THE NATURE OF THE LINKAGE OF KININ IN KININOGENS

J. S. Morley

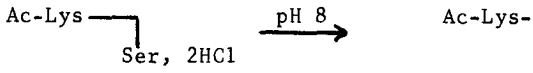
Imperial Chemical Industries Limited, Pharmaceuticals Division,
Alderley Park, Macclesfield, Cheshire, England.

Received October 31, 1968

We recently presented evidence in support of the suggestion that the attachment of kinin in kininogens involves an ester linkage between the carboxyl group of the C-terminal arginine residue of the kinin and the hydroxyl group of an adjacent serine residue (Holman, Lowe, Morley, and Smithers, 1968). After the submission of our manuscript, results apparently contradictory to this suggestion were presented by Kato and Suzuki (1968). Comment is necessary as we believe the conclusions reached by Kato and Suzuki are not justified and may mislead other workers in this field.

Kato and Suzuki (1968) applied the dansyl procedure for detecting terminal amino groups (Gray and Hartley, 1963) to a kinin-containing fragment obtained by cyanogen bromide cleavage of bovine kininogen - II. They did not obtain dansylserine from the series of reactions and concluded that"the possibility that the C-terminal amino-acid residue of kinin links to serine residue with ester bond was excluded completely". This conclusion seems unjustified for the following reason. In the absence of experimental details, it must be assumed that normal alkaline conditions prevailed at the dansylation stage Now our knowledge of the extremely rapid rearrangement of various O-lysylserines to N-lysylserines (O→N shift) under mildly alkaline conditions (the rearrangement of compound I to II, for example, is complete within a few seconds at pH 8) led us to anticipate

prior O→N rearrangement as a certain consequence of these conditions. This expectation has been confirmed using compound I [O-(N^{α}-acetyl-L-lysyl)-L-serine dihydrochloride] as a model. Treatment of I (the constitution of



(I) (II)

which was fully established) with dansyl chloride under the general conditions described by Gray and Hartley (1963) gave, after acid hydrolysis, no dansyl serine. Kato and Suzuki's conclusion must therefore be discounted.

It should be emphasised, assuming the suggestion that the kininogens contain an O-arginylserine residue to be correct, that alkaline conditions must be avoided in degradative work involving the kininogens if the ester linkage is to remain intact. Habermann's kinin-containing fragments, PKFL and PKFS, were obtained from bovine kininogen by peptic digestion (Habermann, 1966). Pepsin is one of the few enzymes which cleaves under acidic conditions, so the ester linkage should be present in PKFL and PKFS. In many other enzymic degradations of kininogens, O→N rearrangement is to be anticipated.

References

Gray, W. R. and Hartley, B. S., Biochem. J., 89, 379 (1963). See also Gray, W. R., in "Methods in Enzymology, Vol XI", edited by C. H. W. Hirs, New York: Academic Press, p. 139 (1967).

Holman, G., Lowe, J. S., Morley, J. S., and Smithers, M. J., Biochem. Biophys. Research Communs., 32 (1968).

Kato, H., Suzuki, T., Biochem. Biophys. Research Communs., 32, 800 (1968).