

The most striking observation, however, was the absence of convulsions in the desiccated dogs, and the presence of severe, spastic convulsions in those with water.

Conclusions:

Dogs, desiccated through water-starvation, when given large doses of insulin developed a more severe anhydremia than the dogs which had water.

Convulsions were not observed in the desiccated animals although they invariably appeared in the others.

Glucose did not prevent the death of the water-starved dogs. The non-desiccated animals immediately recovered after glucose administration.

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### The emetic action of strophanthidin in cats with denervated hearts.

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Strophanthidin is a cleavage product derived by hydrolysing hispidus or Kombé strophanthin. It can also be obtained from cymarin, an active principle of *Apocynum cannabinum*.<sup>1</sup> Its empirical formula,<sup>2</sup> as lately established, is  $C_{23}H_{32}O_6 \cdot \frac{1}{2} H_2O$ . Jacobs and Collins have, moreover, thrown much light upon its structural makeup.<sup>3</sup> Pharmacologically, strophanthidin has been but little studied.

As we have already pointed out,<sup>4</sup> this substance has marked emetic properties. It also acts upon the heart in a manner essen-

<sup>1</sup> Windaus and Hermanns, *Ber. der deutsch. chem. Ges.*, 1915, xlviii, 979, 991.

<sup>2</sup> Jacobs and Heidelberger, *J. Biol. Chem.*, 1922, liv, 253; Thoms and Unger, *Zeit. f. angewand. Chem.*, 1924, xxxvii, 721.

<sup>3</sup> Jacobs, *J. Biol. Chem.*, 1923, lvii, 553, 569; Jacobs and Collins, *ibid.*, 1924, lix, 713, and lxiii, 123.

<sup>4</sup> Dresbach and Waddell, *J. Pharm. and Exp. Therap.*, 1924, xxiii, 152.

tially like that of the strophanthins from which it is derived, when given in suitable doses.

Since strophanthidin is either quite rapidly eliminated from, or destroyed in, the animal body, its emetic action can be advantageously observed repeatedly on the same individual animal. For this purpose, we have used cats (and a few dogs). We have found that emesis occurs promptly after any of the usual modes of injection (except, perhaps, by mouth), but we have employed the intraperitoneal route for the most part, confirming the results by intravenous injections. The average intraperitoneal dose is 0.20 mg. per kg.

The research here reported deals mainly with emesis in cats with partially and completely denervated hearts, though we have previously tested the substance on a large number (more than sixty) of normal cats. The operations performed and the number of animals used were as follows: 13 bilateral stellate ganglion excisions; 7 unilateral vagotomies, 2 double vagotomies; 12 double vagotomies with bilateral stellate ganglion excisions (extrapleural method); 9 bilateral vagotomies with bilateral (intra-thoracic) stellate ganglion excision, together with removal of most of the thoracic sympathetic chain; 5 additional operations of this sort, with removal of the middle cervical ganglia also, thus insuring absolute denervation of the heart; 3 spinal cord sections at level of 7th vertebra; 3 decerebrations.

In the work recently done in order to insure complete denervation of the heart, we have carried out the operations in several stages and have had the animals in good condition, a few being able to eat and retain food after the final vagus section. With one exception, in which only nausea was produced, all of the cats in the above series vomited after injections of strophanthidin intraperitoneally, and in those cases in which intravenous injections could be used the results were also positive. The cats with spinal cord sections were no exceptions, though this operation seriously interferes with the vomiting act. Nevertheless, it rules out the probability of strophanthidin acting on any visceral end organ to produce reflex vomiting.

We conclude that this substance does not bring about emesis by acting on some afferent structure in the heart, or at least not wholly in this way. In the light of our experiments its seat of action is more probably the vomiting center. Other phases of the action of strophanthidin are being investigated.