Vasoconstriction of guinea-pig submucosal arterioles following sympathetic nerve stimulation is mediated by the release of ATP

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Introduction

Although noradrenaline (NA) is present in high concentrations in sympathetic nerve terminals, NA does not mediate all the postjunctional responses elicited by sympathetic nerve stimulation (Ambache & Zar, 1971; Burnstock, 1986). Studies on guinea-pig submucosal arterioles have shown that both the underlying changes in membrane potential (excitatory junction potentials, e.j.ps) and vasoconstrictions following short trains of low or high frequency stimulation of the sympathetic nerves are unaffected by α-adrenoceptor antagonists (Hirst & Neild, 1980, 1981; Shen et al., 1990). Paradoxically these vessels constrict when low concentrations of NA are applied exogenously, and NA released from the sympathetic nerves following electrical stimulation acts through prejunctional α-adrenoceptors to depress transmitter release. Hirst & Neild (1980, 1981) suggested that the α-adrenoceptor resistant responses in this vessel were due to the action of NA through a novel γ-adrenoceptor. In a number of other arteries α-adrenoceptor antagonist resistant contractions following sympathetic nerve stimulation have been recorded (Muramatsu et al., 1989; Sjoblom-Widfeldt et al., 1990; Brizolara & Burnstock, 1990). These are thought to be due to ATP, which is co-released with NA, acting through P2X-purinoceptors because they are abolished following desensitization of P2X-purinoceptors with the stable adenosine 5′-triphosphate (ATP) analogue α,β-methylene ATP (Ramme et al., 1987; Burnstock & Warland, 1987; Hirst & Jobling, 1989; Evans & Cunnane, 1992). Recently the trypanocide, suramin, has been shown to be an antagonist at the P2-purinoceptor in the rodent vas deferens (Dunn & Blakeley, 1988; von Kugelgen & Stucky, 1989) and the guinea-pig taenia caeci (Den Hertog et al., 1989; Hoyle et al., 1990).

The aims of the present study were three fold: (1) to determine if an α-adrenoceptor antagonist sensitive contraction can be recorded in this vessel in response to nerve stimulation using 100 pulses at 10 Hz, parameters that to our knowledge have revealed an α-adrenoceptor-mediated contraction in all arteries studied; (2) to establish if the prazosin-resistant contraction is due to the activation of γ-adrenoceptors by NA or the activation of P2X-purinoceptors by ATP; (3) to test the specificity of suramin for antagonizing P2X-purinoceptors.

Methods

Submucosal plexus preparations were obtained from the small intestine of guinea-pigs (150–250 g); methods of tissue preparation and intracellular recording from submucosal neurones were as detailed previously (Surprenant, 1984). Tissues were superfused at 3–4 ml min⁻¹ with a physiological solution of the following composition (mM): NaCl 126, NaH₂PO₄ 1.2, MgCl₂ 1.2, CaCl₂ 2.5, KCl 5, NaHCO₃ 25, glucose 11; gassed with 95% O₂ and 5% CO₂. Temperature was maintained at 34–36°C.

The perivascular nerves on the surface of the arterioles were stimulated electrically through blunt glass microelectrodes (tip diameter 20–50 μm) filled with physiological saline and placed lightly on the surface of the arteriole about 1 mm away from the recording site. In contractility experiments, magnesium was omitted from the solution because constrictions in response to nerve stimulation or exogenously applied agonists were greater; similar observations have been reported in a variety of other blood vessels (Ramme et al., 1987; Evans & Cunnane, 1991). Test agents were added to
the superfusion medium to give the required final concentration.

Nerve stimulation (100 pulses at 10 Hz, 0.2 ms pulse width at 40 V from a Grass S88 stimulator) was delivered at 5 min intervals with 5–8 sets of these stimuli being given before any drug application; the amplitudes of successive control responses varied by less than ± 5%. Vasoconstrictor substances were applied for a duration of 2–5 min every 20 or 30 min with 2–4 such applications being given before any drug application. Data are expressed as a percentage of the response before drug application; all values are mean ± s.e.mean. Tests of significance were by Student’s t test; P < 0.05 was considered significant. n = number of animals except where stated otherwise.

Vessel diameter recordings

Changes in the outside diameter of the arterioles following nerve stimulation or the application of agonists were monitored by the Diamtrak system (Neild, 1989). This system can track the diameter of small vessels by on-line computer analysis of TV images with an Imaging Technology PCVision-Plus frame grabber board (Imaging Technology Inc., Woburn, Mass., U.S.A.) in an IBM PC/AT computer. The result was converted to an analog signal which was displayed on a conventional chart recorder. The data were sampled at 10–20 Hz and the resolution of the system was less than 1 μm.

