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European Journal of Pharmacology 356 (1998) 59–65

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α_2-Adrenoceptors mediate the effect of dopamine on adult rat jejunal electrolyte transport

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Received 15 May 1998; revised 25 June 1998; accepted 30 June 1998

Abstract

The present study was aimed to characterise the effect of dopamine on rat jejunal electrolyte transport and to evaluate the type of receptors and the intracellular signalling mechanisms involved in the response. Stripped epithelial sheets were mounted in Ussing chambers connected to an automatic voltage current clamp and changes in the short circuit current ($\mu A/cm^2$) were measured continuously as an index of electrogenic ion transfer. Dopamine (0.1–100 μM) produced a concentration dependent decrease in I_{sc} with an EC_{50} of 1.4 ± 0.1 μM; the effect of dopamine was not changed by propranolol (1 μM), prazosin (1 μM and 10 μM) or (±)-sulpiride (1 μM), but was completely abolished by phentolamine (1 μM). The addition of phentolamine (0.3 μM) or yohimbine (0.3 μM) produced a rightward shift of the dopamine concentration-dependent curve with an increase in EC_{50} values up to 30.0 ± 0.2 μM and 11.7 ± 0.1 μM, respectively. The α_2-adrenoceptor-selective agonist, UK14,304 (5-bromo-*N*-(4,5-dihydro-1*H*-imidazol-2-yl)-6-quinoxalinamine), also produced a concentration-dependent decrease in I_{sc} with an EC_{50} of 0.04 ± 0.01 μM; the addition of yohimbine (0.3 μM) increased the EC_{50} value of UK14,304 to 0.68 ± 0.01 μM. The addition of amiloride (100 μM), a Na^+ channel blocker, to the fluid bathing the apical side was found not to change the effect of dopamine on I_{sc}. 5-(*N*-ethyl-*N*-isopropyl)-amiloride (10 μM), a selective Na^+/H^+ exchanger inhibitor, partially antagonised the effect produced by 100 μM of dopamine. The addition of ouabain (1 mM) to the fluid bathing the basal side, antagonised the effect produced by 50 and 100 μM of dopamine. In contrast, frusemide (1 mM) completely abolished the effect of all concentrations of dopamine. Forskolin (10 μM) and N^6,2′-*O*-dibutyryl cyclic AMP (1 mM) added to both the apical and serosal sides completely abolished the effect of dopamine on I_{sc}. It is concluded that the dopamine antisecretory effects in the jejunum of adult rats are mediated through α_2-adrenoceptors. This effect is sensitive to increases in intracellular cyclic AMP and is primarily dependent on the basal Na^+,K^+,$2Cl^-$-co-transport mechanism.

Keywords: Dopamine; α_2-Adrenoceptor; Intestine; Electrolyte transport

1. Introduction

The intestinal tract has been shown to be of crucial importance in the regulation of body fluid and electrolyte homeostasis with particular relevance in the control of changes in fluid and electrolyte intake (Binder, 1983). Previous studies on the neurohumoral control of intestinal transport showed that catecholamines stimulate electrolyte absorption. In rabbits, stimulation of α-adrenoceptors by adrenaline and noradrenaline in the ileal mucosa enhances active absorption of Na^+ and Cl^- and reduces short-circuit current, probably by inhibiting net HCO_3 secretion, whereas β-adrenoceptors agonists were devoid of effect (Field and McColl, 1973; Field et al., 1975).

In the intestine, dopamine is particularly abundant in the mouse and dog mucosal cell layer (Eaker et al., 1988; Esplugues et al., 1985). Studies on the formation of this catecholamine from exogenous 3,4-dihydroxyphenyl-L-alanine (L-DOPA) along the rat digestive tract showed that the highest aromatic L-amino acid decarboxylase activity is located in the duodenum, jejunum, proximal colon and glandular stomach (Vieira-Coelho and Soares-da-Silva, 1993). Exogenous dopamine has been reported to stimulate active Na^+ and Cl^- absorption in the rabbit ileum; both dopamine receptors and α_2-adrenoceptors appear to be involved (Donowitz et al., 1982). In the rat, dopamine was also found to stimulate ileal and colonic fluid absorption via dopamine receptors and α_2-adrenoceptors (Donowitz et al., 1983). An antisecretory effect was also reported for the rat jejunum which is mediated by an action on either an α_2-adrenoceptor or a dopamine receptor with character-

