Effects of Tinuvin 770 on the rate and force of contraction in isolated guinea-pig atria

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Method

White Pirbright guinea-pigs (Tif:DHP; SPF) of either sex, weighing 335-450 g were used. The hearts were excised under urethane anaesthesia (1.5 g/kg i.p.) and the atria dissected. The experiments (N=4) were performed on right spontaneously beating and left, electrically stimulated atria. Stimulation was effected by unipolar square-wave pulses (5 msec, 2.5 Hz) at a voltage up to 50% higher than the threshold. The atria were mounted under isometric conditions with a resting tension of 0.5 g. The rate of the right atrium and the force of contraction of the left atrium were recorded continuously on a Hellige multichannel recorder. The organ-bath contained Krebs-Henseleit solution of the following composition (mmol/l): NaCl 119; KCl 4.8; $CaCl_2$ 2.5; KH_2PO_4 1.2; $MgSO_4$ 1.2; $NaHCO_3$ 24.8; glucose 10. It was maintained at 32°C and saturated with a mixture of 95% O_2 and 5% CO_2.

Tinuvin 770, dissolved in DMSO and DMSO/H_2O mixtures, respectively, was administered to the bath in cumulative doses at intervals of 10 minutes (final concentrattions in the organ-bath: 0.001 - 10 µmol/l). The effects of the highest concentration, 10 µmol/l, were followed for 30 minutes.

Results

In isolated guinea-pig atria, Tinuvin 770 was without effect on force and rate of contraction in concentrations of 0.001 - 1 µmol/l and led to a clear-cut reduction of both parameters with 10 µmol/l. The decrease of force and rate of contraction was already evident after 10 min., but was more pronounced after 20 and 30 minutes (s. table).

Discussion

Calcium antagonists of different chemical classes (eg. nifedipine, verapamil, diltiazem) reduce force and rate of contraction, which are calcium-dependent processes, in isolated guinea-pig atria.

Since Tinuvin 770 had a high affinity to calcium channels in receptor binding studies, it can be assumed that its effects in isolated guinea-pig atria are due to the calcium-antagonistic property of the compound. Tinuvin 770, however, was about 10-times less potent in this test system than diltiazem, a calcium-antagonist of relatively low potency.

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Preparation	Concentration	Time	Force of Contraction[1)]	Rate of Contraction[2)]
	µmol/L	min	Percent changes from initial values (inital values given in brackets)	
Tinuvin 770 (N = 4)	0.001	10	- 1 ± 1 (2.16 ± 0.13 g)	- 0 ± 2 (132 ± 17 bpm)
	0.01	10	- 2 ± 1	- 1 ± 2
	0.1	10	- 4 ± 1	- 2 ± 3
	1	10	- 7 ± 1	- 6 ± 2
	10	10	- 18 ± 1	- 45 ± 10
		20	- 27 ± 2	- 52 ± 8
		30	- 32 ± 2	- 61 ± 8

Values given are mean ± SEM; N = number of experiments
1) In electrically driven (2.5 Hz) left atria
2) In spontaneously beating right atria