0·1 mmoles/kg; $n=15$). The addition of acetylcholine (100 μg/ml) for 5 min induced a further increase of the sodium content (122·2$\pm$0·9 mmoles/kg; $n=13$) and a further decrease of calcium (1·7$\pm$0·1 mmoles/kg; $n=13$). In the presence of angiotensin (10^{-7}M) these ionic changes were reduced.

These observations show that angiotensin induced a net sodium efflux in smooth muscle desensitized by acetylcholine; when the calcium content of the medium was reduced this sodium efflux was associated with a net calcium influx. This could be due to an activation of a coupling between an inward movement of calcium and an outward movement of sodium. Such an activation could explain the increase in tissue responsiveness in the various experimental conditions here described.

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Blockade of the effects of Valyl-5-angiotensinamide II, oxytocin, noradrenaline, 5-hydroxytryptamine and acetylcholine by guancydine

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Guancydine is a 1-cyano-3-*tert*-amylguanidine whose vasodepressor effects were attributed to a specific angiotensin blocking activity (Cummings, Welter, Grace & Lipchuck, 1968).

The contractile responses of the isolated uterus and colon from the rat were tested using a low Ca (0·6 mM) Krebs solution in order to avoid spontaneous contractions. Strips of rabbit aorta were suspended in Krebs solution with normal Ca (1·3 mM). The agonists used were Valyl-5-angiotensinamide II on colon, uterus and aorta; oxytocin on uterus; 5-hydroxytryptamine on uterus; acetylcholine on colon and noradrenaline on aorta. Guancydine, when used in concentrations higher than 10^{-4}M, antagonized in a non-competitive fashion the response to all of the agonists tested.

In another series of experiments, rat uterus and rat colon were suspended in a Krebs solution containing 2·5 mM Ca; the organs developed a strong rhythmic activity. Guancydine in concentrations higher than 10^{-7}M inhibited the spontaneous contractions. In higher concentrations (5×10^{-4}M) guancydine inhibited the action of oxytocin on net water influx of frogs (*Rana esculenta*) bladder epithelium.

In conclusion, guancydine inhibits smooth muscle contractility by a mechanism probably affecting the excitation-contraction coupling and this is the reason for the non-specific, non-competitive antagonism produced by guancydine on the actions of Valyl-5-angiotensinamide II, oxytocin, 5-hydroxytryptamine, acetylcholine and noradrenaline.

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