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0014-2999/98/$19.00
PII: S0014-2999(98)00500-7

istics different from those of peripheral D_1 or D_2 receptors (Wahawisan et al., 1997). Recently, it has been suggested that the α_2-adrenoceptors involved in the antisecretory action in the rat intestinal epithelium are of the α_{2D} or α_{2A}-like subtype (Liu and Coupar, 1997). In contrast with this pro-absorption profile of dopamine, other studies showed that endogenous dopamine reduces jejunal sodium transport in young rats fed a high salt diet (Finkel et al., 1994) and this effect is most probably related to a decrease in Na^+–K^+ ATPase activity (Vieira-Coelho et al., 1997).

The present work was aimed to study the effect of dopamine on rat jejunal electrolyte transport and to evaluate the type of receptors and the intracellular signalling mechanisms involved in the response.

2. Materials and methods

2.1. Tissue preparation

Male Wistar rats, aged 60 days (260–300 g) were fed a standard rat chow (LECTICA I.P.M R20) and received tap water ad libitum. The rats were killed by decapitation under ether anaesthesia and two jejunal segments located 10–15 cm distal from the pyloric sphincter were removed. Each segment (2 cm long) of jejunum was cut longitudinally along the mesenteric border, washed free of luminal contents and the tissue was pinned mucosal side down on a dental wax block. The serosa and muscularis were dissected away to obtain the epithelial sheets, as previously described (Nellans et al., 1974). Two adjacent pieces were routinely prepared from a single jejunum.

2.2. Experimental procedure

Epithelial sheets were mounted in Ussing chambers (exposed area of 0.28 cm^2) equipped with water-jacketed gas lifts bathed on both sides with 10 ml of Krebs–Hensleit solution, gassed with 95% O_2 and 5% CO_2 and maintained at 37°C. D-Glucose (10 mM) was added to the serosal-side reservoir and an equimolar amount of mannitol was added to the mucosal-side reservoir. The Krebs–Hensleit solution contained (in mM): NaCl 118, KCl 4.7, $NaHCO_3$ 25, KH_2PO_4 1.2, $CaCl_2$ 2.5, $MgSO_4$ 1.2; the pH was adjusted to 7.4 after gassing with 5% CO_2 and 95% O_2. The tissues were continuously voltage clamped to zero potential differences by application of external current, with compensation for fluid resistance, by means of an automatic voltage current clamp (DVC 1000, World Precision Instruments, Sarasota, FL, USA). Transepithelial resistance (Ω cm^2) was measured by altering the membrane potential stepwise (± 5 mV) and applying the Ohmic relationship. Changes in the short circuit current ($\mu A/cm^2$) were continuously measured as an index of electrogenic ion transfer. The voltage/current clamp unit was connected to a PC via a BIOPAC MP1000 data acquisition system (BIOPAC Systems, Goleta, CA, USA). The data analysis were analysed using Acq*Knowledge* 2.0 software (BIOPAC Systems, Goleta, CA, USA).

Usually two tissues per animal were mounted in the chambers. After a 30- to 45-min preincubation period, by which time the potential difference had stabilised, dopamine or UK 14,304 was added to the serosal-side reservoir; ascorbic acid (1 mM) was present in the serosal bathing solution to reduce oxidation of dopamine. All agonist concentration–response curves were made cumulatively; each new concentration was added as soon as the potential difference response to the prior concentration reached its nadir. Antagonists were added 20 min before the agonist concentration–response curve was made. All other drugs used were added to the serosal side unless stated otherwise.

2.3. Drugs

The compounds used were: N^6,2′-*O*-dibutyryladenosine 3′:5′-cyclic monophosphate, dopamine hydrochloride, DL-propranolol, prazosin hydrochloride, phentolamine hydrochloride, ($\pm$)-sulpiride, yohimbine hydrochloride, frusemide, amiloride, ouabain and forskolin, all obtained from Sigma (St. Louis, MO, USA). UK14,304 (5-bromo-*N*-(4,5-dihydro-1*H*-imidazol-2-yl)-6-quinoxalinamine) was obtained from Research Biochemicals International (RBI, Natick, MA-01760, USA) and 5-(*N*-ethyl-*N*-isopropyl)-amiloride (EIPA) was kindly donated by Dr. E. Schöming (Pharmakologisches Institut der Universität, Heidelberg, Germany).

