Converting Enzyme Content of Different Tissues of the Rat

The major role played by the lungs as a site of conversion of circulating angiotensin I to angiotensin II has been demonstrated by VANE et al.[1,2] and confirmed by others[3,4]. The fact that such organs as liver and kidney seem to play a negligible part as sources of the converting enzyme, raises the question whether this enzyme is specifically produced by the lungs. This led us to investigate the converting enzyme content of different tissues of the rat. We used a chemical assay[5], in which the conversion of the synthetic substrate, Z-phenylalanyl-histidyl-leucine[6] to Z-phenylalanine and histidylleucine, is used as an index of enzyme activity. This conversion has been shown to be similar to that of angiotensin I to angiotensin II[6].

Male rats weighing from 180–200 g were anaesthetized with ether and decapitated. The organs to be analyzed were removed and homogenized in a glass Potter homogenizer (1 part by weight with 8 parts by volume of 0.25 *M* sucrose). Intestine was homogenized with a blade homogenize. The homogenates were frozen and thawed 6 times. In a number of experiments, the blood contained in organs was removed prior to homogenization by perfusion with a Ringer solution containing 1% heparin. Otherwise, the organs were thoroughly washed with this solution. The heart and intestine were opened with scissors before washing.

To assay the enzyme, 20 µl of homogenate supernatant were incubated 15 or 30 min at 37 °C with 3 ml of 0.05 *M* phosphate-borate buffer (pH 8.0, containing 1% NaCl) and 50 µl of substrate solution (2 mg/ml in methanol). The reaction was stopped by addition of 0.4 ml of 2 *N* NaOH, and histidylleucine was assayed fluorimetrically[5]. The protein concentration of the samples was assayed with the biuret reaction.

Concentration of the converting enzyme in different tissues of the rat

Tissue	Protein (mg/ml)	Converting enzyme (mU/mg protein) Individual samples	Average
Lung	7.9[a]	30	37.2
	6.5[a]	49	
	6.3[a]	60	
	17.6	24	
	14.6	23	
Liver	25.3[a]	0.23	0.23
	22.1[a]	0.23	
Kidney	18.0[a]	0.40	0.63
	17.6[a]	0.80	
	22.0	0.70	
Heart	24.6	0.10	0.15
	20.3	0.20	
Brain	24.2	1.10	1.47
	23.8	1.60	
	21.6	1.70	
Small intestine	13.9	4.30	4.67
	9.9	5.50	
	14.1	4.20	
Stomach	12.9	2.66	2.18
	15.8	1.70	
Muscle	22.9	1.10	0.71
	16.9	0.63	
	22.7	0.40	
Serum	54.3	0.74	1.03
	57.4	0.90	
	54.3	0.82	
	50.2	1.08	
	64.7	0.72	
	57.4	0.95	
	60.5	1.22	
	57.4	1.78	

[a] Perfused organ.

The results (Table) show that the lung contains far more converting enzyme than any other tissue investigated: its content exceeds that of liver by more than 100 times, and that of small intestine, which has the highest content after lung, by about 8 times. These findings are in good agreement with the work of VANE et al.[1,2] who reported that angiotensin I is converted to angiotensin II in the vascular bed of the lung. Few examples of lung-specific enzymes are known so far, and it would be interesting to know whether pulmonary diseases occur in which the converting enzyme level of blood is modified[7].

Résumé. On a dosé l'enzyme de conversion dans différents tissus du rat au moyen d'une méthode chimique mesurant la libération d'histidyl-leucine à partir du substrat synthétique Z-phe-his-leu. Le poumon contient au moins 8 fois plus d'enzyme que tous les autres tissus étudiés. Il en contient notamment plus de 100 fois plus que le foie.

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One Electron Transfer Properties and Phytotoxicity of a Diquaternary Salt from 2,2′:6′,2″-Terpyridine

The bipyridylium salts, diquat and paraquat, are established herbicides[1] but the mode of their biological action is not yet completely clear[2], although much evidence has been obtained[3] to support the view[4,5] that it is associated with their ability to be reduced at a potential (E_o) of about −0.40 volts to free radical cations by a one-electron transfer which is completely reversed by air. A few reports, however, indicate[3] that the size of the molecule is important in determining whether a compound possesses herbicidal properties. In particular, certain diquaternary salts of 4,4′-bipyridyls substituted with 2 aromatic rings are inactive[6], although they meet the requirements thought to be necessary for activity. In view of this report, we have investigated a diquaternary salt of 2,2′:6′,2″-terpyridine which can be considered to be a bipyridyl substituted with one aromatic ring.

2,2′:6′,2″-Terpyridine reacted with boiling ethylene dibromide to give 6,7-dihydro-4-(2-pyridyl)-dipyrido[1,2-