Activity of tyrosine hydroxylase in brains and dopamine-β-hydroxylase in hearts of rats after 17–20 weeks of vitamin E deficient diet

Enzyme	E+	E−
Tyrosine hydroxylase	100 ± 2.0%	108 ± 6.3%
Dopamine-β-hydroxylase	100 ± 0.5%	98 ± 0.6%

The activity of tyrosine hydroxylase in rat brain was estimated in vivo by measuring the formation of ^{3}H-catechols from 0.2 mg/kg of 3,5-^{3}H-tyrosine injected s.c. 1 h prior to decapitation[13,14]. The activity of dopamine-β-hydroxylase was assayed in vivo in the heart of pheniprazine (10 mg/kg)-pretreated rats by the formation of ^{14}C-octopamine from 0.07 mg/kg of 1-^{14}C-tyramine injected s.c. 1 h before[15,16]. For technical reasons tyrosine hydroxylase can hardly be assayed in the rat heart, and the dopamine-β-hydroxylase method is restricted to extracerebral tissues. The figures represent mean ± S.E. of at least 6 determinations.

which have been considered rate-limiting in norepinephrine synthesis[8,9]. Therefore, the decrease of norepinephrine in vitamin E deficiency might have other reasons, such as reduced availability of tyrosine for norepinephrine formation (e.g. by enhanced protein synthesis[12]), decreased decarboxylation of dopa, diminished uptake of norepinephrine in storage organelles, enhanced release or increased catabolism of norepinephrine. These possibilities are at present under investigation.

Zusammenfassung. Viermonatiger Vitamin-E-Mangel bewirkt bei Ratten einen etwa 25 prozentigen Abfall des Noradrenalin-Gehaltes in Gehirn und Herz, der durch DL-α-Tokopherol rückgängig gemacht wird. Die Abnahme des Noradrenalins erfolgt ohne gleichzeitige Verminderung der Tyrosin-Hydroxylase- und Dopamin-β-Hydroxylase-Aktivität.

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Effects of Disodium EDTA on the Cardiovascular Responses to Prostaglandin E_1

Recently, Coceani and Wolfe[1] found that the effect of prostaglandin E_1 (PGE_1) on the contractility of the rat stomach fundus strip was significantly potentiated in high calcium Tyrode solution. Hence, they postulated that PGE_1 initiates the pharmacodynamic action by the release of bound Ca or by the facilitation of Ca influx[1,2]. It has been shown that PGE_1 exerts a positive inotropic action in propranolol-treated dogs[3]. The present study was undertaken to examine whether the Ca chelating agent, disodium EDTA, would influence the cardiovascular effects of PGE_1 in dogs.

Seven male dogs weighing 20–24 kg were anesthetized with sodium pentobarbital (30 mg/kg). The technique used in this study has been described previously[3,4]. In open-chest dogs under artificial respiration, heart rate, mean systemic arterial pressure, and myocardial contractile force were measured continuously with an Electronics for Medicine tachometer (Model TDC-1), a Statham pressure transducer (Model P23AA) and a Walton-Brodie strain gauge arch[5], respectively. Disodium of EDTA was administered continuously at constant rates (2 and 5 mg/kg/min) using a Harvard perfusion pump (Model 600-900). A single dose (1 μg/kg) of PGE_1 was given i.v. prior to and after 15 min infusion of 2 and 5 mg/kg/min of EDTA.

The results of the effects of PGE_1 on the cardiovascular parameters are summarized in the Figure. As shown previously[3], the i.v. administration of 1 μg/kg of PGE_1 decreased mean systemic arterial pressure, and increased

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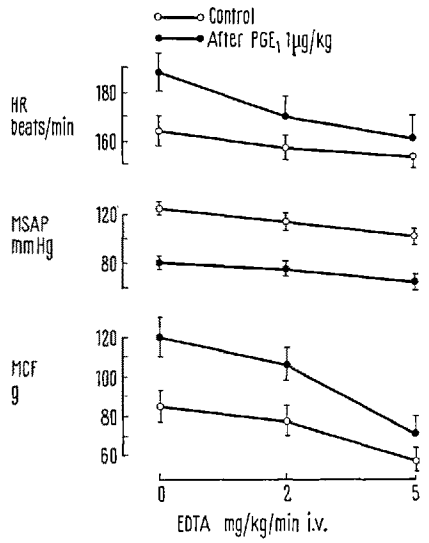
heart rate and myocardial contractile force in all dogs. The i.v. administration of EDTA decreased heart rate, mean systemic arterial pressure and myocardial contractile force essentially in proportion to the dose. As the dose of EDTA increased, the hemodynamic effects of the same dose (1 μg/kg) of PGE_1 decreased progressively except mean systemic arterial pressure. As seen in the Figure, the hypotensive effect of PGE_1 was not affected by the administration of EDTA.