2.4. Analysis of data

The results are given as arithmetic means $\pm$ S.E.M.; EC_{50} and K_D values were calculated using the Graphad Prism software package (Motulsky et al., 1994). Statistical analyses were performed by one-way analysis of variance (ANOVA) followed by the Newman–Keuls test for multiple comparisons or Student's *t*-test. A P value less than 0.05 was assumed to denote a significant difference.

3. Results

Jejunal preparations had a mean basal I_{sc} value of 19.8 ± 2.2 $\mu A/cm^2$ ($n = 48$) and tissue resistance was 151.0 ± 5.8 Ω cm^2 ($n = 48$). Dopamine, when added to the serosal side, rapidly decreased I_{sc} in a concentration dependent manner with an EC_{50} of 1.4 ± 0.1 μM and a maximum decrease of 11.3 ± 2.2 $\mu A/cm^2$ at 100 μM. The delta I_{sc} produced by a single maximal dose of dopamine had the same magnitude as that produced by successive additions of smaller doses, reaching the same final concentration (data not shown). This effect of dopamine on I_{sc} was not changed when the tissues were

pretreated with the non-selective β-adrenoceptor antagonist, propranolol (1 μM) (Fig. 1A). On the other hand, phentolamine (0.3 μM), a non-selective α-adrenoceptor antagonist, produced a rightward shift of the dopamine

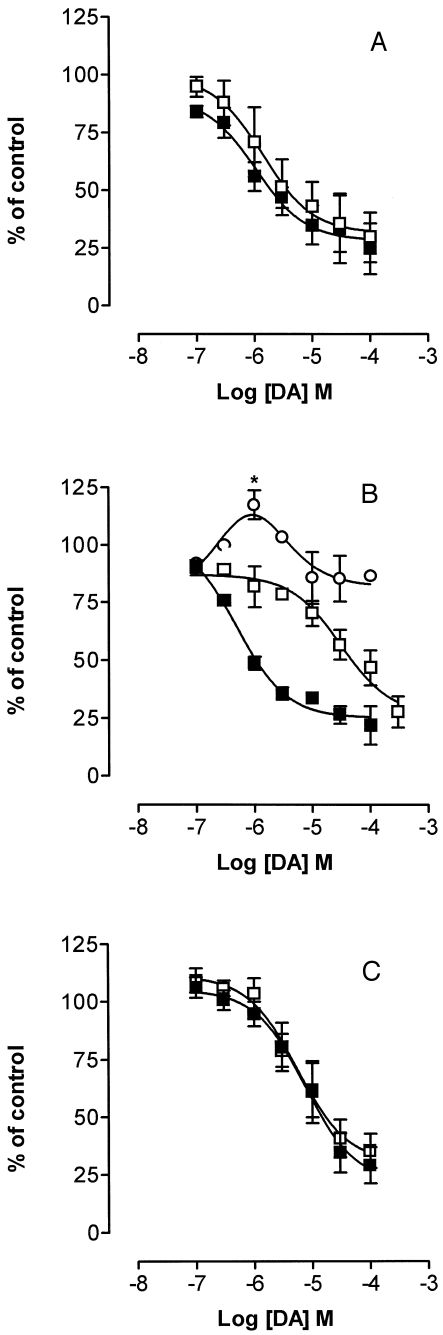

Fig. 1. Concentration–response curves for dopamine (DA) effect on I_{sc} in voltage-clamped rat jejunal epithelial sheets. (A) Response to dopamine in the absence (closed squares) and the presence of 1 μM propranolol (open squares). (B) Response to dopamine in the control (closed squares), in the presence of 0.3 μM phentolamine (open squares) and 1 μM phentolamine (open circles). (C) Response to dopamine in the absence (closed squares) and the presence of sulpiride 1 μM (open squares). Significantly different from corresponding control values (Student's *t*-test, $* P < 0.05$). Symbols represent means of four or five experiments per group; vertical lines show S.E.M.

