TRANSACTIONS.

I.—*The Chemistry of Strophanthidin, a Decomposition Product of Strophanthin.* By THOMAS R. FRASER, M.D., F.R.S., and LEONARD DOBBIN, Ph.D.

(Read 7th December 1891.)

In a paper on the Chemistry and Pharmacology of *Strophanthus hispidus*, it was pointed out by one of us that when strophanthin, the glucosidal active principle present in the seeds and several other parts of this plant, is subjected to the action of dilute acids, it yields, among other products, a crystalline body—strophanthidin. A brief description was also given of processes by which this body may be prepared, and of several of its characters and chemical properties.*

The chemistry of strophanthidin will be more fully described in the present paper.

Preparation.—Strophanthidin may conveniently be prepared by allowing a 5% solution of strophanthin, or of pure extract of *Strophanthus*, in 1·5 or 2% sulphuric acid to stand at the ordinary temperature for a few days. When this is done, the originally nearly clear solution soon becomes hazy, the haziness gradually increases during the following day or two, and then the solution again becomes clear, much glucose is found to be present in it, and a deposit forms, which consists, for the most part, of crystals. The crystals are usually sufficiently large to be apparent to the naked eye,† but sometimes they are so minute that their crystalline form is recognisable only when they are magnified. They are slightly coloured when prepared from the extract, but are almost colourless when prepared from strophanthin.

Crystalline strophanthidin may be produced in the cold not only by the action of dilute sulphuric acid, but also of dilute hydrochloric, nitric, phosphoric, acetic, oxalic, and hydrocyanic acid. It is, however, more rapidly produced by these acids at a temperature of from 50° to 78° C., when it often appears in the form of long friable needles, from six to ten millimetres in length; but at higher temperatures, an amorphous coloured substance, and not an almost colourless crystalline body, is obtained.

By the above process, so much as 37% of crystalline strophanthidin has been obtained

* *Trans. Roy. Soc. Edin.*, vol. xxxv. part iv. pp. 1004–1017.

† *Ibid.*, pl. vii. fig. 10.

from strophanthin, and 30% from the extract, although more frequently the extract yielded from 20 to 25%.

In order to effect the complete decoloration of the crystals, from whatever source they have been obtained, they may be washed with distilled water and digested for a few hours with a little pure charcoal in a hot rectified spirit solution. The filtered hot solution deposits, on cooling, colourless crystals of considerable size, which continue to form on the spontaneous evaporation of the solution. The crystals consist of four-sided, apparently monoclinic, prisms, terminated either by the end faces alone, or also by pyramidal faces. To ensure the absolute purity of the product, it may several times be recrystallised from alcohol, or precipitated by petroleum ether or by water from a concentrated solution in alcohol, or in several of the other solvents afterwards to be mentioned.

General Characters.—The crystals are easily broken down in a mortar, but the particles are somewhat adhesive, and may even form a friable paste during trituration. A solution in water is neutral in reaction, and a moderately persistent froth is produced when it is shaken. A saturated watery solution is strongly, though not intensely, bitter; and slight bitterness can be perceived also in a solution of one part in sixty thousand.

Solubilities.—Unlike strophanthin, strophanthidin is insoluble in glycerine, very slightly soluble in cold water, only moderately soluble in rectified spirit, and more soluble in absolute than in dilute alcohol. Absolute alcohol and acetone, however, dissolve a larger quantity of it than of strophanthin. It resembles strophanthin in being insoluble in olive oil.

The results of determinations of its solubility in various liquids, at the ordinary temperature, are as follows:—

Absolute ethyl alcohol (sp. gr. '796)	.	1 in	30, or 3·3	per cent.
Acetone	.	„	35, or 2·85	„
Rectified spirit (sp. gr. '838)	.	„	47, or 2·1	„
Amyl alcohol (sp. gr. '820)	.	„	165, or 0·606	„
Chloroform (sp. gr. 1·497)	.	„	690, or 0·1449	„
Distilled water	.	„	2150, or 0·0465	„
Ethyl ether (sp. gr. '723)	.	„	2196, or 0·0455	„
Ethyl ether (sp. gr. '730)	.	„	2222, or 0·045	„
Petroleum ether (boiling below 50° C.)	.		Absolutely insoluble.	

