INVESTIGATION INTO THE PHARMACODYNAMIC PRINCIPLES OF *CUCURBITA MAXIMA* (THE PUMPKIN)

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Irritable Bowel Syndrome (IBS) is associated with both increased segmentation and hypomotility of the large bowel. The observation that IBS symptoms (abdominal pain and disordered bowel motility) are exacerbated after eating fruit and vegetables of the family Cucurbitaceae, prompted this investigation into the activity of the pharmacodynamic principles of Cucurbita maxima on ex vivo intestinal smooth muscle.

Methanol extracts of pumpkin flesh were rota-evaporated down and fractionated by ion exchange. All fractions showed similar, though not identical, activity to that of the unfractionated extract. For initial screening guinea-pig ileum was chosen as a well characterised pharmacological preparation. Doses equivalent to 0.5g of pumpkin flesh produced a characteristic response consisting of a sharp contraction followed by relaxation and then slow and prolonged contraction.

The slow prolonged contraction was further explored. Similar dose-response relationships were produced using 10^{-5}M deoxycholic acid. The response to both the pumpkin preparations and deoxycholate were reduced using doses of 10^{-7}M mepyramine and 10^{-6}M methysergide. However neither histamine nor 5HT could be detected chromatographically in the extracts. Responses to pumpkin preparations and to deoxycholate were depleted by prolonged contact time and by repeated dosing. Pre-treatment of the ileum with 10^{-7}M disodium cromoglycate abolished the responses. These results suggest a common mode of action, possibly through release of endogenous mediators from mast cells or other intestinal cells. This supports the suggestion that increased levels of prostaglandin E_2 are present in IBS (Jones et al 1982). The active principle has not been characterised, but it is noteworthy that both deoxycholate and the cucurbitacins (present at least in pumpkin seeds) have steroidal structures and may therefore solubilise the lipid bilayer of cell membranes (Black 1988).

The non-adrenergic, non-cholinergic relaxation was further explored using the rabbit duodenum. Similar dose-dependent relaxations were obtained with pumpkin extract and adenosine and these were antagonised by 10^{-4}M caffeine. This might tentatively suggest involvement of P_1 purinoceptors of the A_2 subtype (Gaion et al 1988). However other reports suggest the existence of relaxatory adenosine receptors distinct from the A_2 subtype (Munshi et al 1988). The non-adrenergic, non-cholinergic initial sharp contraction seen with pumpkin extracts may be mediated by the same principle as the relaxation. Evidence exists that P_1 purinergic agonists act on A_1 purinoceptors at low concentrations to cause contraction of smooth muscle, but at higher concentrations a relaxation is produced via the A_2 purinoceptors (Farmer et al 1988). Both the initial sharp contraction and the relaxation were caused by a principle which was found to degrade following long term storage at -20°C.

These preliminary investigations suggest some foundation to the observation that IBS is aggravated by pumpkin.

In future work it is intended to further characterise the active principles of the pumpkin extracts and also to explore the activity using suitable ex vivo large bowel models.

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