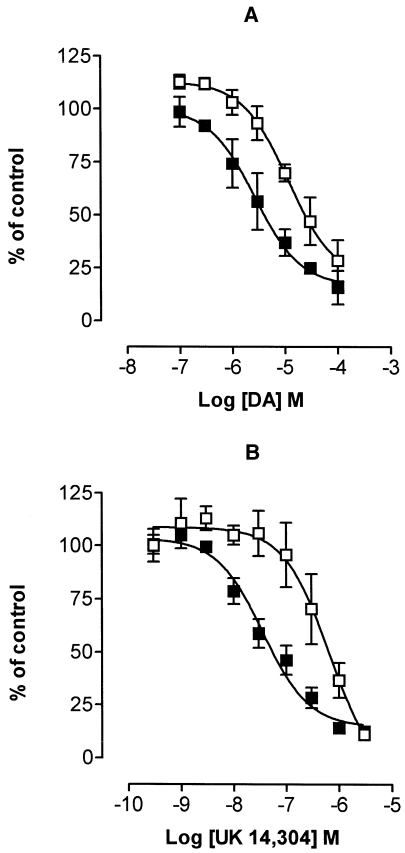

Fig. 2. Concentration–response curves for dopamine (DA) and UK 14,304 on I_{sc} in voltage-clamped rat jejunal epithelial sheets. (A) Effect of dopamine in the absence (closed squares) and the presence of 0.3 μM yohimbine (open squares). (B) Effect of UK 14,304 in the absence (closed squares) and the presence of 0.3 μM yohimbine (open squares). Symbols represent means of four or five experiments per group; vertical lines show S.E.M.

concentration-dependent curve with a significant 20-fold increase in EC_{50} values to 30.0 ± 0.2 μM; 1 μM phentolamine completely abolished the reduction of I_{sc} produced by dopamine (Fig. 1B). In the presence of 1 μM phentolamine, the effect of 1 μM dopamine was converted to a significant increase in I_{sc} (17.6 ± 6.3% increase). The dopamine receptor antagonist, (±)-sulpiride (1 μM), did not change the effect of dopamine on I_{sc} (Fig. 1C). In contrast to dopamine, the dopamine receptor agonist, apomorphine (0.1 to 10 μM), was found not to decrease jejunal I_{sc} (data not shown).

In contrast to phentolamine, prazosin (1 μM and 10 μM), a selective α_1-adrenoceptor antagonist, did not change the effect of dopamine on I_{sc} (data not shown). On the other hand, a selective α_2-adrenoceptor antagonist, yohimbine (0.3 μM), was found to produce a rightward shift of the dopamine concentration-dependent curve with a 5-fold increase in EC_{50} values (2.6 ± 0.1 μM vs. 11.7 ± 0.1 μM; $P < 0.01$) (Fig. 2A). The α_2-adrenoceptor-selective agonist, UK14,304, produced a concentration-dependent decrease in I_{sc} with an EC_{50} of 0.04 ± 0.01 μM; the

