THE EFFECT OF SULFHYDRIL GROUPS ON VERATRINE SENSITIZATION OF MUSCLE TO THE ACTION OF POTASSIUM

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Bacq [6] has published reports which show that veratrine causes a marked increase in the sensitivity of the striped muscle of amphibia to potassium ions. This interesting phenomenon has been subsequently confirmed for a number of substances which are nowadays classified as belonging to the alkaloids of the Veratrum group [7].

P. E. Dyablova [1] has shown that the sensitizing action of veratrine is not shown if the concentration of calcium ions in the Ringer solution is increased, and that there are chemical agents which can depress the sensitivity of muscles to calcium (e.g. novocain). Kh. S. Koshtoyants [2], in his experiments, has shown that the sensitivity of invertebrate (mollusc) smooth muscle to potassium is markedly increased by preliminary treatment with acetylcholine.

In the present article, we report the results of experiments carried out to reveal the role of the sulfhydril groups of protein complexes in the sensitizing action of veratrine.

The experiments represent a follow-up of the first experiment in this direction, which consisted of special investigations, showing that the typical picture of the time course of the contraction and the relaxation of veratrine treated muscle, which occur in response to the action of an electrical stimulus, do not take place when the sulfhydril groups are blocked, but reappear when these groups are reformed (L. S. Bunkina's experiments).

Also, in our laboratory, we have repeatedly demonstrated the dependence of the sensitivity of various muscles as well as chemoreceptors on the condition of the sulfhydril groups [3, 5]. It was shown in special experiments, that the increase in the sensitivity of denervated muscles to chemical stimulators also depends on changes in the concentration of the free sulfhydril groups which occurs at a definite time after the denervation [4]. From among the results reported, we must note that Sevag [8], in his theory of allergy, especially stresses the fact that the formation of sulfhydril and disulfide groups, by interacting with the tissue proteins and foreign substances, forms the basis of the increased sensitivity.

METHODS

The experiments were carried out on the rectus abdominis muscle of the frog. As is well known, when potassium chloride acts on this muscle, a contraction occurs which passes off after washing the solution away with Ringer. In order to induce veratrine sensitization of the muscle to the action of potassium we used a concentration of veratrine of $1 \cdot 10^{-6}$. To block the sulfhydril groups, we used a solution of cadmium chloride in a concentration of $1 \cdot 10^{-3}$; to regenerate the sulfhydril groups, a 1 in $5 \cdot 10^{-2}$ solution of unithiole was used.

The experiments were carried out simultaneously on the two recti muscles of a single frog; one muscle was used for the experiment, and the other as control. Both muscles were first treated with the same concentration

of potassium chloride, which gave about the same muscular contraction, and after this one muscle was treated with a solution of veratrine (control), and the other was treated simultaneously with sol :tion of veratrine and cadmium chloride. The time of action of the solutions in both control and experimental muscles was 10 minutes.

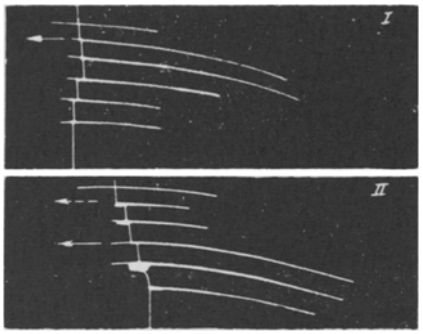

Fig. 1. Veratrine sensitization of the action of potassium (I); absence of veratrine sensitization of potassium action on blocking sulfhydril groups with cadmium chloride (II, first arrow) and subsequent restoration of veratrine sensitization of the action of potassium after regeneration of the sulfhydril groups by unithiole (II, second arrow), in both cases (I and II) the first contraction represents the response of the muscle before treatment with veratrine

RESULTS

In the control, as was to be expected, there was a sharp increase in the effect of potassium in the presence of veratrine, i.e. there was veratrine sensitization(Fig. 1). In this case, when the veratrine acted on the muscle at the same time as the cadmium chloride, the sensitivity of the muscle to the same concentration of potassium chloride was markedly reduced, or remained unchanged, i.e. there was no veratrine sensitization (Fig. 2, first arrow).

If the sulfhydril preparation unithiole acts for 10 minutes on a veratrinized muscle which has been treated with cadmium chloride, then for a given concentration of potassium chloride, there is a considerable increase in the contraction (Fig. II, second arrow), i.e. the veratrine sensitization has been restored. The restoration by means of the sulfhydril preparation unithiole of the veratrine sensitization destroyed by cadmium chloride indicates the part played by the sulfhydril groups in the sensitizing effect of veratrine. Consequently, sensitization to the effect of potassium ions on a muscle does not take place if the muscle is treated simultaneously with solutions of veratrine and cadmium chloride. Veratrine sensitization of a muscle treated simultaneously with veratrine and cadmium chloride can be restored by treating the muscle with a solution of the sulfhydril preparation unithiole.

The results give reason to suppose that the sulfhydril groups of proteins play a particular part in veratrine sensitization. This action is associated with the part played by the sulfhydril groups in the integration of the protein structures.

SUMMARY

If the muscle is simultaneously treated with veratrine and cadmium chloride solutions there is no veratrine sensitization effect of potassium ion action on the muscle. This sensitization may be reestablished after the treatment of the muscle with unithiol, the sulfhydryl preparation solution.

A conclusion is drawn that the sulfhydryl group of protein bodies play a definite role in the sensitization of potassium ions on the muscles with veratrine. This is connected with the special part played by the sulfhydryl groups in the integration of the protein structures.

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