ROLE OF PROSTAGLANDINS IN THE REGULATION OF CATECHOLAMINE UPTAKE BY THE MYOCARDIUM

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The study of the effect of prostaglandin E_1 (PG-E_1) on catecholamine uptake by homogenates of albino rat myocardium showed that in concentrations of 2×10^{-6}M PG-E_1 considerably inhibits the uptake of adrenalin and causes some decrease in the uptake of noradrenalin by the heart muscle. Neither PG-E_1 nor PG-A_1 (in concentrations of between 2×10^{-10} and 2×10^{-6}M) had any effect on interaction between troponin and noradrenalin: The intensity of luminescence of troponin in the presence of noradrenalin was unchanged on the addition of PG-E_1 and PG-A_1. The ability of PG to reduce catecholamine uptake by the myocardium is not due to its effect on the interaction between troponin and catecholamines, but depends on different mechanisms.

KEY WORDS: prostaglandins; catecholamine uptake; myocardium; troponin.

One of the most important yet, at the same time, the least studied aspects of the mechanism of action of prostaglandins (PG) on cardiac function is the relationship between PG and other endogenous physiologically active substances in their action on heart muscle.

From this standpoint the study of the mechanisms of interaction of PG and catecholamines is particularly interesting, for PG is known to have a role in the regulation of noradrenalin secretion [6, 9], and prostaglandins E_1 and F_{2a} are known to reduce the uptake of endogenous adrenalin by the myocardium of the rabbit heart [2, 5]. Meanwhile the blocking of biosynthesis of endogenous PG by indomethacin has been shown to intensify the uptake of both exogenous (in experiments on rabbits) and endogenous (in experiments on rats compelled to undertake physical exertion) adrenalin by the myocardium [2, 5].

This paper describes the results of experiments to study the mechanisms of the effect of prostaglandins on the uptake of catecholamines by heart muscle.

EXPERIMENTAL METHOD

The effect of PG-E_1 on the uptake of adrenalin and noradrenalin by the albino rat myocardium was studied in 40 experiments in vitro. In these experiments male albino rats weighing 190-200 g were decapitated, the heart was quickly removed, the myocardium of the left ventricle (100 mg) was homogenized at 0-4°C with 1 ml of incubation medium, the volume of incubation medium was then adjusted to 3 ml, adrenalin or noradrenalin was added, and the sample was incubated for 45 min at 37°C with constant agitation. The incubation medium consisted of phosphate buffer of the following composition (in mM): NaCl 98, KCl 2.7, $MgSO_4 \cdot 7H_2O$ 1.2, KH_2PO_4 4, $Na_2HPO_4 \cdot 2H_2O$ 17.5, glucose 10. Adrenalin or noradrenalin was added to the incubation medium in a final concentration of 1×10^{-5}M, and PG-E_1 in final concentrations of 2×10^{-6} and 5×10^{-6}M was added only to the experimental homogenates 5 min before the addition of adrenalin or noradrenalin. The concentration of catecholamines in the myocardium was determined spectrofluorometrically [3] using a Farrand (USA) spectrofluorometer.

Considering that unlike other proteins (albumin, myosin, actomyosin), troponin interacts with adrenalin and noradrenalin [4], the effect of PG-E_1 and PG-A_1 on interaction between troponin and noradrenalin was studied by determining the intensity of luminescence of a solution of troponin [4]. Troponin was isolated from fresh rabbit heart muscles [7] and the purity of the troponin preparations was verified by electrophoresis in polyacrylamide gel [8]. The experimental results were subjected to statistical analysis.

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TABLE 1. Effect of PG-E_1 on Uptake of Adrenalin and Noradrenalin by Homogenates of Albino Rat Myocardium (M ± m)

Uptake of adrenalin, %			Uptake of noradrenalin, %		
Control (n = 6)	in presence of PG-E_1 ($2 \cdot 10^{-6}$M) (n = 7)	in presence of PG-E_1 ($5 \cdot 10^{-6}$M) (n = 7)	Control (n = 6)	in presence of PG-E_1 ($2 \cdot 10^{-6}$M) (n = 7)	in presence of PG-E_1 ($5 \cdot 10^{-6}$M) (n = 7)
92±1,6	57±8,8*	58±2,6*	95±1,4	83±3,2*	84±1,5*

*P < 0.05 compared with control.

Legend. Results expressed as percentages of concentration of endogenous catecholamines in tissue.

The adrenalin and noradrenalin used in the experiments were from Calbiochem (Sweden) and the crystalline preparations of PG-E_1 and PG-A_1 were from Upjohn (USA). The PG was dissolved immediately before use by the method described previously [1].

EXPERIMENTAL RESULTS

The results (Table 1) show that PG-E_1 (2×10^{-6} and 5×10^{-6}M) considerably inhibit the uptake of adrenalin and, to a lesser degree, of noradrenalin by homogenates of the albino rat myocardium. No appreciable difference was found in the action of PG-E_1 in the two concentrations tested, and it is evident that PG-E_1, in a concentration of 2×10^{-6}M, already exerts it maximal action on catecholamine uptake. Analysis of the effect of PG-A_1 and PG-E_1 on the interaction between troponin and noradrenalin showed that neither PG-E_1 nor PG-A_1, in concentrations of between 2×10^{-10} and 2×10^{-6}M, affects this interaction: In the presence of noradrenalin (0.8 μg/ml) PG-E_1 and PG-A_1, in the concentrations mentioned above, did not change the intensity of luminescence of troponin (concentration of the troponin solution 0.25 mg/ml, pH 7.4, wavelength of excitation 280 nm).

Data in the literature indicating that catecholamines are firmly bound by the troponin of muscles [4] suggests that adrenalin or noradrenalin has a direct effect on the troponin-like Ca-binding proteins in the myocytes.

It can also be submitted that the inotropic effects of catecholamines may take place through their direct action on troponin, which may perhaps play the role of receptor for adrenalin and noradrenalin [4]. The absence of any effect of PG on interaction between troponin and catecholamines, despite their very strong effect on the uptake of catecholamines by the myocardium, suggests that the ability of PG to reduce the uptake of catecholamines by the myocardium and to prevent their excessive accumulation in heart muscle is not due to their effect on interaction of adrenalin or noradrenalin with troponin, but is realized by different mechanisms.

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