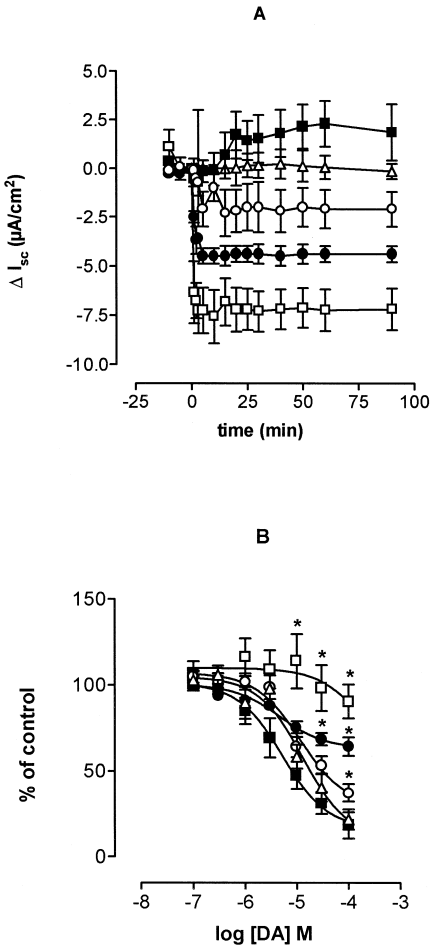

Fig. 3. (A) Time-dependent effect of 100 μM amiloride (closed squares), 10 μM 5-(*N*-ethyl-*N*-isopropyl)-amiloride (EIPA) (open circles), 1 mM ouabain (closed circles), or 1 mM frusemide (open squares) and no drug addition (open triangles) on I_{sc} in voltage-clamped rat jejunal epithelial sheets. For the ouabain and frusemide effects, all values from time 1 to 90 min were found to be significantly different from corresponding control values (Student's *t*-test, $P < 0.05$). (B) Concentration–response curves for dopamine in the absence (open triangles) and the presence of 100 μM amiloride (closed squares), 10 μM 5-(*N*-ethyl-*N*-isopropyl)-amiloride (EIPA) (open circles), 1 mM ouabain (closed circles) or 1 mM frusemide (open squares). Significantly different from corresponding control values (Student's *t*-test, $* P < 0.05$). Symbols represent means and of four or five experiments per group; vertical lines show S.E.M.

addition of yohimbine (0.3 μM) produced a rightward shift of the UK14,304 concentration-dependent curve with a 14-fold increase ($P < 0.01$) of EC_{50} values (0.68 ± 0.01 μM) (Fig. 2B). The dissociation constant found for yohimbine when dopamine was used as the agonist ($K_D = 30 \pm 7$ nM) was not different from the value found when the agonist was UK14,304 ($K_D = 40 \pm 10$ nM).

In order to evaluate the ionic basis of the basal I_{sc} in this tissue preparation, several electrolyte transport pathway modulators were used; the time dependent effects of these compounds are shown in Fig. 3A. The effect obtained on I_{sc} at 10 min (stable responses), was most pronounced for frusemide 1 mM (-7.6 ± 1.4 μA/cm^2) followed by ouabain 1 mM (-4.5 ± 0.4 μA/cm^2). The addition to the mucosal side of amiloride (100 μM), a Na^+ channel blocker, or 5-(*N*-ethyl-*N*-isopropyl)-amiloride (10 μM), a selective Na^+/H^+ exchanger inhibitor, did not significantly change basal I_{sc}. Addition of amiloride 100 μM to the apical side was found not to change the effect of dopamine on I_{sc} (Fig. 3B). Under the same experimental conditions, 5-(*N*-ethyl-*N*-isopropyl)-amiloride (10 μM) partially antagonised the effect produced by 100 μM of dopamine (Fig. 3B). The addition of ouabain (1 mM) to the basal side antagonised the effect produced by 50 and 100 μM of dopamine (Fig. 3B). In contrast, frusemide (1 mM) completely abolished the effect of all concentrations of dopamine (0.1–100 μM) on I_{sc} (Fig. 3B).