Its solubility in several of these liquids, as for example in rectified spirit, is much increased by elevating the temperature. After hot saturated solutions in alcohol have become cool, and have ceased to deposit strophanthidin, they hold in solution a larger quantity than alcohol is capable of dissolving without the aid of heat.

Strophanthidin is precipitated by petroleum ether from solution in absolute alcohol, acetone, rectified spirit, amyl alcohol, ethyl ether, and chloroform; and by water from solution in absolute alcohol and rectified spirit. Precipitation is, however, only slowly produced in rectified spirit and ethyl ether solutions. The precipitates, either imme-

diately or after the lapse of several hours, assume the form of broad or needle-shaped rhombic crystals, which are bright and translucent.

Ethyl ether, which so readily precipitates strophanthin from solution in ethyl and amyl alcohol and in acetone, fails to precipitate strophanthidin when dissolved in these liquids; nor is it precipitated by ethyl alcohol, acetone, amyl alcohol, or chloroform, from solution in any of the liquids in which its solubility was determined. Weak alcoholic solutions are rendered hazy by the addition of water, even when the quantity of added water is itself more than sufficient to dissolve the strophanthidin present; and a similar change is produced in watery solutions by the addition of a little rectified spirit.

Melting point.—Strophanthidin melts at between 170° and 171° C., with incipient decomposition and the disengagement of bubbles of gas. When heated on platinum foil over a Bunsen's burner, it suddenly liquefies, bubbles of gas are profusely disengaged, combustion takes place with a bright flame, and very quickly the whole substance entirely disappears. No decided odour is evolved during the heating and burning.

Specific Rotation.—It possesses positive rotation in alcoholic solution. One gramme dissolved in 50 c.c. of rectified spirit (sp. gr. 0.838) was found to have a specific gravity of 0.85, and, with a 5 decimetres column, it produced a rotation of $+4^{\circ} 7'$, which corresponds with a specific rotation of $+41^{\circ} 12'$.

It was found that the specific rotation of strophanthin, in the same conditions, is $+14^{\circ}$.

Elementary Analysis.—When crystallised from rectified spirit, strophanthidin does not lose weight at 100° C. It does not contain nitrogen. When heated for two hours at 100° C. in 2 per cent. sulphuric acid, it is converted into a brown resin-like substance, but no glucose appears in the solution. A carefully purified specimen, recrystallised from rectified spirit, when subjected to ultimate analysis, yielded the following results, in two combustions:—

1.	0.1134 gramme yielded CO_2 ,	0.2746 gramme,	=	66.04 per cent.	C.
	„	„ H_2O , 0.0857	„	= 8.39	„ H.
2.	0.1150 gramme yielded CO_2 ,	0.2793	„	= 66.23	„ C.
	„	„ H_2O , 0.0866	„	= 8.36	„ H.

These percentages correspond with the formula $\text{C}_{14}\text{H}_{22}\text{O}_4$.

	Found (average of two analyses).	Calculated for $\text{C}_{14}\text{H}_{22}\text{O}_4$.
Carbon, .	66.13 .	66.14 per cent.
Hydrogen, .	8.37 .	8.66 „
Oxygen (by subtraction),	25.50 .	25.2 „

In the absence of knowledge regarding the constitution of strophanthidin, the formula $\text{C}_{14}\text{H}_{22}\text{O}_4$ may, therefore, provisionally be adopted.

Reactions of Dry Strophanthidin.

1. When **strong sulphuric acid** was placed in contact with a little finely powdered strophanthidin, an immediate orange red colour was produced, and slowly a bluish-green colour appeared at the margins. In 40 minutes the green colour had extended itself, and soon afterwards it had entirely displaced the red. The green, in its turn, slowly faded, and the whole then assumed a faint brownish-yellow tint, which persisted for several hours. After the addition of strong sulphuric acid had developed an orange-red colour, the subsequent addition of nitric acid immediately changed the colour to dusky yellow, which slowly faded to pale brownish-yellow.

