nale Innervation nicht auszuschliessen. In diesem Fall würde die Entladung eines Motoneurons bei einer bereits bestehenden Grundaktivität im Muskel nur Fasern erregen, die bisher nicht durch andere Neuronen aktiviert waren. Ein Anwachsen der kontraktilen Antwort würde in einem teilweise aktivierten Muskel mit weniger als einer ganzen motorischen Einheit zustandekommen. Das bedeutet eine Möglichkeit der Kontraktionsabstufung, die allerdings nur erfolgen kann, wenn beide an der Innervation beteiligten Motoneuronen synchron entladen.

Die multiple Innervation von Vocalisfasern steht ohne Zweifel in engem Zusammenhang mit den besonderen Leistungen dieses Muskels bei der Stimmbildung.

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Summary

In contrast to the narrow terminal innervation bands of human skeletal muscles, the vocal muscle shows a particularly extended region of synaptic contacts. A great number of muscle fibres receive two or more motor endings forming individual endplates at a distance of several hundred micra. The physiological significance would be a more rapid activation.

Relationship between the Effectiveness of Cardiac Glycosides in Cats and their Interference with Red Cell Potassium Transport

SOLOMON *et al.*[1] found that, with the exception of lanatoside-B and digoxigenin, the effectiveness of seven other cardiac glycosides in cats was proportional to their interference with red cell K 42 transport. Also KAHN *et al.*[2-4] noted that there is some resemblance between the relative potencies of the cardiac glycosides tested in inhibiting cation exchange in erythrocytes and their relative potency in producing a positive inotropic effect on the heart. WILBRANDT[5] had compared the potencies of ouabain, digitoxin, and digoxin and their dihydro derivatives on heart-lung preparation and on erythrocytes, from the data of KAHN[3] and VICK *et al.*[6], and came to the same conclusion. On the basis of these findings, we decided to exploit this correlation between the effects of cardiac glycosides on the heart and on cation transport in the red cell for a determination and control of potency of different cardiac glycosides. Because of the data published by SOLOMON *et al.*[1], that there are cardiac glycosides for which this relationship is not valid, we have decided to repeat the experiments on the incubated cold stored human erythrocytes with Lanatoside-B, and to add some cardiac glycosides not investigated up to now.

The effect of cardiac glycosides on the flux of potassium was measured as described previously[7] by a similar method used by KAHN *et al.*[2,3] on the human red cells first kept for 5 days at a temperature of 3°C, and after the addition of glucose and the investigated cardiac glycosides (convallatoxin, hellebrin, ouabain, k-strophanthine, digoxin, lanatoside-C, digitoxin, lanatoside-A, lanatoside-B) in four different concentrations, incubated at 37°C for 4 h. Serum potassium was measured in a Zeiss flame photometer.

For every glycoside a concentration-action curve was constructed as is shown in the Figure 1, expressing the relationship between the logarithm of concentration and

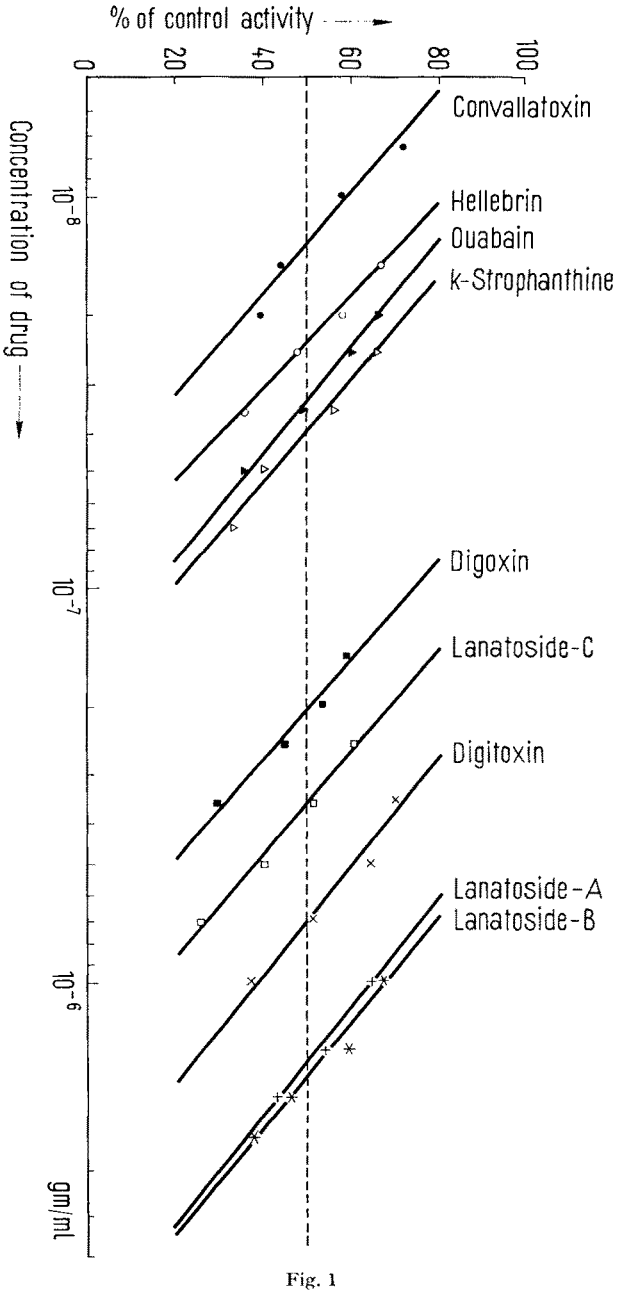

Fig. 1

the % of control activity of each glycoside determined by comparing the values of serum potassium after adding the glycoside used with the control value after adding the same medium in which the glycoside was dissolved[2,3].