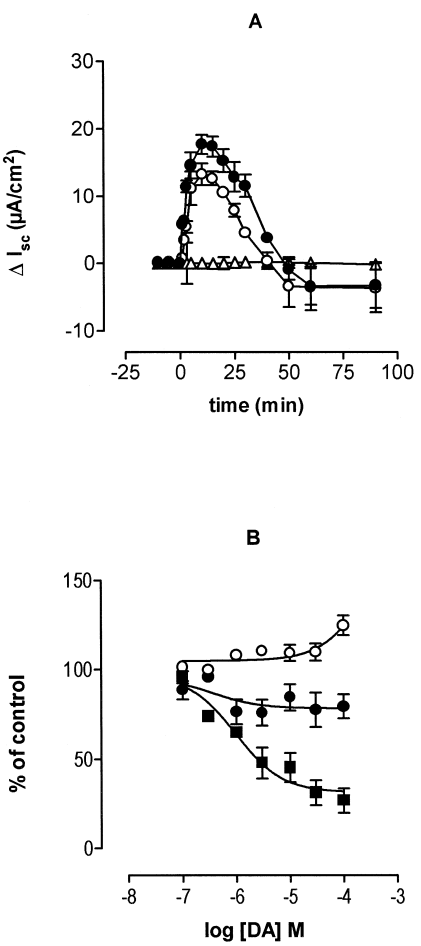

Fig. 4. (A) Time-dependent effect of 10 μM forskolin (open circles) and 1 mM dibutyryl cyclic AMP (closed circles) and no drug addition (open triangles) on I_{sc} in voltage-clamped rat jejunal epithelial sheets. For the forskolin and dibutyryl cyclic AMP effects, all values from time 1 to 40 min were found to be significantly different from corresponding control values (Student's *t*-test, $P < 0.05$). (B) Concentration–response curves for dopamine in the absence (closed squares) and the presence of 10 μM forskolin (open circles) or 1 mM dibutyryl cyclic AMP (closed circles). Symbols represent means of four or five experiments per group; vertical lines show S.E.M.

The addition of forskolin (10 μM), an activator of adenylate cyclase, to both the mucosal and serosal sides of the jejunal epithelium produced a rapid increase in I_{sc} values (up to 13.3 ± 1.6 μA/cm^2, $n = 4$) (Fig. 4A). The addition of dibutyryl cyclic AMP (1 mM) to both the mucosal and serosal sides produced a slightly greater increase in I_{sc} values (up to 17.7 ± 1.4 μA/cm^2, $n = 4$) when compared to the addition of forskolin (Fig. 4A). The increase in I_{sc} produced by both forskolin and dibutyryl cyclic AMP began within 30–50 s after the addition of the compounds and attained its maximum at 10 min. The initial increase in I_{sc} disappeared in about 40–50 min; the potential difference remained stable during the subsequent 60 min (Fig. 4A). Pretreatment with forskolin (10 μM) or dibutyryl cyclic AMP (1 mM) completely abolished the effect of dopamine (0.1–100 μM) on I_{sc} (Fig. 4B). In these experiments, concentration-response curves for dopamine were constructed 50 min after the addition of either forskolin or dibutyryl cyclic AMP.

4. Discussion

The results obtained in this study agree with the view that catecholamines have pro-absorption and antisecretory actions in the intestine and that α_2-adrenoceptors mediate these effects. This is evidenced by a decrease in I_{sc} when dopamine is added from the serosal side of the intestinal epithelium; the same result had been obtained with rabbit ileum (Donowitz et al., 1982). Similarly, results obtained under in vivo experimental conditions show that dopamine stimulates water absorption in the rat ileum and colon (Donowitz et al., 1983); however, the authors claimed that the effect of dopamine was mediated by both specific dopamine receptors and α_2-adrenoceptors. In contrast, the results presented here, for the rat jejunum, show that dopamine receptors appear not to be involved in the effect of dopamine. In fact, the present data shows that the effect of dopamine on I_{sc} was not changed by pretreatment with either propranolol (1 μM), prazosin (1 and 10 μM) or (±)-sulpiride (1 μM); in contrast, phentolamine (0.3 μM) produced a significant 30-fold increase in EC_{50} values for dopamine. This type of evidence rules out the possibility that β-adrenoceptors, α_1-adrenoceptors or dopamine receptors are involved in the effect of dopamine. On the other hand, the involvement of α_2-adrenoceptors in the response to dopamine is a plausible alternative: yohimbine (0.3 μM) produced a rightward shift of the dopamine concentration-dependent response curve with a significant 10-fold increase in EC_{50} values. Two additional findings agree with this suggestion: the effect of UK14,304 was also a concentration-dependent decrease in I_{sc} with an EC_{50} of 0.04 ± 0.01 μM and the addition of yohimbine (0.3 μM) produced a rightward shift of the UK14,304 concentration-dependent curve with a significant 14-fold increase in EC_{50} values. The dissociation constant found for yohimbine was in the nM range when either dopamine or UK14,304 were used as agonists ($K_D = 30 \pm 7$ nM and $K_D = 40 \pm 10$ nM respectively), confirming the involvement of α_2-adrenoceptors in the effect of dopamine on rat jejunum electrolyte transport.

