There is relatively little difference between data concerning fasting and non-fasting patients. This difference concerns the adults predominantly. No significant relationship was found between the blood sugar and the delta activity in a group of 17 subjects of different ages. However, none of these subjects showed a blood sugar below 60 mg % and only 2 presented values above 100 mg %. After glucose injection the delta activity is suppressed or reduced more in adolescents and adults than in children. Subjects with disturbances of carbohydrate metabolism (hypoglycemia, and particularly Addison's Disease) show a great amount of delta activity during hyperventilation,[3] and a slow decrease of this activity with age. Subjects with symptomatic epilepsy generally show a higher amount of delta activity (with shorter latent time) than patients with idiopathic epilepsy. In symptomatic epilepsy the decrease of the slow activity with advancing age is slower than in Groups (1) and (3). Some subjects more than 40 years of age and suffering from organic cerebral diseases (Group 4), show, during hyperventilation, an unusually high increase in delta activity for their age.

On a semi-logarithmic scale the amount of delta activity was plotted against age for the following groups: 1. spontaneous delta activity in epileptics, 2. induced delta activity in (a) non-epileptics, (b) idiopathic epilepsy, (c) symptomatic epilepsy, (d) patients with hypoglycemia, (e) after glucose injection. All curves obtained converge to the same point corresponding to the maximum possible delta activity (100% delta time) and to the age of about 3 years.

Summary. There is a definite relationship between the age and the amount of slow activity during hyperventilation in epileptic and non-epileptic patients. An analogous relationship to age was found for the spontaneous delta activity of patients with idiopathic epilepsy.

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K-Strophanthin-β, K-Strophanthoside, Periplocymarin, and Periplocin.

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From the pioneer work of Arnaud[1] to the elaborate investigation of Brauns and Clossen,[2] the only crystalline principle believed to

[3] Engel, G. L., and Margolin, S. G., to be published.

occur in the seeds of *Strophanthus kombe* was K-strophanthin. It was Jacobs and Hoffmann[3] who demonstrated the latter to be a mixture of cymarin (K-strophanthin-α) and K-strophanthin-β. Recently, Stoll, Renz, and Kreis[4] corroborated Jacobs and Hoffmann's results and, in addition, reported the isolation of a new glycoside, K-strophanthoside.

Periplocin is a digitalis-like principle first obtained by Lehmann[5] from the bark of *Periploca graeca*. Jacobs and Hoffmann,[6] by treating the extract of the same plant with the enzyme strophanthobiase, were able to crystallize periplocymarin. Lately, Stoll and Renz[7] isolated periplocin and revised its empirical formula. They also showed that by splitting a molecule of glucose under the influence of strophanthobiase, periplocin yielded periplocymarin.

According to our previous publication,[8] it seems that a glycoside containing one sugar molecule (monoside) such as convallatoxin is more potent than a bioside such as scillaren A, and that a bioside in turn is more potent than a trioside such as digitoxin. If this were the case, on account of the following chemical relationships, K-strophanthin-β would be expected to be more active than K-strophanthoside, and periplocymarin more active than periplocin:

K-strophanthoside ⟶ K-strophanthin-β + glucose
↓
Strophanthidin + glucose + cymarose

Periplocin ⟶ Periplocymarin + glucose
↓
Periplogenin + cymarose

To test the validity of such a hypothesis, the present investigation was undertaken.

The samples of K-strophanthoside, K-strophanthin-β, and periplocin were generously supplied by Dr. Arthur Stoll, Basel, Switzerland. The specimen of periplocymarin was the same as that used in a previous report.[9] The latter, apparently, had lost its alcohol of crystallization upon standing since there was no decrease in weight

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[8] Chen, K. K., Chen, A. L., and Anderson, R. C., *J. Am. Pharm. A.*, 1936, **25**, 579.

[9] Chen, K. K., Anderson, R. C., and Robbins, E. B., *J. Am. Pharm. A.*, 1938, **27**, 113.

when heated in high vacuum. Stock solutions of 1:1000 with 47.5% of ethyl alcohol by volume were prepared with each substance, and dilutions were made from them in saline.

Two methods of assay were adopted—the U.S.P. frog method[10] and the cat method as described previously.[11] The advantage of employing two methods is the mutual confirmation of results—at least qualitatively. In order to minimize the effect of secular variation, each pair of substances, namely, K-strophanthin-β and K-strophanthoside, and periplocymarin and periplocin, was studied simultaneously in the same lots of cats and frogs, and by the same observers. Furthermore, comparable concentrations of the drugs were used. Thus, a solution of 1:10,000 of K-strophanthin-β and

TABLE I.
Comparison of Median Systolic Doses in Frogs.

