

EFFECT OF FLUNARIZINE ON CONTRACTILE ACTIVITY OF ANTRUM AND FUNDUS OF GUINEA PIG STOMACH

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While studying the effects of diphenylpiperazine calcium channel blockers on gastrointestinal functions it was found that flunarizine prevents gastric damage caused by different ulcerating agents (1). As most of the pro-ulcerogenic mechanisms including gastric wall hypercontractility, increased acid production, gastric wall microcirculation disorders, increased release of monoamines from mastocytes are calcium dependent (2) it is conceivable that calcium channel blockers, in particular flunarizine, could diminish gastric lesions by influencing one or more of these processes. The purpose of the present series of experiments was to determine the effect of flunarizine on contractility of smooth muscle strips obtained from antrum and fundus regions of guinea pig stomach and to explain the possible connection with the previously established ulceroprotective effect of this drug. Male guinea pig weighing 300-400 g were killed by shooting and bleeding. The stomach was removed immediately. Circular muscle strips (2 mm wide and 10 mm long, mucosa removed using blunt dissection) were prepared from antrum or fundus regions. Muscle strips were placed in organ bath (10ml in capacity) filled with Krebs solution (up to 2 strips were suspended in the same organ bath). Mechanical activity was recorded under isometric conditions. Initial tension (1g) was applied to each preparation and tissues were allowed to adapt for a 60 min period before testing. The effects of flunarizine on phasic antral activity and tonic fundal activity were studied. For this purpose normal Krebs solution as well as Krebs solution with high K^+ , Ca^{2+} or Ba^{2+} concentration were used. Flunarizine (Pharmachim) was added directly to the organ bath in increasing concentrations from $5 \cdot 10^{-6}$ up to $5 \cdot 10^{-5}$ M/l. The mechanical activity was measured in mm and the percentage of the contractile response in the percents of flunarizine towards the spontaneous contractile response was calculated. The Krebs solution had the following composition in mM/l: Na^+ 137; K^+ 5,9; Ca^{2+} 2,5; Mg^{2+} 1,2; Cl^- 124; HCO_3^- 25; $H_2PO_4^-$ 1,2; glucose 11,5; equilibrated with 95% O_2 and 5% CO_2 at 36°C, pH 7,4. As shown in fig. 1 flunarizine produced a concentration-related decrease in the spontaneous

phasic activity of antrum while the tonic reaction of the fundus persisted, only slightly reduced in size. The latter can be selectively suppressed by nitroprusside sodium. When concentrations of Ca^{2+} or Ba^{2+} in Krebs solution were increased the effect of flunarizine on phasic activity was significantly reduced (fig. 2). Fig. 3 shows that flunarizine is potent in reducing high- K^+ evoked contraction both in antrum and fundus. These data are in good agreement with the results obtained about the effects of other calcium channel blockers (3). These data indicate that the ability of flunarizine to reduce

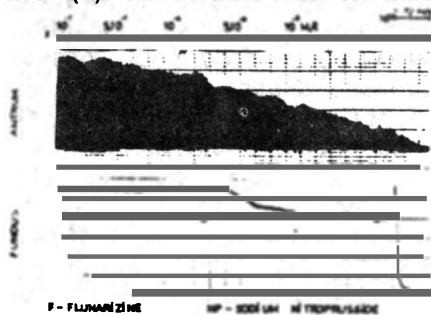


Fig. 1

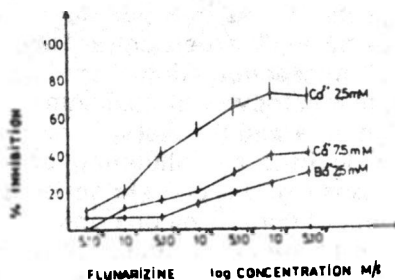


Fig. 2

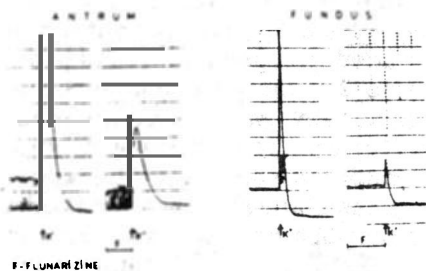


Fig. 3

the spontaneous phasic antral without affecting tonic fundal activity could be in relation with the previously established ulceroprotective properties of this drug. Other calcium channel blockers (nifedipine, verapamil) that can alter gastric contractility in similar way have been found to possess protective effect against gastric mucosal damage (2,4,5).

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