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Mode of Action of "Ribonuclease."

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A thermostable enzyme, first noted by Jones[1] to be present in the pancreas, has received recent attention at the hands of Dubos and Thompson,[2] Schmidt and Levene,[3] Kunitz,[4] and Allen and Eiler.[5] Dubos and Thompson found the enzyme to effect the decomposition of ribonucleic acid from yeast. The enzyme was noted to be without action on the following substances: desoxyribonucleic acid from thymus, egg albumin, hemoglobin, Witte's peptone, a number of plant, animal, and bacterial polysaccharides, ethyl acetate, tributyrin, and an ether-soluble fraction extracted from pneumococci.

The enzyme was named "ribonuclease" and claimed not to be a phosphatase. Schmidt and Levene describe the action of the enzyme to be that of a depolymerase, and consider the name "ribonucleodepolymerase" to offer a more appropriate description of the mode of action. Kunitz has isolated the enzyme in the crystalline state, and claims that its mode of action appears to correspond to the nuclease activity described by Dubos and Thompson. Allen and Eiler have shown that the enzyme effects the liberation of an acidic group of ribonucleic acid. Titration data place the liberated acidic group in the range of a secondary phosphoric acid dissociation. An examination of the structures of the known components of the ribonucleic acid molecule shows that the secondary hydroxyl of the phosphate group conceivably may be linked with any of the following reactive groups: (a) the hydroxyl group of guanine or uracil; (b) the amino group of guanine, adenine, or cytosine; (c) the hydroxyl group of position 5 or of position 2 of the ribose; (d) the hydroxyl of another phosphate group. This last possibility, seemingly, is ruled out by the data of Allen and Eiler. However, the indications are that certain characteristics of the action of the enzyme are those of a phosphatase.

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1 Jones, W., *Am. J. Physiol.*, 1920, **52**, 203.

2 Dubos, R. J., and Thompson, R. H. S., *J. Biol. Chem.*, 1938, **124**, 501.

3 Schmidt, G., and Levene, P. A., *J. Biol. Chem.*, 1938, **126**, 423.

4 Kunitz, M., *Science*, 1939, **90**, 112; *J. Gen. Physiol.*, 1940, **24**, 15.

5 Allen, F. W., and Eiler, J. J., *J. Biol. Chem.*, 1941, **137**, 757.

In an effort to find the exact linkage hydrolyzed by the enzyme, substances that are known to contain the foregoing phosphate-hydroxyl or phosphate-amino linkages were synthesized and subjected to the action of the enzyme. The studies were conducted in the same manner as those in which the action on ribonucleic acid was noted.[5] Sodium β-glycerophosphate, disodium phenyl phosphate, sodium phenyl anilino phosphate, sodium phenyl amido phosphate, potassium diphenyl phosphate, and phenyl phosphoryl guanine were found to be unattacked by the enzyme. Thus, it is clear that the enzyme is not to be classified as any of the non-specific phosphatases, *i. e.*, phosphomonoesterase, phosphodiesterase, or phosphoamidase.

Evidence for positive enzymic action on allonucleic acid, isolated from pancreas, and upon the Hammarsten nucleoprotein of the pancreas was noted. In both of these cases, the liberation of a group characteristic of a secondary phosphate dissociation is obtained. It appears from these data that the action of the enzyme is that of a specific phosphatase. The specificity is satisfied by two conditions that are met in the molecules of ribonucleic and allonucleic acids: (a) the specific arrangement of the mononucleotides in the nucleic acid structures, and (b) the existence of a certain as yet unidentified phosphate-hydroxyl or phosphate-amino linkage.

The nucleoprotein of Hammarsten cannot be said definitely to be an homogeneous substance. It cannot be stated at this time whether or not the action of the enzyme is to hydrolyze the linkage between nucleic acid and protein or one of the components of the nucleic acid while the latter is still combined as nucleoprotein.

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Influence of Local Applications of Turpentine on Mammary Gland Growth and Involution.*†

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Evidence has been presented indicating that the anterior pituitary of pregnant cattle contains a factor which will stimulate the complete

* Aided in part by a grant from the International Cancer Research Foundation.

† Contribution from the Department of Dairy Husbandry, Missouri Agricultural Experiment Station, Journal Series No. 727.