When strophanthidin, moistened with strong sulphuric acid, was slowly heated between 42° and 45° C., the orange-red first produced became a yellowish-red with a slight green tint at the margins, then altogether greenish-yellow, and finally brown.

2. Contact in the cold with **dilute sulphuric acid** (10 per cent.) failed to develop any colour within half an hour. On now heating gradually to 48° C., yellowish-green appeared at the margins and yellow at the centre; the green soon became very dark until it was almost black, and the yellow at the centre changed to brown; and in about an hour and a half the whole assumed a brownish-black colour.

3. **Strong nitric acid** produced in the cold merely a very faint brown tint, which appeared only after prolonged contact, but remained unchanged for several hours. On the addition of strong sulphuric acid, the very faint brown tint immediately became pinkish-yellow, which very soon changed to greenish-yellow.

When strophanthidin was mixed with strong nitric acid, and placed in an air chamber with a temperature of 43° C., which was gradually raised to 52° , in one minute a faint pink tint appeared, which very soon changed to brownish-yellow, and in a few minutes to pale yellow, which slowly deepened in hue until a deep yellow, almost gamboge, was developed. The last colour remained for more than an hour and a half.

4. **Dilute nitric acid** (10 per cent.) produced no change in the cold. When, however, the temperature was slowly raised to 47° and 48° C., a light orange colour was speedily produced, which persisted for several hours.

5. Contact in the cold with **strong hydrochloric acid** merely caused the particles of strophanthidin to become slightly brown, even when the contact was continued for several hours.

On slowly heating to from 43° to 48° C. with strong hydrochloric acid, yellow appeared at the edges and gradually spread over the whole surface of the mixture, and this yellow colour remained for several hours, during which the heating was continued.

6. **Dilute hydrochloric acid** (10 per cent.) produced no change in the cold.

On heating between 47° and 48° C., an orange colour was produced, which persisted for several hours.

7. **Strong sulphuric acid** and bichromate of potassium produced a crimson colour, which

passed slowly into brown with patches of green, and then the whole gradually became very pale brown.

8. Strong sulphuric acid and chlorate of potassium produced a crimson colour, which soon became pale reddish-yellow.

9. Phosphomolybdic acid very slowly developed a pale greenish-blue colour. When an alkali was added along with or after the phosphomolybdic acid, a blue colour was immediately developed.

10. After contact with strong sulphuric acid had developed the usual orange-red colour in powdered strophanthidin, exposure to the vapour of bromine rapidly deepened the colour to a dark salmon-red, in which the undissolved particles of strophanthidin appeared black; and, soon afterwards, the salmon-red became dusky red, and the dusky red, after several hours, changed to green.

11. Solution of potash, soda, ammonia, lime, and baryta, and of carbonate of potash and carbonate of soda failed to produce any colour change; and negative results were also obtained on the addition of iodic acid and starch, of hydrobromic acid and starch, and of nitric acid followed by stannous chloride.

Reactions of Solution of Strophanthidin in Water (saturated, 1 : 2000).

1. Solution of iodide of potassium and of potassio-mercuric iodide produced a light brown colour, and when this had been developed, the addition of starch solution produced the usual blue reaction indicative of free iodine.

2. When to a drop of the strophanthidin solution, placed on a white porcelain slab, a drop of very dilute solution of ferric chloride was added, and then a drop of strong sulphuric acid, a yellow colour was immediately produced, and, on stirring, a faint pink tinge appeared, and in a few seconds the mixture became almost colourless.

Negative results were obtained on the addition of solutions of chloride of gold, nitrate of silver, platinic chloride, cobaltous chloride, acetate and subacetate of lead, mercuric chloride, cupric sulphate, tannic acid, picric acid, ferric chloride, metatungstate of sodium, hydrobromic acid, bromide of potassium, tribromide of potassium and Nessler's reagent.