Electrophysiological recordings

Changes in membrane potential of submucosal neurones and from the smooth muscle cells of submucosal arterioles were recorded with glass microelectrodes, filled with 1 M KCl with tip resistances of 130–180 MΩ. Signals were recorded with an Axoclamp 2A amplifier and displayed on a Gould 2400S chart recorder. Changes in membrane potential of arterioles were measured following nerve stimulation with short trains of stimuli (10–15 pulses) at 1 or 2 Hz from the stimulating electrode used for contraction studies. The same stimulating electrode was also used to evoke nicotinic excitatory postsynaptic potentials (e.p.s.ps; 0.1 Hz, pulse width 0.1 ms, 5–10 V) and noradrenergic inhibitory postsynaptic potentials (i.p.s.ps; 6 pulses 20 Hz, pulse width. 0.2 ms, 50 V) from the submucosal neurones following the stimulation of adjacent ganglia.

Reserpine pretreatment

Animals were pretreated with reserpine (5 mg kg⁻¹) i.p. 18 h before the experiment. The extent of the depletion of tissue NA was estimated histologically by the glyoxylic acid staining technique for catecholamines (Lindvall & Björkland, 1974; Furness & Costa, 1975).

Drugs

Adenosine 5′-triphosphate, α,β-methylene ATP, (+)-amphetamine, (−)-noradrenaline bitartrate, (−)-phenylephrine hydrochloride, reserpine, and tetrodotoxin were obtained from Sigma. P₂,P₅-di(adenosine-5')pentaphosphate (Boehringer), guanethidine sulphate (Ciba Geigy), idazoxan (Reckitt & Coleman), prazosin hydrochloride (Research Biochemicals) and suramin hexasodium salt (Bayer) were obtained from the sources given in parentheses.

Results

Contractility studies

Electrical stimulation of guinea-pig submucosal arterioles with trains of 100 pulses at 10 Hz every 5 min evoked reproducible vasoconstrictions measured as changes in the outside diameter of the vessel. The diameter of the arteriole quickly returned to its control value on cessation of stimulation. In the majority of experiments the vasoconstriction could be resolved into a rapidly rising transient peak within the first 30–40 s followed by a smaller amplitude maintained constriction (Figure 1). Electrically evoked responses were abolished by tetrodotoxin (0.3 μM, n = 8).

Effects of α-adrenoceptor antagonists The α₁-adrenoceptor antagonist, prazosin (0.1 μM), had no effect on either the resting tone of the vessel, or the nerve-evoked vasoconstriction measured either at the initial peak amplitude or during the maintained plateau phase (Figure 1). Constrictions elicited by the selective α₁-adrenoceptor agonist, phenylephrine (1 μM), of similar amplitude to the nerve-evoked constriction were abolished by 0.1 μM prazosin (n = 5) (see also Vanner et al., 1990).

The α₂-adrenoceptor antagonist, idazoxan (0.1 μM), significantly increased both the initial peak amplitude of the neurally evoked vasoconstriction as well as the maintained plateau phase (Figure 2). The potentiation of the nerve-evoked constriction by idazoxan was unaffected by prazosin (0.1 μM) (peak height, idazoxan 165 ± 22%, idazoxan + prazosin 184 ± 36%; maintained vasoconstriction, idazoxan 242 ± 21%, idazoxan + prazosin 204 ± 35%, n = 4).

Figure 1 Constrictions of submucosal arterioles following nerve stimulation are not mediated by the activation of α₁-adrenoceptors by noradrenaline. (a) Nerve evoked constrictions (100 pulses at 10 Hz) were unaffected by the α₁-adrenoceptor antagonist, prazosin (0.1 μM); (b) Constrictions elicited by the exogenous application of the α₂-adrenoceptor agonist, phenylephrine (PE; 1 μM) were abolished by prazosin (0.1 μM), an effect reversed on washout. (c) Summary of the effects of prazosin (0.1 μM) on the initial peak and plateau amplitude of nerve-evoked constrictions. Data are plotted as mean (± s.e.mean shown by vertical bars) % of the nerve-evoked constriction before prazosin application (n = 5; control, open columns, prazosin, solid columns). Periods of nerve stimulation (NS) and phenylephrine applications are indicated by bars.
Guanethidine (3 μM) had no effect on the amplitude of nerve-evoked constrictions after reserpine treatment. (c) Summary of the effects of idazoxan (0.1 μM) on nerve-evoked contractions from normal and reserpinized guinea-pigs. Results from normal animals (n = 5) were quantified both as initial peak amplitude and the amplitude of the maintained response. Peak amplitude only was measured from reserpinized animals because these preparations did not show two distinct phases of constriction (n = 5). Data are plotted as mean (± s.e.mean, vertical bars) of the % of the nerve evoked constriction before idazoxan application (control, open columns; idazoxan, solid columns). Periods of nerve stimulation (NS) are marked by bars. ***P < 0.001.

