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LETTER TO THE EDITOR

EFFECT OF CALCIUM, STRONTIUM, AND BARIUM ON THE PERISTALTIC ACTIVITY IN FROG STOMACH AND THEIR MODIFICATION BY VERAPAMIL

Sir,

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In an earlier study with skeletal and cardiac muscles, Ca^{2+}, Sr^{2+}, and Ba^{2+} were found to exhibit many similar actions (1). In smooth muscle, excitation - contraction coupling is intricate in as much as Ca^{2+} is involved in several different processes which are interconnected and influence the ultimate mechanical output through variations in $[Ca^{2+}]i$ (2). It was therefore of interest to study how Ca^{2+}, Sr^{2+}, and Ba^{2+} modify the normal peristaltic activity in frog stomach, wherein the effect on the neuronal tissue as well as on the smooth muscle can be studied at a time without the interference of other spasmogens.

Trendelenburg's method (3) was followed for recording the peristaltic activity in frog stomach with slight modifications as described by Sharma et al (4). Frog stomach, after washing the lumen with frog Ringer solution, was mounted in a bath (100 ml) containing frog Ringer solution at 37°C, bubbled with 0_2. The peristaltic activity was induced by raising the reservoir to a critical height for 2 min at 5 min intervals. After obtaining reproducible peristaltic activity, the effect of the drugs was studied by adding the drug to the bath for 2 min. The bath was washed out during rest periods. The interaction with verapamil was studied by adding the drug 2 min prior to the administration of cation under study.

Ca^{2+}, Sr^{2+}, and Ba^{2+} in low doses (Table I) enhanced the peristaltic activity in frog stomach. The effect was reversible and full recovery was obtained within two or three washes. Higher doses of the cations (Table I) inhibited the peristaltic activity in frog stomach. The inhibition was reversible on washing.

TABLE I : Effect of cations on induced peristalsis of frog stomach in presence and absence of verapamil.

Drug/Drug combination with dose	*Height of peristaltic contraction in cm M±SEM*	
Nil (Control)	2.25 ± 0.24	
$CaCl_2$ 10 µg/ml	3.08 ± 0.26*	
$CaCl_2$ 100 µg/ml	0.4 ± 0.19**	
Verapamil 0.13 µg/ml + $CaCl_2$ 100 µg/ml	1.16 ± 0.38	N.S.
Nil (Control)	1.98 ± 0.44	
$SrCl_2$ 20 µg/ml	3.43 ±0.38*	
$SrCl_2$ 80 µg/ml	0.23 ± 0.45**	
Verapamil 0.13 µg/ml + $SrCl_2$ 80 µg/ml	0.91 ± 0.27	N.S.
Nil (Control)	2.05 ± 0.45	
$BaCl_2$ 0.6 µg/ml	3.21 ± 0.38*	
$BaCl_2$ 3.0 µg/ml	0.14 ± 0.45***	
Verapamil 0.13 µg/ml + $BaCl_2$ 3.0 µg/ml	0.27 ± 0.06	N.S.

Significantly different from control, n = 6,
* = P<0.05; ** = P<0.01; *** = P<0.001.

N.S. = Not significant at P>0.05.

Verapamil itself inhibited the peristaltic activity in frog stomach when given in the dose range of 0.1 to 0.25 µg/ml. A submaximal dose of 0.13 µg/ml was however sufficient to adequately inhibit the peristalsis with verapamil. In presence of this dose, the effect of higher dose of the cations was partially inhibited (Table I). Full recovery from the inhibitory effect of verapamil was seen within 15 to 20 min when the

preparation was washed. This antagonism, however, was not seen when Ca^{2+}, Sr^{2+}, and Ba^{2+} were used in small doses.

There is no report readily available about the effect of the three cations on peristalsis and their antagonism by verapamil, although verapamil antagonism of vascular smooth muscle contraction by the three ions is known (5). We observed that Ca^{2+} Sr^{2+}, and Ba^{2+} act in the same way on the peristaltic activity just as their effect on other preparations like skeletal muscle, cardiac muscle, and other smooth muscles (6,7,8). Sr^{2+} and Ba^{2+} potentiate the spasmogenic effect of acetylcholine and block the K^+-induced contracture in frog rectus (8). On frog heart, all the three cations show stimulant effect (1). Furthermore, they potentiate the spasmogenic action of histamine on the intestinal smooth muscle (1). It is therefore presumed that all these bivalent cations have similar mechanisms of action, and that Sr^{2+} and Ba^{2+} like Ca^{2+} act directly at the target site, i.e., actomyosin complex (9), or indirectly through the liberation of Ca^{2+} (10).

As verapamil, a selective voltage dependent Ca^{2+} channel blocker, could only produce a partial recovery of the inhibitory effects of Ca^{2+}, Sr^{2+}, and Ba^{2+} on peristalsis in our experiments, we suggest that these cations may induce their effects by their direct action on the actomyosin complex as well as by mobilizing the extra-cellular Ca^{2+} through voltage dependent Ca^{2+} channel as has been suggested for Ba^{2+} (11) and for Sr^{2+} (12) in smooth muscle contractions.

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