Failure of peristaltic stimulants to restore peristalsis previously blocked by 2,4-dinitrophenol

The action of metabolic inhibitors on the active transport of cations in nerve fibre (Hodgkin & Keynes, 1955), on mammalian striated muscle (Barnes & Duff, 1954) and on the electrical and mechanical activity of the smooth muscle of the guinea-pig taenia coli (Bülbring & Lüllman, 1957) have been described. We have attempted to relate the peristaltic block produced by 2,4-dinitrophenol (DNP) with active cationic transport in nerves or smooth muscles (or in both structures) involved in the peristaltic reflex.

A modified method of Trendelenburg (1917) to record the peristaltic activity (Beleslin & Varagić, 1958) was used. Volume changes in the intestinal segment were recorded by means of a float recorder and movements of the longitudinal muscle by an isotonic lever. The intestine was suspended in a 20 ml bath containing Tyrode solution at 36° gassed with oxygen. The peristaltic reflex was elicited by increasing the intraluminal pressure by 3–4 cm H_2O for about 90 s; the increase in pressure was kept constant throughout.

The effect on the peristaltic reflex of DNP was studied by introducing it (10–500 μg/ml) into the lumen of the isolated intestine or by adding it to the bath. By both routes DNP depressed or blocked the peristaltic reflex and this was reversible within 10–20 min. DNP in concentrations higher than 100 μg/ml contracted the longitudinal muscle and blocked the peristaltic reflex.

Peristaltic stimulants such as acetylcholine (500–600 μg/ml), arecoline (0·05–0·25 μg/ml), nicotine (100–200 μg/ml) and eserine (0·02–5·0 μg/ml) acting from the serosal side did not antagonize the inhibitory effect of DNP on the peristaltic reflex obtained either from mucosal or serosal side. When the peristaltic reflex was blocked by DNP, acetylcholine and eserine contracted the circular and longitudinal smooth muscles and caused a few small waves which were not typical peristaltic waves. In similar experiments serosal and mucosal application of 5-hydroxytryptamine (1–15 μg/ml) and histamine (1–50 μg/ml) failed to restore the peristaltic waves previously inhibited by DNP on either surface of the gut.

When the peristaltic reflex was depressed or abolished by serosal application of DNP, adenosinetriphosphate (ATP) and adenosinediphosphate (ADP) in concentrations from 10 to 250 μg/ml within 20 min failed to restore this reflex.

Serosal application of potassium chloride in concentrations from 1–4 mg/ml contracted both the longitudinal and circular smooth muscles, but failed to restore the peristaltic reflex previously blocked by serosal application of DNP. There was no restoration of the reflex, but a few small waves appeared which were not typical peristaltic waves. Calcium chloride and magnesium chloride were without effect on the peristaltic reflex previously blocked by serosal application of DNP.

It is evident that the peristaltic stimulants, ATP, ADP and cations cannot restore the peristaltic reflex previously blocked by DNP. Moreover, acetylcholine, eserine and potassium chloride contracted both longitudinal and circular smooth muscles in the presence of DNP. Evans, Schild & Thesleff (1958) have shown that drugs may activate the contractile elements of plain muscle without the mediation of membrane depolarization. The present experiments suggest that a contraction in smooth muscles may be produced by acetylcholine, eserine and potassium chloride in the presence of DNP when the active cationic transport is blocked. However, acetylcholine, eserine and potassium chloride cannot produce peristaltic waves when the active cationic transport is blocked, though both longitudinal and circular smooth muscles are contracted.

Department of Pharmacology,
Medical Faculty,
Beograd 11105, Yugoslavia.

D. B. BELESLIN
Z. MALOBABIĆ

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Relaxing potency of terbutaline and orciprenaline on rat uterus

The inhibitory effects of the selective β-receptor stimulating agent terbutaline (Persson & Olsson, 1970) and of orciprenaline have been compared on carbachol-induced contractions in the rat isolated uterus.

Female rats, Sprague-Dawley, 130–150 g, had 0·2 μg 17-β-oestradiole benzoate subcutaneously 24 h before being killed by a blow on the head and bled. The middle part of each uterus horn, of about 2 cm length, was put in an organ bath (25 ml) containing calcium-poor Locke solution (45 g NaCl, 2·1 g KCl, 0·3 g $CaCl_2$, 2·5 g $NaHCO_3$, 2·5 g glucose in 5 litre of glass-redistilled water) at 25° and gassed with 5% carbon dioxide in oxygen. Isometric tension changes were recorded. Dose-response measurements of carbachol-induced contractions, and a dose of carbachol (1·0–4·0 μg/ml) corresponding to about 80% of maximum contraction was then selected for use in the test of inhibitory activity of both drugs. These were administered at 0·008–0·8 μg/ml 90 s before carbachol. The decrease of carbachol-induced contraction was recorded. The dose of carbachol was then given every 8 min until a stable response again was obtained and the next β-adrenoceptor effect was evaluated.

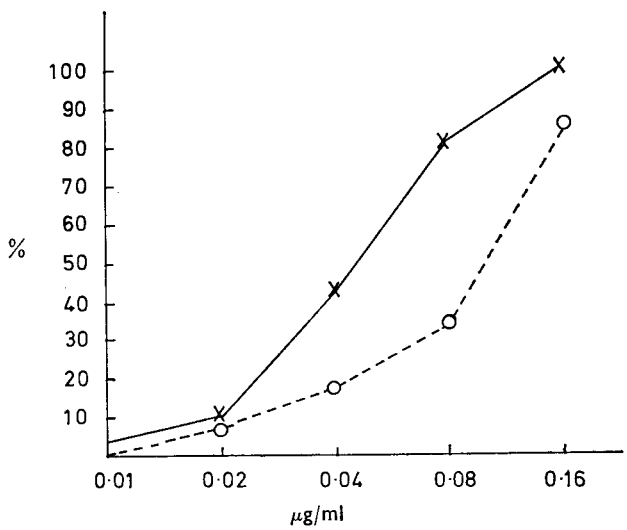

FIG. 1. The inhibition (%) of carbachol-induced contractions by different doses of terbutaline (×) and orciprenaline (○).