Reserpinization Dense catecholamine fluorescence was present in all control preparations of the submucosal plexus (Figure 3a) (see also Furness & Costa, 1987). No catecholamine fluorescence was observed following glyoxylic acid staining of submucosal plexus preparations from reserpin pretreated guinea-pigs (Figure 3b) indicating an apparent absence of tissue noradrenaline. However, nerve evoked constrictions of similar magnitude to control were still recorded following reserpine treatment. Control vasoconstrictions were 21.2 ± 2.4 μm and vasoconstrictions in reserpinized animals were 28 ± 3.2 μm (n = 8 arterioles from 4 animals). In contrast to control tissues, these responses were not potentiated by idazoxan (0.1 μM, n = 6 arterioles from 4 animals, Figure 2b).

Effects of the adrenergic neurone blocker guanethidine Guanethidine (3 μM) abolished vasoconstrictions evoked by nerve stimulation, an effect reversed by the concomitant application of amphetamine (3 μM, n = 4, Figure 4). A similar reversal of the effects of guanethidine by amphetamine has been shown in the guinea-pig vasa deferens (Brock & Cunnane, 1988) and rabbit jejunal artery (Evans, 1990). The mechanism of action of amphetamine was not examined in this study; however, Brock & Cunnane (1988) suggest that amphetamine probably acts by displacing guanethidine from sympathetic nerve terminals. The abolition of the response to electrical stimulation with the adrenergic neurone blocker, guanethidine, further demonstrates that the nerve-evoked, α-adrenoceptor antagonist-resistant vasoconstriction was generated by the release of transmitter from sympathetic nerves.

Determination of the α-adrenoceptor antagonist resistant component of constriction In a number of arteries where α-adrenoceptor antagonist resistant contractions have been reported the residual constraction appears to be due to the activation of P2X-purinoceptors by ATP (for review, see von Kugelgen & Starke, 1991). Application of exogenous ATP (3 μM) to the submucosal arterioles produced transient vasoconstrictions which reached peak amplitude in the first 30 s of application and returned towards the control diameter on maintained application. Reproducible responses to exogenously applied ATP were obtained if the interval between successive applications was greater than 30 min. The stable ATP analogues α,β-methylene ATP (mATP) (0.1–3 μM) and P1,P'-di-(adenosine-5')pentaphosphate (DADPP) (0.1–3 μM) produced transient constrictions, which peaked in the first 2 min of application. The vasoconstriction did not return to

Figure 2 Noradrenaline released following nerve stimulation acts through pre-junctional α2-adrenoceptors. (a) Constrictions of submucosal arterioles were potentiated in the presence of the α2-adrenoceptor antagonist, idazoxan (0.1 μM). (b) Idazoxan (0.1 μM) had no effect on the amplitude of nerve-evoked constrictions after reserpine treatment. (c) Summary of the effects of idazoxan (0.1 μM) on nerve-evoked contractions from normal and reserpinized guinea-pigs. Results from normal animals (n = 5) were quantified both as initial peak amplitude and the amplitude of the maintained response. Peak amplitude only was measured from reserpinized animals because these preparations did not show two distinct phases of constriction (n = 5). Data are plotted as mean (± s.e.mean, vertical bars) of the % of the nerve evoked constriction before idazoxan application (control, open columns; idazoxan, solid columns). Periods of nerve stimulation (NS) are marked by bars. ***P < 0.001.

