increase in overflow evoked by 30 mM K^+ was 4–5 × the basal level in slices compared with only 1.5–2 × the basal level in synaptosomes ($n > 12$).

PGE_2 (2.8×10^{-5} M) and indomethacin (5.6×10^{-5} M) were without effect on the spontaneous efflux of [^{3}H]-NA from slices, however the 30 mM K^+ evoked overflow was increased by indomethacin (5.6×10^{-6} M) to 139.3 ± 10.7% (mean ± s.e.) of control levels ($P < 0.05$) while PGE_2 (2.8×10^{-6} M) reduced the overflow to 70.5 ± 1.6% of control ($P < 0.001$). PGE_2 (5.6×10^{-6} M) and U46619 (2.85×10^{-6} M) also reduced the evoked overflow, but not significantly. Since indomethacin increased the overflow, endogenous PGs may normally limit NA release and thus could mask the effects of exogenous PGs. The effect of PGE_2 was, therefore, studied in preparations where endogenous PG synthesis was blocked throughout by indomethacin (5.6×10^{-5} M). PGE_2 (0.28, 1.4, 2.8, 5.6, 14.0 and 28.0×10^{-6} M) reduced the evoked overflow to 83.7 ± 5.1 (n.s.), 78.6 ± 5.6 (n.s.), 57.9 ± 16.2 ($P < 0.05$), 56.3 ± 1.8 ($P < 0.01$), 55.8 ± 9.8 ($P < 0.05$) and 60.7 ± 13.6 ($P < 0.05$)% of control respectively ($8 \geqslant n \geqslant 4$).

The reduction in [^{3}H]-NA overflow by PGE_2 could be partially prevented by addition of the PG receptor blocker SC19220 (1-acetyl-2-(8-chloro-10,11-dihydrodibenz[b, f][1, 4]oxazepine-10-carbonyl) hydrazine) to the perfusion medium. Using indomethacin treated preparations, in the presence of SC19220, PGE_2 (0.28, 1.4, 2.8 and 14.0×10^{-6} M) now reduced overflow to 101.7 ± 22.2, 88.5 ± 17.7, 87.4 ± 5.5 and 87.9 ± 6.3% of control respectively ($6 \geqslant n \geqslant 5$). The effects of PGE_2 were now not significantly different from control at any concentration.

It is unclear why the PGE_2 mediated feedback should be evident in slices but not in synaptosomes. The discrepancy may perhaps be attributable to the difference in preparation times (0.25 versus 3.5 h) and the greater mechanical disruption required for the preparation of synaptosomes.

It appears that a PGE_2 mediated negative feedback, similar to that shown in peripheral systems, does operate in the central nervous system, however, the physiological importance of this effect has not been ascertained.

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Release of [^{3}H]-noradrenaline from the guinea-pig vas deferens by ethacrynic acid

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Ethacrynic acid (EA), a potent diuretic and Na^+, K^+-ATPase inhibitor, increases the force and rate of contractions of isolated atria (Pousti, Zarrindast, Sadeghi & Khoyi, 1973; Khoyi, Pousti, Powis & Zarrindast, 1978) and contracts the vas deferens of the guinea-pig (Khoyi, Pousti & Zarrindast, 1974). The cardiac effects are blocked by propranolol or reserpine but not by desipramine or colchicine. The effect on the vas deferens is prevented by phentolamine or reserpine. In the present work, the effect of EA on the release of tritium from guinea-pig vasa deferentia preloaded with [^{3}H]-noradrenaline was studied. EA (200 μg/ml) increased the rate of tritium outflow from 0.49 ± 0.07% to 1.57 ± 0.33% per min ($P < 0.005$). Repeated exposure to EA at 15 min intervals produced tachyphylaxis. The tachyphylaxis was not crossed with ouabain (5 μg/ml). Desipramine (1 μM) did not prevent the effect of EA. Removal of calcium from the incubation medium and increasing the magnesium concentration to 20 mM did not prevent the effect of EA.

It is concluded that EA releases noradrenaline from guinea-pig vas deferens by a mechanism different from that of tyramine and ouabain. The results suggest that the mechanism of action is calcium independent.

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