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EFFECTS OF PG E_2 AND PG I_2 ON THE ADENYLATE CYCLASE ACTIVITY IN RAT INTESTINAL EPITHELIAL CELLS.

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Prostaglandins of the E-type act as intestinal secretagogues and are believed to be important in the pathogenesis of certain diarrheal syndromes (1 , 2 , 3 , 4). The intestinal adenylate cyclase / cAMP-system has been implicated in the secretion of fluid induced by these compounds : It has been demonstrated that prostaglandins of the E-type increase cyclic AMP levels in association with the production of ion secretion in animal models (3 , 5).

The recently discovered prostacyclin (PG I_2) displays in addition to its potent platelet antiaggregation activity various gastrointestinal effects : Like PG E_2 it is a strong inhibitor of gastric acid secretion in vivo (6 , 7 , 8) and has comparable activity to PG E_2 in inhibiting indomethacin-induced gastric erosions (8).

In contrast to prostaglandin E_2 , however , PG I_2 did not stimulate intestinal fluid and electrolyte accumulation : In the rat enteropooling test system, this labile prostaglandin compound was virtually without effect (9).

We have examined the effects of prostaglandin E_2 and prostaglandin I_2 on the adenylate cyclase in homogenates of isolated rat mucosal intestinal cells.

The cells were isolated essentially according to the method of Weiser (1o). Cells were gently homogenized (3-5 strokes) with a Teflon glass homogenizer (Zell-Homogenisator, Colora-Messtechnik,Lorch, Württemberg,F.R.G.) in 5 mmol/l ice-cold Tris-HCl buffer, pH 7.5, containing 3 mmol/l $MgCl_2$, 1 mmol/l EDTA and 3 mmol/l mercaptoethanol.

Adenylate cyclase activity was assayed in the cell homogenates according to Salomon et al. (11), at pH 8.0 and 30°C. The protein content of the samples was measured according the Lowry-method (12). Statistical analysis was done by the Wilcoxon-test for paired samples.

Table 1

Effects of increasing concentrations of PG E_2 and PG I_2 on adenylate cyclase activity in isolated rat epithelial cells.

	Adenylate Cyclase Activity pmoles cAMP/ mg protein/ 15 min	
Concentration (mol/l)	Prostaglandin E_2	Prostaglandin I_2
None (basal)	150 ± 20	150 ± 20
3×10^{-8}	150 ± 18	140 ± 18
3×10^{-7}	165 ± 22	150 ± 16
3×10^{-6}	225 ± 30 *	155 ± 20
3×10^{-5}	310 ± 40 *	160 ± 22
1×10^{-4}	350 ± 45 *	160 ± 22
3×10^{-4}	350 ± 40 *	160 ± 20

Values are mean ± SD of six separate experiments, each carried out in triplicate. * significantly lower ($p \leq 0.05$) than the corresponding controls.

Basal adenylate cyclase activity in homogenates of isolated rat intestinal cells averaged 150 pmol cAMP/ mg protein/ 15 min.

Over a concentration of 3×10^{-8} mol/l to 3×10^{-4} mol/l prostaglandin E_2 and prostaglandin I_2 were tested on the rat enzyme system. As shown in Table 1, PG E_2 stimulates the activity of adenylate cyclase in a concentration-dependent manner. Effects were detectable at 3×10^{-7} mol/l and maximal at 1×10^{-4} mol/l. At this concentration, PG E_2 induced an about 2.3-fold maximal increase over basal enzyme activity.

By contrast, prostacyclin (PG I_2) did not produce stimulation of rat adenylate cyclase activity up to 3×10^{-4} mol/l (Table 1). The lacking effect of PG I_2 was not attributable to biological inactivity of the prostacyclin preparation used, because the same charge was able to activate the enzyme system in human gastric and colonic mucosa (not shown).

Prostaglandin E_2 and prostaglandin I_2 have similar actions, particularly on the adenylate cyclase in different tissues (13 , 14). It is, therefore, often assumed that both prostaglandins act via similar receptor sites. Our studies reveal, however, that in rat small intestinal epithelial cells both prostaglandins have clearly distinct actions on the enzyme system: PG E_2 is a potent activator of adenylate cyclase, whereas PG I_2 is without effect. Considering the lacking effects of PG I_2 on fluid and electrolyte movement in the rat small intestine, our data emphasize the important role of the adenylate cyclase /cAMP-System in the secretory process in this organ.

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