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## Detoxification of Dendrobine by 'Sodium Amytal'.

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Work in this laboratory<sup>1, 2</sup> has demonstrated that 'Sodium Amytal' (Sodium Iso-amyl Ethyl Barbiturate, Lilly) can save rabbits poisoned with 35 minimal lethal doses of strychnine sulphate, 40 minimal lethal doses of picrotoxin, and 45 minimal lethal doses of coriamyrtin. In cocaine poisoning, only 4 minimal lethal doses can be antidoted by the same hypnotic, and this requires almost simultaneous administration of the convulsant subcutaneously and the barbiturate intravenously.<sup>3</sup> In view of the fact that dendrobine, an alkaloid of the Chinese drug Chin-shih-hu (a species of *Dendrobium*),<sup>4</sup> causes convulsions of central origin,<sup>5</sup> it was thought interesting to find out whether or not there was any antagonism between dendrobine and 'Sodium Amytal'.

Our preliminary experiments were made in mice by mixing and injecting subcutaneously the calculated doses of dendrobine hydrochloride and 'Sodium Amytal'. One per cent solution of each was employed. As shown in Table I, the minimal lethal dose of dendrobine HCl by subcutaneous injection is 120 mg. per kg., as contrasted with 20 mg. by vein.<sup>5</sup> By the addition of 'Sodium Amytal', at least 2½ minimal lethal doses of dendrobine HCl (300 mg. per

TABLE I.  
Detoxification of Dendrobine by 'Sodium Amytal' in Mice by Subcutaneous Injection.

Dendrobine HCl	'Sodium Amytal'	No. of Mice Used	No. of Mice Died
mg. per kg.	mg. per kg.		
110	0	5	0
120	0	4	4
150	0	1	1
120	75	5	2
180	75	3	0
240	75	5	5
240	100	5	1
300	100	8	3
360	100	5	3
360	125	5	5

<sup>1</sup> Swanson, E. E., *J. Lab. and Clin. Med.*, 1933, **18**, 933.

<sup>2</sup> Swanson, E. E., and Chen, K. K., *J. Pharm. and Exp. Therap.* (in press).

<sup>3</sup> Swanson, E. E., *J. Lab. and Clin. Med.*, 1932, **17**, 325.

<sup>4</sup> Chen, K. K., and Chen, A. L., *J. Biol. Chem.*, 1935, **111**, 653.

<sup>5</sup> Chen, K. K., and Chen, A. L., *J. Pharm. and Exp. Therap.*, 1935, **55**, 319.

kg.) were detoxified. Apparently, the optimal dose of 'Sodium Amytal' in the detoxification of dendrobine in mice, in the manner described, is 100 mg. per kg.

The next series of experiments were carried out in rabbits (gray chinchilla) by giving dendrobine HCl subcutaneously. Upon the appearance of the first convulsion, 'Sodium Amytal' was injected intravenously, and repeated when convulsions reappeared. The strength of solution of each substance was 10% in water. The initial dose of the barbiturate was 25 mg. per kg. ( $\frac{1}{2}$  of the minimal anesthetic dose), and all subsequent doses were reduced to 12.5 mg. per kg. ( $\frac{1}{4}$  of the minimal anesthetic dose). From Table II, it may be seen that the subcutaneous minimal lethal dose of dendrobine HCl in rabbits is 100 mg. per kg., as compared with 17 mg. by intravenous injection.<sup>5</sup> By repeated administration of 'Sodium Amytal,' convulsions ceased, rapid breathing diminished, and 3 out of 4 animals recovered from 500 mg. of dendrobine HCl per kg. of body weight (5 minimal lethal doses). The remaining rabbits, except one, all died from doses amounting to 600 or more mg. per kg., in spite of treatment.

TABLE II.  
Detoxification of Dendrobine by 'Sodium Amytal' in Rabbits.

Rabbit No.	Sex	Body Wt.	Dendrobine HCl (Subcutaneous)	'Sodium Amytal' (Intravenous)	Result
		kg.	mg. per kg.	mg. per kg.	
1	—*	2.355	90	0	survived
2	—*	2.200	90	0	"
3	—*	2.730	90	0	died
4	—*	2.071	90	0	"
5	—*	1.584	90	0	survived
6	—*	1.800	100	0	died
7	—*	2.340	100	0	"
8	—*	2.570	100	0	"
9	M	1.350	200	50.0 in 3 doses	survived
10	F	1.847	400	62.5 " 4	"
11	M	1.500	500	25.0 " 1	died
12	F	1.640	500	50.0 " 3	survived
13	F	1.670	500	75.0 " 5	"
14	F	1.641	500	75.0 " 5	"
15	F	1.300	600	50.0 " 3	"
16	M	1.634	600	62.5 " 4	died
17	F	1.416	600	50.0 " 3	"
18	F	1.740	600	37.5 " 2	"
19	M	1.435	700	62.5 " 4	"
20	F	1.602	800	50.0 " 3	"
21	F	1.528	1000	37.5 " 3	"

\*Not recorded.

*Summary.* 'Sodium Amytal' detoxifies dendrobine. In rabbits it can antidote 5 minimal lethal doses of the alkaloid after definite signs of intoxication have been observed.