PHARMACOLOGY

CHARACTERISTICS OF THE BATHMOTROPIC ACTION OF STROPHANTHIN

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Because of the conflicting nature of data in the literature on the action of the cardiac glycosides on the excitability of the heart [4, 5, 7], and the inadequacy of methods used to study this problem, it was decided to investigate the bathmotropic action of strophanthin by means of a phasing device making it possible to determine the threshold of excitability in a strictly determined phase of the cardiac cycle.

EXPERIMENTAL METHOD

The bathmotropic action of strophanthin was studied by means of a device consisting of a phasing apparatus, a two-channel electrocardiograph, and an electronic stimulator [3]. The phase device, working in isolation, was triggered off by the R wave of the ECG, which was recorded by means of a plate electrode from the surface of the ventricle. Test stimuli of increasing strength (duraction of impulse 0.01 msec, voltage 1-30 V, time lag of impulse behind R wave 0.43 sec) were applied by means of a silver needle electrode, inserted subepicardially into the base of the frog's heart until the appearance of an extrasystolic complex. Introduction of the electrode beneath the epicardium abolished the usually observed fluctuations in the threshold of excitability associated with drying of the heart surface and possible movement of the electrode. The experiments were carried out on the frog's heart in situ with simultaneous recording of the ECG and the amplitude and frequency of the cardiac contractions. The excitability of the myocardium was studied in the initial state and 5, 15, 30, and 45 min after administration of the preparations.

The effect of strophanthin on the excitability of the frog's myocardium was studied in doses of 0.2, 0.4, and 1.0 mg/kg. In order to analyze the bathmotropic action of strophanthin, its effect on the excitability of the heart (in a dose of 0.2 mg/kg) was investigated after atropinization (20 mg/kg), and also after administration of dihydroergotoxin (3 mg/kg). The preparations were injected subcutaneously. When both drugs were used together, they were injected at the same time. Altogether 61 experiments were carried out.

EXPERIMENTAL RESULTS

In a preliminary series of experiments on intact frogs, the excitability of the myocardium and the amplitude and frequency of the cardiac contraction were found to vary only very slightly during the period of observation (see figure, curve 7).

Strophanthin in a toxic dose (0.4 mg/kg) caused a persistent increase in the threshold of excitability, reaching its maximum after 30 min (curve 6). In three frogs of this series of experiments, the heart stopped in systole after 45 min. A toxic effect was also observed in the experiment in which strophanthin was given in a dose of 1.0 mg/kg and in which a considerable fall was observed in the threshold of excitability (by 61.4% after 30 min; curve 8). Asynchronous contractions of the individual areas of the ventricular myocardium and arrest of the heart in systole could be seen visually in all the experiments after 35 min. Strophanthin, in toxic doses, thus caused a sharp increase in the level of excitability of the myocardium. In a conventionally therapeutic dose (0.2 mg/kg), strophanthin raised the threshold of excitability in all the experiments (by 36.8% after 30 min; curve 1), and increased the amplitude (by 7.8%) and slowed the rhythm (by 7.8-26.3%) of the cardiac contraction.

To discover in more detail the mechanism of the bathmotropic action of strophanthin, two series of experiments were carried out to study the action of strophanthin (0.2 mg/kg) after the preliminary administration of atropine and of dihydroergotoxin.

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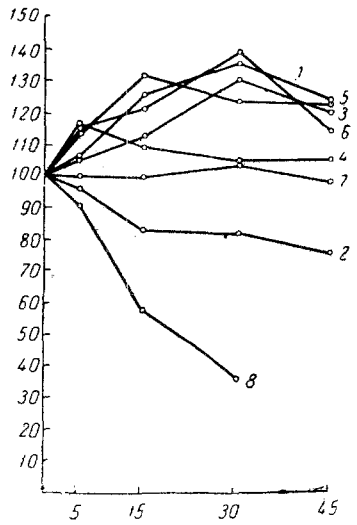

Effect of strophanthin on the excitability of the frog's myocardium. Along the axis of abscissas—time (in min); along the axis of ordinates—changes in the threshold of excitability (in percent of initial level). 1) Strophanthin (0.2 mg/kg); 2) atropine (20 mg/kg; 3) strophanthin (0.2 mg/kg) + atropin (20 mg/kg); 4) dihydroergotoxin (3 mg/kg); 5) strophanthin (0.2 mg/kg) + dihydroergotoxin (3 mg/kg); 6) strophanthin (0.4 mg/kg); 7) intact frogs; 8) strophanthin (1 mg/kg).

The results of the control group of experiments in which atropine was injected (20 mg/kg) showed that after atropinization the threshold of excitability was lowered (curve 2), and the amplitude and rhythm of the cardiac contractions were increased.

When strophanthin was injected against a background of atropinization, its bathmotropic action was essentially unchanged (curve 3).

After administration of dihydroergotoxin (3 mg/kg) the negative bathmotropic effect of strophanthin was practically unchanged (curve 5), its positive effect on the amplitude of the cardiac contractions was more marked, whereas, the characteristic negative chronotropic action of the glycoside was replaced by tachycardia.

The experimental results described above show that strophanthin, in small doses, lowers the excitability of the frog's myocardium, while at the same time increasing the amplitude of the cardiac contractions and slowing their rhythm. The toxic action of strophanthin is characterized by a sharp increase in excitability, which may be associated with a deficiency of K^+ ions in the myocardium [6]. The negative bathmotropic effect of strophanthin after the preliminary administration of atropine was not significantly changed, although there are reports in the literature that atropine causes a marked increase in its toxicity in experiments on albino mice [2].

The partial blocking of the adrenergic systems of the heart by dihydroergotoxin, which, from the results of experiments on the isolated cat's heart, possesses an amphoteric effect on the lability of the myocardium [1], also left the character of the action of the glycoside on the excitability of the heart practically unchanged. The presence of the negative bathmotropic action of strophanthin during inhibition of the adrenergic systems and following administration of atropine demonstrates the leading role of the direct influence of the glycoside on the excitability of the heart.

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