In addition to the lack of effect of (±)-sulpiride (1 μM) on the dopamine-induced I_{sc} decrease, another piece of evidence suggesting that dopamine receptors are not involved in this effect is that apomorphine (0.1 to 10 μM) does not reduce rat jejunal I_{sc}. The putative involvement of specific dopamine receptors in the effect of dopamine, as reported by (Donowitz et al., 1982), may be explained by the fact that the authors used non-selective dopamine receptor antagonists (haloperidol and domperidone), which are known to antagonise α-adrenoceptors (Lefebvre, 1992; Leuschner et al., 1980; Musso et al., 1992).

The pro-absorption effect of dopamine now observed contrasts with the result reported by Finkel et al. (1994), suggesting that endogenous dopamine reduces jejunal sodium absorption. The effects reported by Finkel et al. (1994) were observed only in weanling rats and not in adult rats. These authors also suggested that the regulation of jejunal sodium transport by endogenous dopamine might be an important contributor to the maintenance of sodium homeostasis in immature animals exposed to a high salt intake. In renal epithelia, dopamine inhibits Na^+,K^+-ATPase activity (Bertorello and Katz, 1993) and sodium permeability by inhibiting the Na^+/H^+ exchanger activity (Felder et al., 1990). These effects are expected to reduce the net sodium transport along the tubular epithelium and, thereby, increase its excretion. The results reported by Finkel et al. (1994) suggest that dopamine would affect the activity of a selective membrane ion transport system in the intestinal mucosa in the same way as that in the renal proximal tubule. It is interesting that, in the presence of 1 μM phentolamine, the effect of 1 μM dopamine was a significant increase in I_{sc} that was not observed for higher concentrations of the amine. It is possible that this results from inhibition of Na^+,K^+-ATPase activity. This would be in agreement with results obtained recently, where dopamine was found to inhibit Na^+,K^+-ATPase activity in isolated epithelial cells from the rat jejunum (20-day-old animals) (Vieira-Coelho and Soares-da-Silva, 1993). A characteristic common to these two studies (Finkel et al., 1994; Vieira-Coelho et al., 1997), in which dopamine was found to have a negative effect on sodium absorption, is the age of the animals used; both studies were performed in young animals. The present and other studies, in which dopamine clearly increased electrolyte absorption, were performed with adult animals. Therefore, it might be hypothesised, that during ontogeny, namely during postnatal development, dopamine would have a protective role in the intestine in the maintenance of sodium homeostasis, and that this role of dopamine is lost on reaching adulthood, when renal function attains maturity. It is also important that complete α-adrenoceptor blockade in adult animals

allowed the appearance of an opposite effect of dopamine on intestinal ion transport that could be explained by the inhibition of Na^+,K^+-ATPase activity, as already described for young animals. Apparently, a high noradrenergic tone is present in adult animals, which may mask the effects of dopamine on specific receptors.

Multiple transport pathways involved in Na^+ and Cl^- transfer are present in the jejunum (Fig. 5). Under our experimental conditions, the effect of dopamine, a decrease in I_{sc}, could have been due to an increase in sodium absorption, to a decrease in chloride or bicarbonate secretion or to both. Amiloride, a Na^+-channel blocker, was found to alter neither basal I_{sc} nor the effect of dopamine. The selective Na^+/H^+ exchanger inhibitor, 5-(*N*-ethyl-*N*-isopropyl)-amiloride, when added alone, did not alter basal I_{sc} and only partially antagonised the effect produced by 100 μM dopamine. These results rule out the possibility of direct involvement of apical Na^+-channels or of the Na^+/H^+ exchanger in the dopamine-induced decrease in I_{sc}. In contrast, ouabain decreased basal I_{sc}, indicating that I_{sc} is dependent on the basolateral Na^+–K^+-ATPase activity. Because the antagonist effect of ouabain on the dopamine-induced decrease in I_{sc} was observed at the highest concentrations of the amine, it appears that Na^+–K^+-ATPase is not the primary ionic mechanism mediating the effect of dopamine. On the other hand, the basal Na^+,K^+,$2Cl^-$ cotransporter, involved in chloride electrogenic secretion, is more likely to be the primary ionic mechanism, since frusemide when added to the basal side was the most potent compound to reduce I_{sc} and completely abolished the effect of all concentrations (0.1–100 μM) of dopamine on I_{sc}.

