

## Theophylline is not an antagonist of intramural inhibitory nerve activity in rabbit and guinea pig intestine

R.C. SMALL & A.H. WESTON

*Department of Pharmacology, Materia Medica and Therapeutics, University of Manchester*

Attempts to assess the validity of the purinergic transmission hypothesis (Burnstock, Campbell, Satchell & Smythe, 1970) have been frustrated by the absence of a selective antagonist of purine action on smooth muscles.

Sawynok & Jhamandas (1976) showed that adenosine and ATP suppressed twitches of the transmurally stimulated guinea pig ileum by inhibiting acetylcholine release, an action antagonized by theophylline. In rabbit duodenum Ally & Nakatsu (1976) showed that theophylline selectively antagonized adenosine-induced relaxation. A report (Okwuasaba, Hamilton & Cook, 1977) that theophylline selectively antagonized ATP and intramural inhibitory nerve activity in guinea pig fundic strips seemingly confirmed theophylline's antagonism of purines in the intestine and provided evidence in favour of purinergic transmission.

We have subsequently investigated the ability of theophylline to antagonize noradrenaline, ATP, adenosine and inhibitory nerve activity in several intestinal tissues. In each tissue the concentration of theophylline used was below that which caused marked loss of muscle tone. Where the effects of inhibitory nerve activity were studied, hyoscine ( $3 \times 10^{-5}\text{M}$ ) and guanethidine ( $10^{-5}\text{M}$ ) were present throughout.

We have confirmed the findings of Sawynok & Jhamandas (1976) in that theophylline ( $5 \times 10^{-5}\text{M}$  —  $10^{-3}\text{M}$ ) antagonized the twitch suppression evoked by adenosine and ATP in the transmurally stimulated guinea pig ileum, but not that evoked by noradrenaline. We have confirmed the findings of Ally & Nakatsu (1976) in that theophylline ( $10^{-4}\text{M}$ ) antagonized adenosine's relaxation of rabbit duodenum. However, theophylline did not antagonize

noradrenaline, ATP or inhibitory nerve activity in this tissue.

Theophylline ( $10^{-4}\text{M}$ ) did not antagonize noradrenaline, ATP or inhibitory nerve activity in guinea pig taenia caeci or fundic strip preparations and these observations have been confirmed in other laboratories (Hooper, Spedding, Sweetman & Weetman, 1978; Baer & Frew, personal communication, 1978). Cook & Hamilton (personal communication) have been unable to repeat the experiments of Okwuasaba *et al.* (1977) and confirm that theophylline does not specifically antagonize post synaptic purinergic receptors of the guinea pig fundic strip.

Collectively these observations call into question the evidence for purinergic transmission offered by the theophylline experiments of Okwuasaba *et al.* (1977). Indeed, the ability of theophylline to sometimes antagonize purines but not inhibitory nerve activity may be construed as evidence against the purinergic hypothesis.

### References

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