MECHANISM BY WHICH PEPPERMINT OIL EXERTS ITS RELAXANT EFFECT ON GASTROINTESTINAL SMOOTH MUSCLE

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Traditionally peppermint oil has been used as a carminative agent in the relief of flatulence and colic pain. However, more recently attention has focussed on its use in providing symptomatic improvement in patients with the irritable bowel syndrome (Rees et al 1979). It has also been demonstrated that peppermint oil possesses a relaxant effect on rectosigmoid motility when administered topically (Duthie 1981). Using guinea pig isolated ileum we have already shown that peppermint oil possesses marked smooth muscle inhibitor properties (Taylor et al 1983) and it is the purpose of this study to examine the possible mechanism by which this takes place.

Peppermint oil consists of a number of constituents such as menthol (44%), menthone (33%), cineole (12%) and menthyl acetate (4.4%), and so it was firstly necessary to determine which of these components is responsible for the biological activity of peppermint oil. Using guinea pig isolated ileum suspended in Tyrode's solution bubbled with 5% CO_2 in O_2 at 37°C, relaxation curves to cumulative doses of peppermint oil and each of its constituents were carried out using carbachol as the agonist. Doses required to bring about 50% relaxation (ID_{50}) were then compared. Menthol (3.0×10^{-5} w/v) was the most active constituent, being more active than peppermint oil (4.4×10^{-5} v/v) while menthone, menthyl acetate and cineole were considerably less active than peppermint oil.

Using strips (30 x 3 mm) of human isolated taenia coli suspended in normal Krebs' solution bubbled with 5% CO_2 in O_2 at 37°C, peppermint oil and menthol inhibited basal tone and contractions to carbachol (10^{-7}-10^{-4}M) and to potassium chloride (5 - 150mM) in a non-competitive manner. In calcium - free, depolarising Krebs' solution (mM: NaCl 82.7; KCl 40.0; $NaHCO_3$ 25.0; NaH_2PO_4 1.4; glucose 11.5) parallel shifts in dose response curves to calcium (0.1 - 20 mM) indicated that peppermint oil and menthol possess specific calcium antagonist activity. To further investigate this effect we studied the influx of $^{45}Ca^{2+}$(μ mole/kg wet weight) into carbachol (10^{-6}M) or potassium (80mM) stimulated rings of guinea pig ileum (7 - 15 mg) suspended in buffered HEPES solution containing $^{45}Ca^{2+}$ (10^{-3} mCi/ml). Following carbachol or potassium stimulation the extracellular concentration of Ca^{2+} increased significantly ($p < 0.001$). However, in the presence of menthol (0.64 mM) no such influx was observed. The calcium antagonist, verapamil (10^{-5}M) likewise inhibited $^{45}Ca^{2+}$ uptake in response to carbachol and potassium stimulation. In addition, peppermint oil and menthol inhibited carbachol - induced contractions of the guinea pig isolated ileum suspended in calcium - free Tyrode's solution on the readmission of calcium ions, further indicating that peppermint oil and menthol are able to inhibit carbachol - induced influx of extracellular calcium ions.

It is concluded that menthol is the constituent mainly responsible for the relaxant activity of peppermint oil on gastrointestinal smooth muscle. The mechanism by which this is brought about is associated with the ability of menthol to decrease the influx of extracellular calcium ions through potential dependent channels.

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