Figure 3 Reserpin pretreatment abolishes catecholamine fluorescence in guinea-pig submucosal plexus following glyoxylic acid staining. (a) In control preparations dense catecholamine containing nerve fibres are associated with submucosal arterioles as well as adjacent ganglia. (b) No fluorescence was observed after reserpine treatment. Calibration bar = 100 μm.
baseline on prolonged application but declined to a maintained level; the amplitude of the maintained vasoconstriction elicited by mATP (1 µM) or DADPP (1 µM) was 30.6 ± 7.3% and 30.7 ± 1.9% of the peak response respectively (n = 3, Figure 5). The diameter of the vessel returned to control values within 3–5 min of washout of mATP or DADPP.

The putative P2-purinoceptor antagonist, suramin (100 µM), had no effect on the resting diameter of the vessel or the vasoconstriction to exogenously applied NA (3 µM), but abolished both the nerve-evoked constriction and the response to exogenously applied ATP (3 µM, Figure 6). Constrictions evoked by nerve stimulation or the exogenous application of ATP were partially reversed following a 20 min washout period. Suramin also abolished the potentiated vasoconstrictions obtained following the removal of the α2-autoinhibitory input with idazoxan (n = 3), as well as the neurally evoked constrictions recorded in reserpine-treated tissues (n = 2). These results strongly suggest that sympathetic vasoconstriction in submucosal arterioles is mediated solely by the action of ATP.

**Intracellular recordings from submucosal neurones**

Following ganglionic stimulation nicotinic fast e.p.s.ps and noradrenergic i.p.s.ps were recorded (see North & Surpre-

![Figure 4](image)

**Figure 4** Vasoconstrictions of the guinea-pig submucosal arterioles elicited by electrical stimulation are mediated by transmitter released from sympathetic nerves. Vasoconstrictions to nerve stimulation (100 pulses at 10 Hz) were abolished by guanethidine (3 µM), an effect reversed by the indirectly acting sympathomimetic, amphetamine (3 µM).

![Figure 5](image)

**Figure 5** Vasoconstrictions of submucosal arterioles in response to superfusion with P2-purinoceptor agonists. (a) ATP (3 µM) and α,β-methylene ATP (mATP, 1 µM) were perfused for the durations indicated by the bars; (b) ATP (3 µM) and P2,P2-di-(adenosine-5')pentaphosphate (DADPP, 1 µM) were applied as indicated. Responses shown in (a) and (b) are from different preparations.

![Figure 6](image)

**Figure 6** Constrictions of submucosal arterioles in response to nerve stimulation are mediated through the activation of P2-purinoceptors. (a) Nerve-evoked constrictions (100 pulses at 10 Hz) were abolished by the putative P2-purinoceptor antagonist, suramin (100 µM); the response is partially reversed on washout (20 min). (b) Constrictions to exogenously applied ATP (3 µM) were abolished by suramin (100 µM). (c) Suramin (100 µM) had no effect on the contraction evoked by the exogenous application of noradrenaline (NA, 3 µM). (d) Summary of the effects of suramin, data are expressed as mean (± s.e.mean shown by vertical bar) of the % of constriction before suramin application in response to nerve stimulation (n = 6), and the responses to exogenously applied ATP (n = 4) or NA (n = 4). Open columns = control responses; solid = suramin. Periods of nerve stimulation (NS) or the superfusion of ATP or NA are indicated by bars. ***P < 0.001.
nant, 1985). These two events were used to assess further the specificity of suramin as an antagonist at the P₂₅-purinoceptor.

Suramin had no effect on the amplitude (control 18.7 ± 1.6 mV, suramin 18.9 ± 3.2 mV, \( P = 0.94, n = 4 \)) or the time constant of decay of nicotinic fast e.p.s.ps (control 21.4 ± 5.1 ms, suramin 17.2 ± 4.1 ms, \( P = 0.49 \)) evoked by nerve stimulation (0.1 Hz) when the membrane potential was held at −90 mV so that action potential initiation was prevented. At the resting membrane potential (−45 to −65 mV) many e.p.s.ps were suprathreshold for initiation of action potentials; suramin had no effect on action potential threshold, amplitude or duration (Figure 7a).