Compound	Dose, γ per g	No. in systole / No. of frogs used	SD_{50} ± Standard error, γ per g
K-Strophanthin-β 1:10,000	0.60	1/5	0.982 ± 0.043
	0.70	1/5	
	0.80	1/10	
	0.90	1/5	
	1.00	6/15	
	1.10	12/15	
	1.20	12/15	
	1.30	9/10	
	1.40	9/10	
	1.50	4/5	
K-Strophanthoside 1:10,000	0.80	1/5	1.341 ± 0.099
	1.00	2/5	
	1.10	2/10	
	1.20	0/10	
	1.30	6/10	
	1.40	8/10	
	1.50	3/5	
	2.00	4/5	
Periplocymarin 1:4,000	2.00	1/5	3.161 ± 0.115
	2.50	0/15	
	3.00	4/15	
	3.50	8/10	
	4.00	10/10	
Periplocin 1:4,000	1.50	0/5	2.815 ± 0.112
	2.00	0/15	
	2.25	2/10	
	2.50	5/15	
	3.00	6/10	
	3.50	8/10	
	4.00	5/5	

[10] U. S. P. XI, 1936, 397.

[11] Chen, K. K., Anderson, R. C., and Robbins, E. B., *J. Pharm. and Exp. Therap.*, **1940, 69**, 279.

TABLE II.
Comparison of Mean Lethal Doses in Cats.

Compound	Cat No.	Sex	Body wt, kg	Heart wt, g	Fatal dose by: Body wt, γ per kg	Fatal dose by: Heart wt, γ per g	Mean lethal dose ± standard error: Body wt, γ per kg	Mean lethal dose ± standard error: Heart wt, γ per g
	2	F	2.200	8.0	132.7	36.5		
	3	F	1.916	7.8	132.3	32.5		
	7	M	2.049	7.9	124.9	32.4		
	8	F	2.302	9.1	127.3	32.2		
K-Strophanthin-β	11	F	2.652	9.9	127.1	34.0	128.2	33.4
	12	M	2.150	8.7	134.0	33.1	± 3.1	± 0.5
	13	M	2.007	8.0	139.5	35.0		
	16	M	2.657	9.5	112.9	31.6		
	19	M	2.362	8.1	113.5	33.1		
	20	M	2.198	9.2	141.9	33.9		
	1	F	1.700	6.6	210.6	54.2		
	4	F	2.363	8.6	191.7	52.7		
	5	M	2.681	8.1	158.1	52.3		
	6	F	2.263	7.5	218.7	66.0		
K-Strophanthoside	9	F	2.630	10.7	141.1	34.7	186.5	50.8
	10	M	1.884	7.9	246.0	58.7	± 11.1	± 2.9
	14	F	2.243	9.2	195.7	47.7		
	15	M	2.560	8.5	142.2	42.8		
	17	F	2.270	8.1	176.7	49.5		
	18	F	2.159	8.2	213.1	56.1		
	27	M	1.972	6.7	133.9	39.4		
	29	M	2.235	9.6	112.8	26.2		
	32	F	2.509	10.4	157.8	38.1		
	33	F	2.756	8.6	112.1	35.9		
Periplocymarin	36	M	2.136	6.8	163.4	51.3	156.1	40.3
	37	F	2.349	9.3	212.8	53.8	± 10.5	± 2.7
	39	F	2.490	9.2	185.5	50.2		
	40	M	2.287	9.6	177.5	42.3		
	41	F	2.133	8.7	155.2	38.0		
	42	F	2.524	12.6	180.3	36.1		
	23	F	2.746	10.2	123.1	33.1		
	24	F	2.403	10.1	126.3	30.0		
	25	F	2.030	8.7	127.6	29.8		
	26	F	2.212	8.5	140.8	36.6		
Periplocin	28	F	2.674	9.3	114.8	33.0	120.5	31.7
	30	F	2.093	7.9	116.6	30.9	± 6.0	± 1.3
	31	F	2.257	9.3	114.5	27.8		
	34	M	2.752	8.2	91.2	30.6		
	35	M	2.695	10.6	102.8	26.1		
	38	F	2.469	9.6	161.2	41.5		

K-strophanthoside, and one of 1:4000 of periplocymarin and periplocin, were administered to frogs; and a dilution of 1:100,000 of each of the 4 substances was injected intravenously into cats at the rate of 1 cc per minute.

The results are summarized in Tables I and II. As postulated, K-strophanthin-β, a bioside, proves to be more potent than K-stro-

phanthoside, a trioside, by the comparison of the median systolic doses in frogs, and the mean (geometric) lethal doses in cats based on either body weight or heart weight. The differences are highly significant statistically. On the other hand, periplocin, a bioside, shows a tendency of having a stronger action than periplocymarin, a monoside. The difference in frogs approaches significance at the 5% point, and in cats the difference is definitely significant. The median emetic doses in pigeons by intravenous injection of periplocin and periplocymarin showed a similar relationship as disclosed in a previous note.[11]

The above data clearly indicate that the cardiac action of a glycoside does not necessarily decrease as the number of sugar molecules increases. The position of linkage, perhaps, partly determines the potency of the product. It will require an investigation of many other compounds of the same type before any generalization can be safely made.

Summary. K-Strophanthin-β is more potent than K-strophanthoside in frogs and cats, while periplocymarin is less potent than periplocin. The decrease in the number of sugar molecules of a cardiac glycoside, therefore, may or may not be accompanied by an increase in activity.

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Substituted Sulfanilamidopyrimidines.*

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Experimental[1, 2] and clinical[3, 4, 5] bacterial chemotherapeutic activity has been reported for 2-sulfanilamidopyrimidine (sulfadiazine). Modification of the pyrimidine portion of this compound, without concurrent loss of chemotherapeutic effectiveness, appears possible

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