Inhibitory actions of adenine nucleotides and adenosine on transmission in rat vas deferens

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During nerve stimulation, adenosine 5'-triphosphate (ATP) is released with catecholamines from the adrenal medulla (Smith & Winkler, 1972) and probably also with noradrenaline (NA) from adrenergic nerve endings (Burnstock, 1976). The physiological role of ATP or its metabolites following release is unclear (Burnstock, 1976). ATP inhibits release of acetylcholine from cholinergic nerves (Sawynok & Jhamandas, 1976) and adenosine may exert a similar presynaptic inhibitory action on noradrenergic neurones (Hedqvist & Fredholm, 1976).

We have examined the effects of ATP, adenosine 5'-pyrophosphate (ADP), adenosine 5'-phosphate (AMP) and adenosine on isometric responses of rat vas deferens *in vitro*.

ATP (10^{-6}–10^{-4}M) and adenosine (3×10^{-6}–10^{-4}M) inhibited responses to field stimulation (150 pulses, 5 Hz, 1 ms, supramaximal voltage) in a dose-dependent manner, the initial 'twitch' response (Swedin, 1971) being more sensitive than the second, 'sustained' response (Figure 1). ADP (10^{-4}M) and AMP (10^{-4}M) also inhibited the responses and were equipotent with ATP but significantly less potent ($P < 0.05$) than adenosine. The inhibition was presynaptic in origin as motor responses elicited by exogenous NA (5×10^{-6}M) were not altered by ATP or adenosine. The inhibition was not mediated indirectly by prostaglandin liberation as indomethacin (3×10^{-5}M) had no effect on the inhibitory effects of ATP and adenosine.

Theophylline (10^{-4}M) inhibits the postsynaptic actions of adenosine (Burnstock, 1975) and also antagonized its presynaptic action in this preparation (Figure 1). The inhibitors of adenosine uptake (Stafford, 1966; Paterson, Kim, Bernard & Cass, 1975), dipyridamole (10^{-5} M) and 2-amino-6-[(2-hydroxy-5-nitro) benzythio]-9-β-D-ribofuranosyl-purine (compound 555) (10^{-5}M) significantly potentiated the effects of adenosine (Figure 1), and those of ATP, ADP and AMP.

These results indicate that ATP and its metabolites can inhibit the release of NA from noradrenergic nerves.

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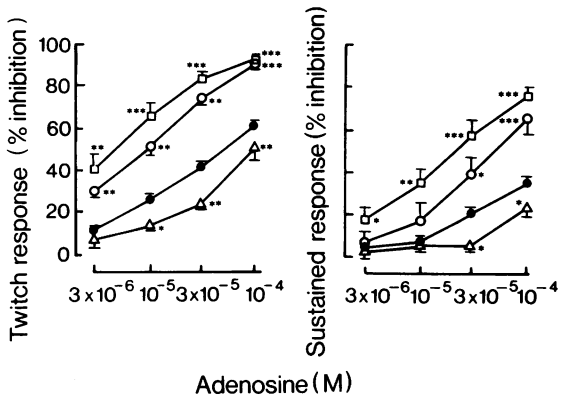

Figure 1 Percentage inhibition (ordinates) of the 'twitch' (left panel) and 'sustained' (right panel) responses of rat vas deferens to field stimulation by different concentrations of adenosine (abscissae) in control Krebs (●, $n=12$) and in the presence of theophylline (10^{-4} M, △, $n=6$), dipyridamole (10^{-5} M, ○, $n=6$) and compound 555 (10^{-5} M, □, $n=6$). Values are given as mean (±s.e. mean) for n observations. The significance of the difference between control and experimental groups was estimated by the paired Student's t-test. Asterisks indicate: * $0.05 > P > 0.01$; ** $0.01 > P > 0.001$; *** $P < 0.001$.

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