accurate comparisons of various cardiac principles in frogs, it has been our custom to recalculate the dose by proportion as if every batch of frogs has the same minimal systolic dose to ouabain, namely, 0.0005 mg. per Gm. In the present work no such correction was made because the main point of interest was to find the difference of sensitivity between frogs and toads.

In the previous paper (1), it was shown that the toad was 150 times more tolerant to *G*-strophanthin than the frog. The ratio was redetermined with a new lot of ouabain-Merck (*G*-strophanthin), and it was found, as shown in Table I, to be 1:77, practically one-half of the former figure. It is difficult to account for the discrepancy of results at present, except to mention that the former tests were carried out in the fall, and the present ones in the spring although both were made at 20° C.

SUMMARY.

The nebulous toad, *Bufo valliceps*, has a natural tolerance to cardiac glycosides as well as alkaloids. When compared with the common frog, *Rana pipiens*, it is 167 times less sensitive to cymarin, and 58 times less sensitive to coumingine hydrochloride. In the present investigation it is also found that the ratio of susceptibility to ouabain between the same species of the frog and the toad is 1:77 as contrasted with that of 1:150 reported previously.

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DIGITALIS ASSAY BY THE CAT METHOD UNDER "SODIUM AMYTAL" ANESTHESIA.*

BY WILLIAM E. FRY AND EDWARD E. SWANSON.[1]

In the assay of digitalis by the Hatcher-Brody Cat Method (1), the question of anesthesia has been a problem of much discussion. Rowe (2) and Chopra and Chowhan (3) suggested the substitution of chlorobutanol in place of ether, assuming that this would not affect the size of the cat unit. Epstein (4) found that paraldehyde lowered the resistance of the cat to digitalis. With ether, chlorobutanol, urethane, chloralose and paraldehyde, David and Rajaminchan (5) observed that the choice of anesthetic was of much importance in the results of the cat unit. Haskell (6) noted a larger cat unit with dial-urethane anesthesia. With urethane, Edmunds, Moyer and Shaw (7) reported more of an increase in the cat unit for the U. S. P. Standard Powder than with ether, and concluded that the effect of anesthetics has a marked influence upon the amount of digitalis in the cat unit. Bauer and Fromherz (8) in the assay of ouabain obtained a larger cat unit with allylisopropyl barbituric acid than with ether.

EXPERIMENTAL.

In the present work, experiments were carried out with two short-acting barbituric acid derivatives as anesthetics. The compounds used were "Sodium Amytal" (Sodium Iso-amyl

* Scientific Section, A. PH. A., New York meeting, 1937.

[1] Eli Lilly & Co., Research Laboratories.

Ethyl Barbiturate, Lilly) and "Seconal" (Sodium Propyl-methyl-carbinyl Allyl Barbiturate, Lilly). As previously reported (9), (10), (11), "Seconal" has a smaller minimal anesthetic dose (M. A. D.), a smaller minimal lethal dose (M. L. D.), and a distinctly shorter duration of action than "Sodium Amytal." In cats, intraperitoneally, the M. A. D. was 70 mg. per Kg. for "Sodium Amytal" and 35 mg. per Kg. for "Seconal."

The digitalis preparations used in these experiments were the U. S. P. Standard Digitalis Powder and two tinctures of digitalis U. S. P. With each preparation, not less than forty-eight cats were used, sixteen under ether and sixteen under each of the barbituric acid compounds. All females were non-pregnant and non-lactating. The barbituric acid derivatives were injected intraperitoneally. In each experiment the blood pressure was recorded.

As shown in Table I, and summarized in Table II, under ether anesthesia the average fatal dose of a 10 per cent solution of the U. S. P. Standard Digitalis Powder is 0.0558 Gm. per Kg. With "Seconal" anesthesia, the U. S. P. Standard has an average fatal dose of 0.0685 Gm. per Kg. as against 0.0777 Gm. per Kg. under "Sodium Amytal" anesthesia.

TABLE I.—COMPARISON OF TWO BARBITURIC ACID DERIVATIVES WITH ETHER IN THE DIGITALIS ASSAY IN CATS.