It has been reported for other catecholamines, namely adrenaline and noradrenaline (Chang et al., 1982; Field and McColl, 1973), that stimulation of intestinal electroneutral NaCl absorption and inhibition of HCO_3 secretion is mediated by α_2-adrenoceptors. The electroneutral NaCl absorption mechanism (Fig. 5), one of the most important absorptive mechanisms in the mammalian small intestine, comprises an apical Na^+/H^+ exchange working in concert with a Cl^-/HCO_3 exchange, bringing Na^+ and Cl^- into the cell. Intracellular Na^+ is then pumped out via the sodium pump located in the basolateral membrane. However, in the present study, electrogenic chloride secretion appears to have been directly involved in the dopamine-induced decrease in I_{sc}. Jejunal secretion of Cl^- (Fig. 5) in mammals involves Na^+,K^+,$2Cl^-$ co-transport in the basolateral membrane, that serves as the Cl^- uptake step; the Na^+–K^+-ATPase pump provides the driving force and recycles the Na^+, which might explain the results with ouabain. Excess K^+ is recycled via K^+ channels at the basolateral membrane, and Cl^- exits via a channel on the apical membrane. Regulation of the Cl^- secretory process occurs primarily at the Cl^- or K^+ channels.

Physiological responses specifically linked to α_2-adrenoceptors have been associated with inhibition of adenylate cyclase (Garcia-Sainz et al., 1980; Sabol and Nirenberg, 1979; Yamashita et al., 1980). The data presented here shows that pre-treatment with either forskolin or N^6,2′-*O*-dibutyryl cyclic AMP completely abolished the effect of dopamine on jejunal electrolyte transport. These results suggest that the dopamine-induced decrease in I_{sc} may be dependent on a reduction in intracellular cyclic AMP levels, but do not directly suggest that dopamine inhibits adenylate cyclase. However, this suggestion is consistent with the finding that both forskolin and N^6,2′-*O*-dibutyryl cyclic AMP, when added alone, increase I_{sc}. It is also in agreement with the finding that adrenaline, in the ileal mucosa, decreases cholera toxin- and prostaglandin-augmented cyclic AMP levels (Field et al., 1975).

It is concluded that the antisecretory effects of dopamine in the jejunum of adult rats are mediated through α_2-adrenoceptors. The response to dopamine appears not to involve the activation of specific dopamine receptors. Furthermore, the decrease in I_{sc} produced by dopamine ap-

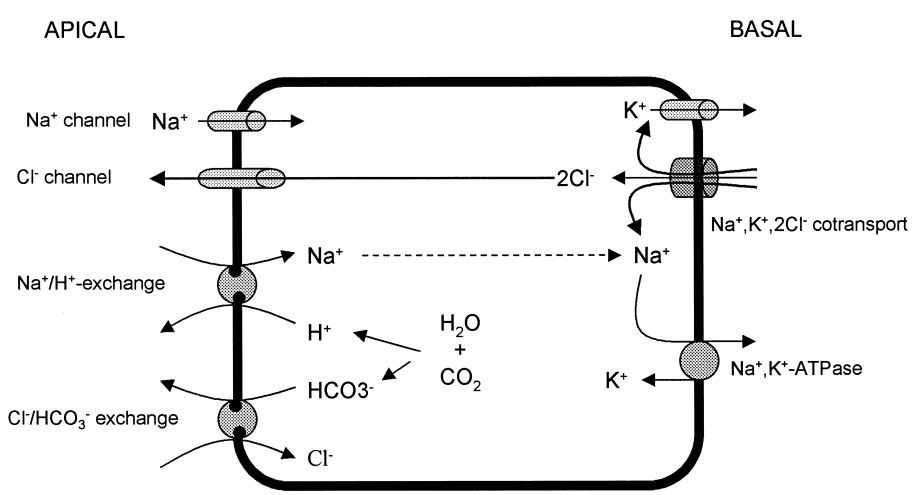

Fig. 5. Electroneutral NaCl absorption and Cl^- electrogenic secretion in mammalian jejunum.

pears to be sensitive to increases in intracellular cAMP and is primarily dependent on the basal $Na^+,K^+,2Cl^-$ co-transport mechanism involved in chloride secretion.

Acknowledgements

The present study was supported by grant number PECS/C/SAU/29/95 from the Fundação para a Ciência e a Tecnologia.

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