Previous studies have characterized the i.p.s.p. recorded in normal preparations as being due to the action of NA released from sympathetic nerves onto \( \alpha \)-adrenoceptors on the submucosal neurones (North & Surprenant, 1985), although a non-adrenergic i.p.s.p. has also been observed (Mihara et al., 1987; Bornstein et al., 1988). In this study i.p.s.ps recorded in control animals were abolished by 1 μM idazoxan. Suramin had no effect on the amplitude of the i.p.s.p. (control 30 ± 4.1 mV, suramin 30 ± 3 mV, \( n = 4 \)), or the time taken for the i.p.s.p. to decay by 50% (control 750 ± 330 ms, suramin 5 min 300 ± 380 ms, \( P = 0.73 \); suramin 10 min 1000 ± 350 ms, \( P = 0.51, n = 4 \); Figure 7b). After reserpine treatment noradrenergic (ie. idazoxan-sensitive) i.p.s.ps were not recorded in neurones which were hyperpolarized by superfusion with the \( \alpha \)-adrenoceptor agonist, UK14304; it has been shown previously that all submucosal neurones which are hyperpolarized by \( \alpha \)-adrenoceptor agonists also exhibit noradrenergic i.p.s.ps in response to nerve stimulation (Surprenant & North, 1988). These observations further strengthen the conclusion that reserpine treatment does produce complete functional depletion of NA from sympathetic nerves in the submucosal plexus.

**Intracellular recordings from submucosal arterioles**

Idazoxan (0.1 μM) increased the steady-state amplitude of e.j.ps in a train (\( n = 3 \), Figure 8a). Suramin (100 μM) abolished all e.j.ps recorded in control solution (\( n = 2 \)) or in the presence of idazoxan (\( n = 2 \), Figure 8c). The blockade of the e.j.ps by suramin was only partially reversed (to approximately 50% of control amplitude) after 15–20 min of wash (Figure 8d).

**Discussion**

The vasoconstriction of guinea-pig submucosal arterioles evoked by 100 pulses at 10 Hz was unaffected by the \( \alpha \)-adrenoceptor antagonist, prazosin. This is despite the fact that both in the present and a previous study (Shen et al., 1990) NA has been demonstrated to be released from sympathetic nerves in the submucosal plexus following nerve stimulation and activates inhibitory prejunctional \( \alpha \)-adrenoceptors on both submucosal and sympathetic neurones. Moreover, vasoconstrictions of similar amplitude to the neurogenic response can be evoked by the exogenous application of low concentrations of \( \alpha \)-adrenoceptor agonists (Shen et al., 1990; Vanner et al., 1990). Resistance to \( \alpha \)-adrenoceptor blockade is not a new phenomenon and has been described in many vascular tissues (for review, see Burnstock, 1990). However it is usually only a component that is resistant. Purely \( \alpha \)-resistant contractions in response to short trains of low frequency stimuli have been reported in two vessels, the rabbit jejunal artery (Ramme et al., 1987; Evans & Cunnane, 1992) and the rabbit saphenous artery (Burnstock & Warland, 1987); even in these vessels a substantial component of the contraction can be demonstrated to be noradrenergic in origin following prolonged high frequency stimulation. The present study on the guinea-pig submucosal arterioles has failed to reveal an \( \alpha \)-adrenoceptor-sensitive component of the vasoconstriction at stimulation parameters that have demonstrated a substantial noradrenergic contraction in all arteries studied to date. It would thus seem that neurally released NA fails to reach a concentration sufficient to activate postjunctional \( \alpha \)-adrenoceptors and mediate vasoconstriction of submucosal arterioles. These results also support the idea (Hirst & Edwards, 1989) that classical \( \alpha \)-adrenoceptors are

![Figure 7: Effects of suramin (100 μM) on synaptic potentials recorded from guinea-pig submucosal neurones following electrical stimulation of adjacent ganglia.](image-url)
an a2-adrenoceptor antagonist, idazoxan. Contractile responses and e.j.ps were potentiated in the presence of idazoxan indicating that NA acts through prejunctional a2-adrenoceptors to depress transmitter release. Potentiation of nerve-evoked transmitter release by a2-adrenoceptor antagonists has been reported for a number of blood vessels and other tissues (Starke, 1977; 1987; Mishima et al., 1984). The potentiation of the contractile response, in particular the maintained component, suggests that the decline of the nerve-evoked vasoconstriction following the transient peak response can be explained at least in part by a2-adrenoceptor activation.

