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EFFECT OF CARDIAC GLYCOSIDES ON POTASSIUM CONTENT OF SKELETAL MUSCLE OF RANA PIPIENS

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Introduction

To the surprise of many clinicians, cardiac glycosides affect tissues other than cardiac muscle. This paper is intended to be a preliminary report concerning the effect of certain cardiac glycosides on the potassium content of amphibian skeletal muscle.

Methods

In the experiments where whole-leaf digitalis was used, the material was prepared as follows: a quantity of dried powdered whole leaf digitalis (S. B. Penick and Co., Chicago) was placed in a beaker with a quantity of modified Ringer's solution (Aronson, 1954). The mixture was slowly brought to a boil; it was allowed to stand, covered, at room temperature for 72 hours, and the solution was filtered and stored under refrigeration until needed.

Where percentages are indicated they refer to the amount of the prepared digitalis solution in Ringer's solution. In those experiments where the frogs are said to be digitalized, the frogs had been injected intraperitoneally with 1.25 cc. of the undiluted digitalis solution per 20 gms. of body weight. It had previously been determined that 2.5 cc. of the digitalis solution per 20 gms. of frog weight represented the L.D. 60 of this preparation.

Where digitoxin was the agent to be tested, the solution was made up in Ringer's solution in proportion to the human digitalizing dose of 1.25 mgm/70 kgm. body weight. The muscle was then equilibrated in this solution. Where a fraction of the digitalizing dose was indicated, the aforementioned solution was diluted with an appropriate amount of Ringer's solution.

The gastrocnemius muscle of the frog was excised and then equilibrated in Ringer's solution for one hour. After equilibration, the muscle was placed either in the Ringer's solution containing the material tested or in fresh Ringer's solution for two hours in the case of the controls.

Muscles from digitalized frogs were treated as though they were weighed. Muscles were then placed in a 50% solution of trichloroacetic acid for at least 24 hours. The denatured tissue and the solution, in which it had been bathed, were blended in a Waring blender. The volume of the blend was measured. An aliquot of the homogenate was diluted to determine the potassium content with a Coleman flamespectrophotometer model No. 21. The potassium content was calculated in terms of mEq.K/kgm. wet weight of muscle.

Results

The data are summarized in Table 1.

TABLE 1.—Effect of Cardiac Glycosides on Skeletal Muscle.

	No. muscles	mEqK/kgm.	S.D.	P
		whole leaf digitalis		
Control	22	62.2	13.8	.....
10% digitalis	12	44.9	10.9	>5%
5% digitalis	12	48.6	13.3	>5%
1% digitalis	14	76.6	9.9	>1%
		digitalized frogs		
Control	11	58.6	7.6	>0.1%
Digitalized frogs	11	78.0	5.9	.....
		digitoxin		
Control	13	70.9	14.8	.....
Digitalizing dose/4	13	70.0	21.3	.....
Digitalizing dose/2	13	90.4	20.0	>5%
Digitalizing dose/1	13	74.7	16.9	.....

DISCUSSION AND SUMMARY

One may conclude from the data in the table that there is an optimum concentration of cardiac glycosides which, when applied to skeletal muscle of frogs, will enhance the potassium content of this muscle. It is also apparent that when this level is exceeded, there is a loss of potassium from skeletal muscle. In Goodman and Gilman's text of pharmacology (1955), as well as in other pharmacology texts, there are statements indicating a rise in serum potassium following digitalization. These observations correlate quite well with the data presented and indicate a possible source of the excess potassium. No attempt is made at this time to set up any hypothesis concerning either the mechanism of action of digitalis or that through which potassium binding may be altered.

LITERATURE CITED

ARONSON, J. K. 1954. The influence of metabolic agents on the potassium content of frog muscle. State Univ. Iowa, doctoral thesis.

GOODMAN, LOUIS S., and ALFRED GILMAN. 1955. The pharmacological basis of therapeutics. New York, Macmillan Co., 1831 pp.