Drug.	Ether.				Anesthetic. "Seconal."				"Sodium Amytal."			
	Cat No.	Sex.	Weight. Kg.	Fatal Dose. Gm. per Kg.	Cat No.	Sex.	Weight. Kg.	Fatal Dose. Gm. per Kg.	Cat No.	Sex.	Weight. Kg.	Fatal Dose. Gm. per Kg.
U. S. P. Standard Powder Digitalis, 10% Solution in 80% Alcohol.	201	F	1.738	0.0587	217	F	2.475	0.0715	233	F	1.950	0.0815
	202	F	1.828	0.0459	218	F	2.010	0.0896	234	F	1.979	0.0879
	203	F	1.787	0.0520	219	F	2.000	0.0810	235	F	1.856	0.0792
	204	F	2.300	0.0509	220	F	1.710	0.0509	236	F	2.270	0.0687
	205	F	2.167	0.0581	221	F	2.320	0.0582	237	F	2.222	0.0810
	206	F	1.885	0.0597	222	F	2.495	0.0643	238	F	1.946	0.0748
	207	F	2.310	0.0591	223	F	2.068	0.0689	239	F	1.820	0.0808
	208	F	2.310	0.0526	224	F	2.168	0.0747	240	F	1.900	0.0726
	209	M	2.137	0.0660	225	M	2.780	0.0680	241	M	2.455	0.0733
	210	M	2.585	0.0441	226	M	2.212	0.0854	242	M	2.664	0.0698
	211	M	2.451	0.0575	227	M	2.487	0.0784	243	M	2.563	0.0720
	212	M	2.820	0.0691	228	M	2.535	0.0615	244	M	1.956	0.0840
	213	M	2.556	0.0528	229	M	2.496	0.0553	245	M	1.908	0.0849
	214	M	2.091	0.0545	230	M	2.393	0.0577	246	M	2.773	0.0800
	215	M	1.971	0.0533	231	M	2.591	0.0533	247	M	2.220	0.0831
	216	M	2.328	0.0586	232	M	2.559	0.0668	248	M	2.535	0.0704
			Average	0.0558			Average	0.0685			Average	0.0777
Tincture Digitalis U. S. P. A.	249	F	2.295	0.0497	265	F	1.820	0.0725	281	F	2.256	0.0718
	250	F	2.976	0.0489	266	F	1.839	0.0571	282	F	2.595	0.0566
	251	F	2.050	0.0644	267	F	2.155	0.0529	283	F	1.825	0.0986
	252	F	1.961	0.0474	268	F	2.281	0.0566	284	F	2.096	0.0558
	253	F	2.289	0.0472	269	F	1.955	0.0775	285	F	2.190	0.0657
	254	F	2.356	0.0420	270	F	2.197	0.0643	286	F	1.680	0.0786
	255	F	1.679	0.0608	271	F	2.119	0.0792	287	F	2.112	0.0625
	256	F	2.275	0.0527	272	F	2.545	0.0737	288	F	2.130	0.0662
	257	M	2.403	0.0449	273	M	2.169	0.0650	289	M	1.880	0.0798
	258	M	2.072	0.0637	274	M	2.581	0.0744	290	M	2.663	0.0676
	259	M	2.204	0.0408	275	M	2.058	0.0751	291	M	2.696	0.0612
	260	M	2.375	0.0559	276	M	2.640	0.0682	292	M	2.055	0.0788
	261	M	2.098	0.0536	277	M	2.720	0.0704	293	M	2.669	0.0539
	262	M	2.246	0.0628	278	M	2.910	0.0752	294	M	1.960	0.0627
	263	M	2.514	0.0596	279	M	1.805	0.0598	295	M	2.645	0.0749
	264	M	2.565	0.0456	280	M	2.098	0.0715	296	M	1.691	0.0798
			Average	0.0524			Average	0.0684			Average	0.0696

Tincture Digitalis U. S. P. B.

297	F	1.636	0.0623	313	F	2.128	0.0916	331	F	2.446	0.0944
298	F	1.922	0.0601	314	F	1.921	0.0734	332	F	2.095	0.0759
299	F	2.394	0.0514	315	F	2.720	0.0684	333	F	2.475	0.0715
300	F	1.803	0.0524	316	F	2.302	0.0730	334	F	2.024	0.0741
301	F	2.489	0.0596	317	F	2.720	0.0684	335	F	2.000	0.0750
302	F	1.912	0.0706	318	F	2.295	0.0680	336	F	2.915	0.0664
303	F	2.381	0.0623	319	F	2.172	0.0753	337	F	2.311	0.0753
304	F	2.404	0.0624	320	F	2.347	0.0575	338	F	1.980	0.0818
305	M	1.785	0.0504	321	M	2.491	0.0915	339	M	2.754	0.0980
306	M	2.776	0.0567	322	M	2.041	0.0661	340	M	2.125	0.0918
307	M	2.399	0.0714	323	M	1.976	0.0760	341	M	1.748	0.0971
308	M	2.300	0.0620	324	M	2.842	0.0855	342	M	2.704	0.0739
309	M	2.248	0.0647	325	M	2.052	0.0935	343	M	2.435	0.1041
310	M	2.263	0.0497	326	M	2.993	0.0631	344	M	2.510	0.0705
311	M	2.774	0.0595	327	M	1.817	0.1024	345	M	2.888	0.0727
312	M	2.067	0.0581	328	M	2.488	0.0687	346	M	2.843	0.0971
...	..	...	....	329	M	1.891	0.0872	...	..	...	....
...	..	...	....	330	M	2.365	0.0749	...	..	...	....
		Average	0.0596			Average	0.0764			Average	0.0824

TABLE II.—SUMMARY OF RESULTS.