Results obtained with reserpine provide considerable evidence that a transmitter other than NA is responsible for mediating vasoconstriction of submucosal arterioles following sympathetic nerve stimulation. Following reserpine treatment, vasoconstrictions elicited by nerve stimulation were of similar magnitude to those recorded in control tissues. Our results are similar to those in the guinea-pig vas deferens (Kirkpatrick & Burnstock, 1987) and rabbit saphenous artery (Warland & Burnstock, 1987), in which reserpine did not significantly alter the magnitude of the prazosin-resistant (presumably purinergic) nerve-evoked contraction. The functional depletion of NA from the sympathetic nerves innervating the submucosalplexus was demonstrated both by the absence of catecholamine fluorescence and by the failure to record idazoxan-sensitive noradrenergic i.p.s.ps in submucosal neurons following reserpine treatment. Previous studies in the guinea-pig have shown that the reserpine pretreatment regime used in the present study depletes the NA content of the vas deferens, a tissue with a dense sympathetic innervation, by more than 95% (Wakade & Krusz, 1972; Kirkpatrick & Burnstock, 1987), and abolishes the potentiating effects of the a2-adrenoceptor antagonist, yohimbine (Brock et al., 1990). Similarly, NA-mediated electrophysiological responses recorded from the rat brain slice preparation are abolished following reserpine treatment (Pan & Williams, 1989).

In a number of vessels where α-antagonist resistant responses have been recorded, they have been shown to be due to the activation of P2X-purinoceptors by ATP co-released with NA from sympathetic nerves (von Kugelgen & Starke, 1985; Burnstock & Warland, 1987; Brizzolara & Burnstock, 1990; Sjöblom-Widfeldt et al., 1990). In the present study, arteriolar constrictions were evoked in response to the exogenous application of ATP, mATP and DADPP. The finding that mATP and DADPP were more potent than ATP is in keeping with the pharmacological profile of the P2X-purinoceptor (see Burnstock, 1991).

In other studies (MacKenzie et al., 1988; Evans & Cunnane, 1992) mATP and DADPP produced contractions that faded completely in the continued presence of the agonist. This full desensitization of the response has been used to quantitate the degree to which the neurally mediated contraction is due to the activation of P2X-purinoceptors. In the present study neither mATP nor DADPP produced a vasoconstriction that fully desensitized during the maintained presence of these agonists. Therefore mATP and DADPP were considered unsuitable for adequately characterizing the P2X-purinoceptor mediated response in submucosal arterioles.

Suramin abolished nerve evoked e.j.ps and constrictions of submucosal arterioles elicited by either exogenously applied ATP or sympathetic nerve stimulation, but had no effects on the arteriolar constriction to exogenously applied NA, nor on the noradrenergic i.p.s.ps or nicotinic e.p.s.ps recorded from submucosal neurones. A similar specificity of suramin in antagonizing P2-purinoceptors has been reported in the rodent vas deferens (Starke, 1987; Den Hertog et al., 1989; von Kugelgen et al., 1989a). The finding that suramin has no effect on the noradrenergic i.p.s.p. taken with the lack of effect on the constriction to exogenously applied NA, implies not only that suramin does not affect the postjunctional response to NA but also has no effect on transmitter release from sympathetic nerves. The lack of prejunctioanl actions of suramin on transmitter release from sympathetic nerves has been reported from studies of the overflow of trytiated NA following nerve stimulation in the mouse vas deferens (von Kugelgen et al., 1990b). In the present study responses to ATP (3 μM) and nerve stimulation were both abolished, suggesting that in submucosal arterioles, suramin is an effective antagonist of
the constrictor response mediated through the activation of P2-purinoceptors.

The results obtained with suramin, taken together with the agonist potencies of ATP, mATP and DADPP, are consistent with the view that vasocostrictions and the underlying changes in membrane potential, the e.p.s, following nerve stimulation are mediated through the action of ATP or a structurally related purine nucleotide through P2-purinoceptors. These data, particularly those from reserpinized tissues, provide no evidence to suggest that the α-adrenoceptor-resistant vasocostriction and underlying changes in membrane potential are due to the activation of γ-adrenoceptors by NA as suggested by Hirst & Neild (1980, 1981).

In summary we have described for the first time a blood vessel in which all the postjunctional responses evoked by stimulation of the sympathetic nerves are mediated by the activation of P2-purinoceptors by ATP or a related purine nucleotide. Submucosal arterioles comprise the resistance vessels of the gastrointestinal microcirculation and have been estimated to contribute up to 40% of the total mesenteric-planachnic resistance (Lundgren, 1984; Parks & Jacobsen, 1987; Granger et al., 1987), as well as contributing significantly to the maintenance of systemic blood pressure. Thus, purinergic transmission may play a major role in the neural regulation of the gastrointestinal microcirculation. The functional role of neurally released NA in submucosal arterioles appears to be restricted to its prejunctional modulation of transmitter release.

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References


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