There are three reasons why the increase in acid activatable kinin-forming enzyme was not simply the result of passage of the enzyme or substrate from the plasma into the lymph. First the kinin-forming activity increased up to 70-fold whereas the overall lymph protein increased less than twice. Second, although in some experiments there was an increase in the acid activatable kinin-forming enzyme in the plasma, in others the increase was observed only in the lymph. Third, the increase in the activity of the plasma was sometimes less than, and sometimes occurred at a different time from, that in lymph.

A possible explanation of some of these findings is as follows: prekallikrein leaks into the injured tissue where it is activated by tissue activators (Lewis, 1959). The active enzyme is, however, rapidly neutralized by kallikrein inhibitor to form a complex which is dissociated by acid (Kraut, Frey & Werle, 1930). The acid activatable enzyme measured in the present experiments was therefore probably a measure of the kallikrein which had been activated and subsequently neutralized.

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Possible existence of different types of angiotensin II receptors

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The actions of five structure analogues of Valyl-5-angiotensinamide II on the contractility of three different smooth muscle preparations were studied. For this purpose, isolated colon and uterus from the rat and strips of rabbit aorta were suspended in a temperature regulated, oxygenated Krebs solution.

Dilutions of analogues and of Valyl-5-angiotensinamide II were compared by finding the concentration of each that was required in the tissue bath to cause an equal and moderate response of the muscle (at around the ED50 of Valyl-5-angiotensinamide II). The ratio of activity was often substantially different for each one of the organs tested (Table 1). Theoretically, if the receptors in the three different organs are the same, a similar ratio of activity of the analogues compared with Valyl-5-angiotensinamide II should be expected.

TABLE 1. *Ratio of activity of analogues of Valyl-5-angiotensinamide II*

	Rat colon	Rat uterus	Rat aorta
Valyl-5-angiotensinamide II	100	100	100
Ornithine-2-angiotensinamide II	5·00±0·57*	4·18±0·19	0·38±0·08
Phenylalanine-4-angiotensinamide II	5·16±0·04	0·66±0·04	0·24±0·01
Phenylalanine-4-angiotensin II	5·65±0·68	3·87±0·46	2·00±0·20
Tyrosine-5-angiotensin II	0·25±0·04	0·5±0·05	0·03±0·00
Proline-9-phenylalanine-10-angiotensinamide I	0·41±0·03	0·52±0·03	0·62±0·01

* Mean±S.E.M., effect of the analogue in per cent of Valyl-5-angiotensinamide II activity, considered as 100%. All the analogues were obtained by courtesy of Dr. B. Riniker (CIBA Research Laboratories, Basle).

The results suggest the existence of receptors of different structures. It is not yet possible to say if there are three different types of receptors, each one particular for rat colon, rat uterus and rabbit aorta, or if instead there are two types, which have variable concentrations in the different organs tested.

Angiotensin auto-potentiation

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It has been reported that the response to angiotensin is influenced by a preceding administration of the peptide. On whole animals as well as on isolated preparations, tachyphylaxis occurred after repeated administration (Khairallah, Page, Bumpus & Türker, 1966; Godfraind, 1968a). However, in the longitudinal smooth muscle of the guinea-pig ileum, either auto-potentiation or tachyphylaxis occurred according to the rate of dissociation from the receptor (Godfraind, 1968b).

The present experiments were designed to determine whether the potentiation was due to a specific modification of the angiotensin receptor or to a non-specific change in tissue responsiveness. Helical strips of guinea-pig aorta, bathed in Krebs solution, were contracted by cumulative increments of angiotensin dosage (from 10^{-10} to 10^{-6}M). When the period at rest between two successive treatments was 90 min, the maximum response was increased to 153% (mean of ten experiments); however, the ED50 was in both successive series equal to 10^{-8}M.

In other experiments performed on the longitudinal smooth muscle of the guinea-pig ileum, the maximum response of the preparation stimulated by acetylcholine was increased by the presence of angiotensin (10^{-8}M). Furthermore, the aspecific desensitization evoked by acetylcholine, according to Paton & Rothschild (1965), was reduced when the desensitizing dose was added in the presence of angiotensin. This action was associated with a reduction of tissue ionic changes due to acetylcholine.

Longitudinal smooth muscles were immersed in a phosphate-free solution at 37° C for 2 h after dissection. The composition (mM) of this solution was as follows: NaCl 122, $NaHCO_3$ 15, KCl 5·9, $CaCl_2$ 2·5, $MgCl_2$ 1·25 and glucose 11·5. Thereafter, the muscles were transferred for 5 min in the same solution containing acetylcholine (100 μg/ml); the Na, K and Ca content were measured and compared with that of controls. A loss of 12·3 mmoles K/kg wet weight was compensated by a gain of 12·8 mmoles Na/kg ($n=10$), the Ca remaining constant. When acetylcholine was added to the solution containing angiotensin (10^{-5}M), ionic changes due to acetylcholine were reduced: the gain of Na was 4·5 mmoles/kg and the loss of K was 4·5 mmoles/kg ($n=10$). Na, K and Ca content of muscles treated with angiotensin (10^{-5}M) were not modified as compared with controls.

In another series of experiments, after 2 h in the phosphate free solution as above, the muscles were incubated for 1 h in the same solution but containing only 0·5 mM $CaCl_2$.

The reduction of the calcium concentration of the incubating fluid altered the ionic content, there was a net gain in Na (from $101{\cdot}7\pm0{\cdot}8$ mmoles/kg; $n=15$ to $114{\cdot}4\pm0{\cdot}8$ mmoles/kg; $n=15$), and a net loss of Ca (from $4{\cdot}6\pm0{\cdot}1$ mmoles/kg; $n=15$ to $2\pm$