Effects of the i.v. administration of PGE_1 (1 μg/kg) on heart rate (HR), mean systemic arterial pressure (MSAP) and myocardial contractile force (MCF) in 7 dogs before and during the continuous i.v. administration of disodium EDTA. Open and closed cycles denote the average values, respectively, before and after the administration of PGE_1. I-shaped bars denote standard errors of the means.

The present study shows that Ca chelation with EDTA causes decreases in positive chronotropic and inotropic actions of PGE_1. Presently, the precise underlying mechanisms of the effect of PGE_1 on the myocardial contractility are poorly understood. NAKANO and MCCURDY[3] found that the administration of propranolol did not modify the positive inotropic actions of PGE_1 in anesthetized dogs. The role of Ca on the pharmacodynamic actions of PGE_1 remains to be rather speculative at present. However, as described by COCEANI and WOLFE[1] on the gastric fundus strip preparations, this study also indicates that the cardiodynamic actions of PGE_1 could be influenced by the intracellular concentration or availability of Ca in dogs. In the present study, the administration of EDTA did not affect the hypotensive effect of PGE_1. The hemodynamic mechanism responsible for this cannot be explained satisfactorily. Since systemic arterial pressure is hemodynamically modified by 2 determinants, cardiac output and total peripheral resistance, it is conceivable that the 2 counteracting determinants may hemodynamically offset each other to possibly keep systemic arterial pressure unchanged in the present experiment. Further experimentations are necessary to elucidate the interaction between PGE_1 and Ca at subcellular levels.

Zusammenfassung. Die Wirkung des Dinatrium-EDTA auf die Kreislaufreaktionen des Prostaglandin E_1 (PGE_1) wurde an narkotisierten Hunden untersucht. Das Ausmass der positiv chronotropen und inotropen Einflüsse des PGE_1 war während der Infusion von EDTA bedeutend geringer als das des PGE_1 vor der EDTA-Gabe. Die Gegenwart oder das Einströmen von Kalziumionen scheint in der pharmakologischen Wirkung des PGE_1 eine Rolle zu spielen.

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On some Potassium-Like Qualities of the Thallium Ion

Univalent thallium compounds resemble potassium compounds in several respects. The chlorides of the 2 metals form mixed crystals. A number of minerals are known in which thallium can replace potassium. The ionic radii of the 2 metals are close to each other (K^+ 1.33 Å; Tl^+ 1.49 Å).

Though thallium had long been studied for its biological actions, it was only in the last decade that some of them could be convincingly shown to be potassium-like. MULLINS and MOORE[1] found that, similarly to potassium, thallium accumulated in muscle fibres and depolarized membranes. GEHRING and HAMMOND[2] produced evidence that thallium substituted for potassium in the same molar concentration activated adenosine triphosphatase. The present communication reports further investigations into the interrelations between thallium and potassium by examining their influence on muscular activity.

Isolated hearts mounted on Straub cannulas, and isolated rectus abdominis muscles of *Rana esculenta* were used. In the first few experiments using heart preparations, we worked with the poorly soluble thallium chloride; in all the others, with thallium nitrate dissolving readily in a Cl^--free medium. Two solutions were used: one contained NaCl, 6.43 g; KCl, 0.3 g; $CaCl_2$, 0.17 g; $NaHCO_3$, 0.36 g; glucose, 0.7 g, in 1000 ml of distilled water; the other was composed of $NaNO_3$, 9.35 g; KNO_3, 0.41 g; $Ca(NO_3)_2$, 0.25 g; $NaHCO_3$, 0.36 g; and glucose, 0.7 g, in 1000 ml of distilled water.

2–8 washings with a potassium-free solution arrested the activity of the isolated frog heart and 1 or 2 subsequent washings with a solution containing 4 m*M* of potassium restarted it. It could also be restarted with a solution in which 2 m*M* of thallium took the place of potassium. 4 m*M* of thallium in the solution stopped the heart beating. With potassium, 8 m*M* were not enough; a 12 m*M* concentration was required to arrest cardiac activity. The toxic effect both of potassium and thallium was found to

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