Evidence for $A_1$ adenosine receptor–mediated inhibition of peristalsis in the guinea-pig isolated ileum

Eurek Ranjit, Diana Wood, Robert Naylor, Bishwa Tuladhar

University of Bradford, Bradford, West Yorkshire, United Kingdom

Adenosine is an established endogenous neuromodulator that inhibits acetylcholine release in the guinea-pig ileum. In the present study, we investigated the modulation of peristalsis by adenosine in the isolated guinea-pig ileum and attempted to characterise the adenosine receptor involved in its effect.

Segments of ileum (5-30 cm from the caecum) were obtained from male guinea-pigs (Dunkin Hartley, 300-500g), cannulated at the oral and aboral ends and secured horizontally in 10 ml baths containing Krebs’ solution maintained at 37°C and oxygenated with 95%O₂ and 5%CO₂. Regular peristalsis was obtained by infusing saline solution into the lumen using the method described previously (Costall et al., 1993). All drugs were added to the serosal side, antagonists and the vehicle were equilibrated for at least 30 min before the addition of adenosine. Adenosine was added cumulatively at 6-8 min intervals once a regular peristalsis was obtained. Any increase in the threshold for peristalsis was measured from the maximum threshold in the 6 min period before the addition of adenosine and expressed as a percentage change to the possible maximum increase in threshold (taken as 4 cm, the position of the outlet tube) when peristalsis was abolished. All values are presented as mean±s.e.mean and statistical comparisons between the different treatments were made using one way ANOVA followed by Dunnett’s t test.

In all control tissues, adenosine (1-100 µM) caused a concentration-related increase in the threshold for peristalsis until finally, the peristalsis was abolished. The pEC₅₀ value for the inhibition of peristalsis, calculated at 50% increase in the threshold, was 4.52±0.15, n=10. The concentration response curve for adenosine was shifted rightwards in a surmountable manner by the $A_1$ adenosine receptor selective antagonist PSB 36 (0.01-1µM, Abo-Salem et al., 2004). pEC₅₀ values for adenosine in the presence of 0.01, 0.1 and 1 µM of PSB 36 were 3.61±0.02, 3.31±0.12 and 2.98±0.14 respectively, n=5 all, P<0.001. Unlike PSB 36, the $A_2A$ adenosine receptor selective antagonist SCH 58261 (0.1 µM, Zocchi et al., 1996) and the $A_2B$ adenosine receptor selective antagonist PSB 1115 (5 µM, Abo-Salem et al., 2004) failed to significantly alter the concentration response curves to adenosine. pEC₅₀ values for adenosine in the presence of SCH 58261 and PSB 1115 were 4.50±0.10 and 4.27±0.13 respectively, n=5 both, P>0.05.

The results indicate that the inhibitory effect of adenosine in the peristaltic reflex in the guinea-pig ileum is mediated by $A_1$ adenosine receptors. The data also indicate that $A_2$ adenosine receptors are unlikely to be involved in the effect of adenosine. The presynaptic location of $A_1$ adenosine receptors mediating inhibition of acetylcholine release in the guinea-pig ileum has been previously reported (Lee et al., 2001), which may explain the mechanism of the inhibitory effect of adenosine on peristalsis in the guinea-pig ileum.


Costall, B et al. (1993) Br J Pharmacol 110, 1572-1578