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Every point in the Figure 1 represents an average of at least four experiments. Because in the previous experiments[2,3,7] the linear relationship between the logarithms of concentrations and % control activities in the explored region and the parallelism of these curves was demonstrated, it was possible to express the relative potencies of cardiac glycoside as a distance between the curves on the ordinate 50, that is as a potency index 50. We compared the pI 50 of the different cardiac glycosides with their mean lethal doses in the cat expressed in mg/kg[8]. It may be noted from the Figure 2 that there is a direct relationship between the mean lethal doses and pI 50 of the cardiac glycosides, the correlation coefficient being 0.99 ($p = 0.001$). In contrast to the findings of SOLOMON *et al.*[1], this direct relationship is valid also for the lanatoside-B, when investigated on cold-stored erythrocytes.

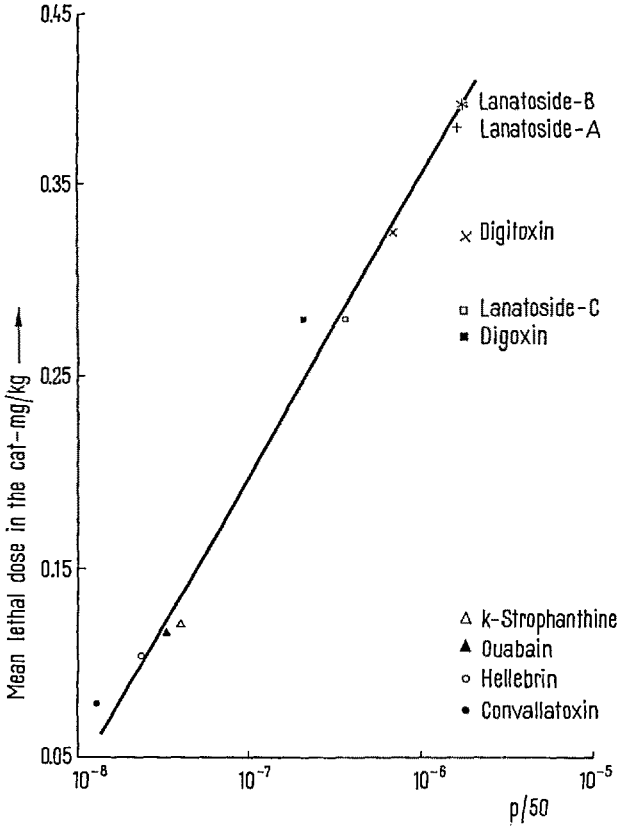

Fig. 2

On the basis of our results and those of the other authors[1-3,6], we suppose that the determination of the doses of cardiac glycosides necessary to produce a 50% blockade of the active potassium reentry into the incubated red cells may be used for evaluating potencies of the glycosides investigated. If the hypothesis about the mechanism of the cardiotonic action of cardiac glycosides by influencing the electrolyte metabolism should prove correct, the proposed method would actually be specific. At the same time, our results support this hypothesis. The quantity of the glycoside that is necessary to determine its potency is minimal and the method is relatively simple and inexpensive. In contrast to the methods currently used of evaluating the effectiveness of cardiac glycosides on animals, which are characterised by a great variability of results, we did not see a similar variability in the case of the method described.

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Zusammenfassung

Bei neun untersuchten Herzglykosiden konnte eine direkte Beziehung zwischen der Kardiotoxizität und dem Grad der Beeinflussung des aktiven Kaliumtransportes festgestellt werden.

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[9] The able assistance of Mrs. G. TÓTHOVÁ is gratefully acknowledged. Statistical analysis of the data was performed by Ing. R. ŠTUKOVSKÝ. Digitoxin, ouabain, and *k*-strophanthine were kindly supplied by E. Merck A.G., digoxin by C. F. Boehringer & Söhne GmbH and Lanatoside-A,- B, -C by Richter Gedeon.

Further Observations on the Effects of Selenium and Antioxidants on Exudative Diathesis in Chicks

The ability of trace amounts of dietary selenium to replace vitamin E under some experimental conditions has raised questions about the metabolism of the biologically active form of this element[1]. It is well established that some selenium compounds will completely replace vitamin E in preventing exudative diathesis in the chick[2,3], but there has, to our knowledge, so far been no information on the tissue storage of the biologically active selenium compound(s). Therefore, we have examined how long the protection by selenium against exudative diathesis would last after selenium was removed from the diet. Also, in continuation of previous studies[4] on the replacement of vitamin E by antioxidants, two substances not previously tested in this laboratory have been examined.

Two vitamin E-free basal diets, differing primarily in the protein source, were used. Diet 2304 contained 60% Torula yeast 3N (Lake States Yeast Corporation, Rhinelander, Wisconsin), 3% gelatine, 5.17% salt mixture no. 4[5], 0.1% B vitamin mixture[5], 0.2% choline chloride, and 31.53% sucrose. Diet 2343 contained 30% of isolated soybean protein (ADM Assay Protein C-1, Archer-Daniels-Midland), 5.17% salt mixture no. 4[5], 0.1% B vitamin mixture[5], 0.2% choline chloride, 1% lard, and 63.53% sucrose. The diets were supplemented with 1 mg% dicalcium salt of 2-methyl-1,4-naphthohydroquinone diphosphoric acid ester (Synkavit «Roche»). Vitamins A and D_3 in aqueous solution[6] were given orally twice weekly. Dayold chicks (New Hampshire × White Leghorn) were fed a commercial starter ration for the first week and then placed in groups of 9 or 10 and given the experimental diets. They were examined daily for exudates.

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