Digitalis.	Ether. Average Fatal Dose. Gm. per Kg.	"Seconal" Average Fatal Dose. Gm. per Kg.	"Seconal" Difference between "Seconal" and Ether. Gm. per Kg.	Anesthetic. Increase over Ether. Per Cent.	"Sodium Amytal." Average Fatal Dose. Gm. per Kg.	"Sodium Amytal." Difference between "Sodium Amytal" and Ether. Gm. per Kg.	Increase over Ether Per Cent.
U. S. P. Standard Powder	0.0558	0.0685	0.0127	22.7	0.0777	0.0219	39.0
Tincture A	0.0524	0.0684	0.0160	30.5	0.0696	0.0172	32.8
Tincture B	0.0596	0.0764	0.0168	28.3	0.0824	0.0228	38.2

For the tincture of digitalis U. S. P. sample A, the average fatal dose under ether anesthesia is 0.0524 Gm. per Kg. With "Seconal" anesthesia, the average fatal dose is 0.0684 Gm. per Kg. With the same tincture under "Sodium Amytal," the average fatal dose is 0.0696 Gm. per Kg.

The tincture of digitalis U. S. P. sample B under ether anesthesia has an average fatal dose of 0.0596 Gm. per Kg. With "Seconal" and "Sodium Amytal" anesthesia, the average fatal doses are 0.0764 and 0.0824 Gm. per Kg., respectively.

As summarized in Table II, under "Seconal" anesthesia, it required 0.0127 Gm. per Kg. (22.7 per cent) more of the U. S. P. Standard Digitalis Powder than when ether was used, and 0.0219 Gm. per Kg. (39 per cent) more under "Sodium Amytal" anesthesia. For tincture A, with "Seconal" anesthesia, 0.0160 Gm. per Kg. (30.5 per cent) more was necessary to cause death and 0.0172 Gm. per Kg. (38.2 per cent) more with "Sodium Amytal" than under ether anesthesia. Sample B tincture with "Seconal" and "Sodium Amytal" anesthesia required 0.0168 Gm. per Kg. (28.3 per cent) and 0.0218 Gm. per Kg. (38.2 per cent) more, respectively, than when ether was used. Thus, both barbituric acid derivatives, more marked with "Sodium Amytal" than with "Seconal," increased the amount of digitalis required to kill more than ether, or the size of the cat unit depends upon the anesthetic employed.

CONCLUSIONS.

(1) As anesthetics, in the assay of digitalis by the cat method, two short-acting barbituric acid derivatives were compared with ether.

(2) When the cats were anesthetized with the barbituric acid compounds, it required more digitalis to kill than with ether.

(3) The size of the cat unit for digitalis varies with the anesthetic agent used.

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A CRITICAL STUDY OF THE TANNIN-BEARING GALENICALS.*[1]

BY S. W. ARNETT[2] AND C. O. LEE.[3]

This study was undertaken for the purpose of finding answers to several problems which have been raised concerning the official tannin-bearing galenicals. The objectives for this investigation briefly were as follows:

1. To determine the effects of the changes in menstrua, as specified in the recent revisions of the United States Pharmacopœia and National Formulary, upon the permanency, astringency and total extractive of the official tannin-bearing galenicals.
2. To determine the effect of precipitation upon the astringency of these galenicals.
3. To find out whether there is any correlation between the astringency, total extractive and precipitation in such preparations.
4. To determine whether precipitation in such galenicals can be prevented by the use of selective menstrua or other means.
5. Most important of all, perhaps, to determine whether these products can be reliably assayed for tannin.

THE ESTIMATION OF THE PRECIPITATE.

The sixteen galenicals which were studied are given in Table I and are arranged in the increasing order of the weights of their precipitates. The amounts shown here were obtained from 50-cc. sealed ampul samples of each of the preparations which had stood for five months. At the end of this period the ampuls were opened, the precipitate collected in Gooch crucibles and dried to constant weight.

An attempt was made to estimate the relative amounts of precipitates which formed in these preparations by examining liter portions of them after they had stood in Erlenmeyer flasks for about four months. Variations in the densities, and other physical differences in the precipitates, makes such readings difficult, especially when so many different drugs are involved.

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[2] National Formulary Fellow, of the AMERICAN PHARMACEUTICAL ASSOCIATION, 1936–1937.

[3] Professor of Pharmacy, Purdue University, School of Pharmacy.