystals separated out, but nothing was done with them for lack of time. This solution after shaking out with chloroform was mow rendered alkaline with sodium carbonate and again shaken out with ether and with chloroform, but from neither solution could any crystals be obtained.

The ethereal extract(B), after evaporation of the solvent, consisted of a yellow crystalline mass which was taken up with alcohol, in which it dissolved readily to a dark brown solution. Upon rapid evaporation in a crystallizing dish, a mass of fine golden yellow needles arranged in dense clusters separated out (Alk.X.). These were purified by recrystallizing several times from alcohol, being finally obtained in short

fine needles, melting at 219-220°. Though resembling berberine in color, their identity with this base is disproved by their melting point, as well as their solubility. Their reaction toward general alkaloidal reagents is given below.

Concentrated sulphuric acid produced a yellow color, changing to a lighter yellow and remaining so for 15 minutes.

Froede's Reagent: Green, changing gradually to a darker shade, then to a dirty brown color; after five minutes becoming bbrown.

Erdmann's reagent: greenish yellow, gradually turning to a light brown color.

Mandelin's reagent: brown, gradually getting darker.

Concentrated nitric acid: brown, then reddish brown, changing on standing to yellow.

In dilutions of 1-10,000, prepared with the aid of a few drops of hydrochloric acid , precipitates occurred as follows:

Potassium mercuric iodide	precipitate formed
Tannin	Gelatinous precipitate
Potassium cadmium iodide	precipitate
Potassium bismuth iodide	dark brown precipitate
Platinum chloride	light precipitate

Upon very slow evaporation of another portion of the solution from which alk.X. had separated, and entirely dif-

ferent kind of crystal deposited in the bottom of the flask, (Alk.Y). They were large and colorless, octohedral in form and difficultly soluble in chloroform, ether, and alcohol. Purified by several recrystallizations from hot alcohol, they melted with decomposition at 175°-176°.

With general alkaloidal reagents they reacted as follows:

Concentrated sulphuric acid: gradually assumes a violet color, then indigo, slowly changing to a darker shade.

Froede's reagent: blue, indigo, then deep Prussian blue.

Erdmann's reagent: gradually turns violet, fading on standing.

Mandelin's reagent: purple, brown, gradually getting darker then lighter brown and remaining so after 12 hours.

Concentrated nitric acid: reddish brown, gradually becoming lighter in color.

In dilutions of 1-10,000 prepared with the aid of a few drops of hydrochloric acid, precipitates occurred as follows:

Mayer's reagent	white precipitate
Tannin	faint opalescence
Potassium bismuth iodide	slight precipitate
Lugol's solution	precipitate formed
Sonnenschein's reagent	white precipitate

In solutions of 1-100,000 Sonnenscheins reagent still produced a slight cloudiness.

The ammoniacal filtrate from A was repeatedly passed in a

fine stream through columns of chloroform in a special apparatus adapted for that purpose, the excess of chloroform being regained by distillation, and used over and over again. These united chloroformic extracts on evaporation yielded a dark colored mass, which was taken up with alcohol. This solution, however, instead of yielding crystals on partial evaporation as might be expected, deposited an amorphous bblack mass similar to the one deposited from the original solution. This mass was then taken up with acidulated hydrochloric acid water, filtered from a dark resin, and shaken out with ether (a) and chloroform(b); rendered alkaline with sodium carbonate and again shaken out with ether(c) and chloroform(d).

Neither of the ethereal solutions yielded more than traces of crystals. From the chloroformic solution(b) a heavy mass was deposited, having a greenish gray color, and somewhat crystalline in character. This residue was fairly soluble in water, more readily in dilute hydrochloric acid; this latter solution gave a heavy precipitate with Mayer's reagent. For purposes of purification the mass was treated several times with hot alcohol in which it was only slightly soluble. The greenish color was thus removed while a white powder remained behind. This was purified by dissolving in a large quantity of boiling alcohol, cooling and allowing the solution to slowly evaporate.

A colorless crystalline powder separated out which upon heating turned green at 200°, darkened in color above this temperature, and finally melted with decomposition at 257-258 .

Since these crystals were so readily soluble in water and as they had been shaken out with chloroform from a hydrochloric acid solution, it seemed quite probable that the substance in hand was the hydrochloride of an alkaloid (Z). That such was actually the case was proved by the formation of silver chloride when silver nitrate test solution was added to an aqueous solution of the substance. Upon standing, the solution turned a violet to purple color and finally a precipitate of the same color was formed. Since not sufficient time was left for the preparation of the free alkaloid the following reactions of the salt with general alkaloidal reagents were tried.

Concentrated sulphuric acid: no color reaction at first, effervesces upon standing , changing to a very faint green.

Froede's reagent: immediately turns emerald green with effervescence, gradually fading to a lighter shade.

Erdmann's reagent: at first effervesces but no color, then very faint darkening slowly fading away.

Mandelin's reagent: effervesces, assuming dark color, then light green, changing to a dark green and remaining so.

Concentrated nitric acid: dark red, immediately changing to brown.

In dilutions of 1-10,000 prepared with the aid of a few drops of hydrochloric acid, precipitates occurred as follows.

Potassium mercuric iodide	white precipitate
Potassium bismuth iodide	dirty brown precipitate
Tannin	slight opalescence
Lugol's solution	heavy precipitate
Sonnenschein's reagent	white precipitate

In dilutions of 1-100,000 potassium mercuric iodide and Sonnenschein's reagent both still produced a slight cloudiness.

From the chloroformic solution (d) a black amorphous mass resulted. This was dissolved in alcohol, but no crystals had separated out at the time of this writing.

Another base of which no mention was made above, was obtained from one of the ethereal extracts from precipitate(A). Two other bases X and Y were obtained from alcoholic solution of this extract, while this one was obtained directly by evaporation of the ethereal mother liquor. The crystals thus obtained (alk.W) were small prismatic needles, slightly greenish in color, melting at 191-192°. Recrystallized from alcohol they were obtained colorless with unchanged melting point. The following color reactions were observed.

Concentrated sulphuric acid: faint yellow color changing slowly

to a very light brown, brick red on standing.

Froede's reagent: very light green, becoming more intense and darker, then dirty green, becoming black.

Erdmann's reagent: assumes light yellow color, becoming more intense, then dirty green, color gradually fading away.

Mandelin's reagent: brick red, light brown, dark brown, then black on standing.

Concentrated nitric acid: yellowish brown gradually becoming lighter & fading away.

In dilutions of 1-10,000, prepared with the aid of a few drops of hydrochloric acid, precipitates occurred as follows.

Potassium mercuric iodide	white precipitate
Potassium cadmium iodide	white precipitate
Potassium bismuth iodide	dark brown precipitate
Picric acid	yellow precipitate formed but dissolved
Lugol's solution	brown precipitate

In dilutions of 1-100,000 potassium mercuric iodide and Sonnenschein's reagent both still produced a slight cloudiness.

As far as could be determined from melting points and color reactions there are present in Dicentra canadensis at least four distinct alkaloids differing from any so far described in chemical literature.

Approved ..... Richard Fischer .....

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