

# LETTERS TO THE EDITOR

## The Effects of Smooth Muscle Stimulants on the Movement of Calcium-47 in the Guinea-pig Ileum *in vitro*

SIR,—In depolarised strips of rabbit ileum, acetylcholine increases calcium-45 uptake (Robertson, 1960), and Schatzman (1961) has shown that it increases calcium efflux in the guinea-pig taenia coli, and he concluded that during stimulation there was a net calcium uptake. Chujyo and Holland (1962) showed that pilocarpine increased calcium-exchange in a tubular segment of guinea-pig ileum and Durbin and Jenkinson (1961a,b) suggested that the carbachol-induced contracture of the depolarised taenia coli of the guinea-pig was due to a net increase in calcium influx, caused by a drug-induced increase in membrane permeability.

TABLE I

DRUG EFFECTS UPON  $^{47}\text{Ca}$  UPTAKE AND RELEASE IN STRIPS OF GUINEA-PIG ILEUM

Drug	Dose ( $\mu\text{g./ml.}$ )	Effect on $^{47}\text{Ca}$ release	Effect on $^{47}\text{Ca}$ uptake
Acetylcholine chloride .. .. .	100	Increased (12) $P < 0.001$	Increased (16) $0.001 < P < 0.01$
Carbachol .. .. .	6	No change (12) $0.05 < P < 0.10$	Increased (12) $0.02 < P < 0.05$
Histamine acid phosphate .. .. .	10	Increased (12) $P < 0.001$	No change (12) $0.05 < P < 0.10$
5-Hydroxytryptamine creatinine sulphate..	10	Increased (12) $P < 0.001$	Increased (12) $0.02 < P < 0.05$
Barium chloride .. .. .	1 mg.	Increased (12) $P < 0.001$	Increased (12) $0.02 < P < 0.05$
Papaverine sulphate .. .. .	200	Decreased (11) $0.02 < P < 0.05$	No change (12) $0.70 < P < 0.80$
Lysergic acid diethylamide .. .. .	10	No change (8) $0.20 < P < 0.30$	No change (12) $0.60 < P < 0.70$
Atropine sulphate .. .. .	10	No change (8) $0.60 < P < 0.70$	No change (12) $0.40 < P < 0.50$
Mepyramine maleate .. .. .	10	No change (8) $0.90 < P$	No change (12) $0.50 < P < 0.60$
Adrenaline Hydrogen-tartrate .. .. .	500	No change (12) $0.40 < P < 0.50$	No change (12) $0.50 < P < 0.60$
Noradrenaline bitartrate .. .. .	500	Increased (12) $0.02 < P < 0.05$	No change (12) $0.20 < P < 0.30$

Figures in parentheses indicate the number of paired strips of guinea-pig ileum used.

We have investigated the effects of some drugs which stimulate smooth muscle, and some of their antagonists upon the influx and efflux of calcium-47 in strips of guinea-pig ileum maintained isotonicly in oxygenated Krebs' fluid at  $37^\circ$ . Replicate experiments were made for each dose of drug used, employing not less than eight to twelve paired strips of ileum, one member of each pair serving as control. In the experiments on calcium efflux, the loss of calcium-47 from the tissue during a 1-min. period was estimated; calcium-47 uptake was measured for a period of 10 min. In the former, the total counts released are added to those remaining in the tissue at the end of the experiment, so as to obtain the total initial radioactivity. From this, the percentage of

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counts released during exposure to the drug was calculated and compared with those released during exposure to the control solution.

In the influx experiments the counts taken up by the tissue from the drug-containing, radioactive bathing medium were measured, expressed as a percentage and compared with those taken up by a control muscle strip.

In both cases the differences between the drug-treated and control preparations were tested for significance, using Student's 't' test. The results are shown in Table I.

Acetylcholine significantly increased calcium-47 release. This confirms the results of Schatzman (1961), who used a lower dose-10  $\mu\text{g./ml.}$  Carbachol did not significantly increase the release at the dose used but histamine, 5-hydroxytryptamine (5-HT) and barium chloride did increase the release as did nor-adrenaline. Adrenaline, however, had no significant effect, but papaverine sulphate decreased calcium-47 release. Atropine sulphate, mepyramine maleate and lysergic acid diethylamide caused no significant change in release. Eichler, Appel and Staib (1960), using an *in vivo* preparation of rat intestine, showed, however, that 100  $\mu\text{g./ml.}$  of adrenaline increased calcium excretion into the lumen of the intestine.

A significantly increased uptake of calcium-47 was caused by acetylcholine chloride, carbachol, 5-HT and barium chloride. The other compounds tested had no significant effect. The results with acetylcholine and carbachol confirm those of Robertson (1960) and Durbin and Jenkinson (1961a,b).

It is possible that compounds which stimulate the guinea-pig ileum increase both the release and uptake of calcium ions and therefore increase their mobility. Of particular interest is the finding that papaverine sulphate, which causes relaxation of smooth muscle, decreases the release of calcium-47. It has also been shown that papaverine sulphate (0.2 mg./ml.) depressed both the release ( $P < 0.001$ ) and uptake ( $P < 0.001$ ) of potassium-42 in similar preparations.

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