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[16] The acid polysaccharides, hyaluronic acid and heparin precipitate acid-soluble collagen immediately upon mixing but no LS fibrils have thus far been found in this fibrous precipitate. Of two samples of protein-free chondroitin sulfate, kindly furnished by Dr. Karl Meyer, of the College of Physicians and Surgeons, Columbia University, one produced LS fibrils while the other did not. Further information is required to clarify this matter. No evidence is as yet available concerning the possible role of the protein component of MP, which may be an α_1 globulin. Experiments on this subject are in progress.

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*AN HYPOTHESIS OF PROTEIN SYNTHESIS POTENTIATED BY CITRIC ACID**

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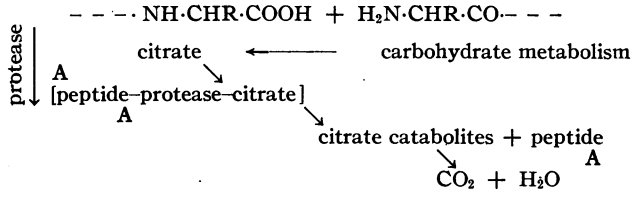
The need for understanding protein synthesis is sufficiently great to warrant the presentation of any hypothesis which is frankly recognized as such in the accurate meaning of this term, and which is not intrinsically untenable. The hypothesis presented here concerns the potentiation of peptide bond synthesis by citric acid metabolites. The essential suggestion arises from observations on the effect of increasing concentrations of citrate buffer on the papain-catalyzed synthesis of acylamino acid anilides.[1, 2]

The energy barrier in peptide bond synthesis has been evaluated as a figure within the range of 1400–3700 cal.[3] and this approximate range of figures has been used in a number of interpretations. Some of these statements are so limiting as to exclude reversal of proteolysis as a mechanism

of biological synthesis of peptide bonds (for a variety of inferences, cf. references 4–10). The values employed in such considerations have been calculated from heat capacity and heat of combustion values for solid amino acids and peptides. While it is theoretically sound, of course, to extend such values to aqueous systems, physiological fluids do not consist of pure water as solvent for such reactions, and if there are demonstrable effects of other solutes they must be considered.

The suggestion that citrate buffer may not be without biological significance in this connection, has been made;[1] this acid represents a natural metabolite. The effect of citrate concentration upon the speed of the forward synthetic reaction for anilides has been demonstrated to be a profound one,[1] and indicates that a similar effect should not be ignored in drawing conclusions on peptide bond formation, regardless of the type of intimate mechanism involved. While such experiments have been carried out with concentrations of substrate, enzyme, and buffer citrate that are many orders of magnitude greater than physiological values, the ratios of concentrations of enzyme to substrate to organic acid are not so unphysiological.

In considering more specifically how citrate might aid in this conversion, a reaction sequence such as the following deserves attention.



The forward reaction A would be joined to citrate as is the glassware counterpart; with citrate subject to catabolism directly from the complex, a favorable over-all equilibrium could result. The possibility of potentiation of peptide bond synthesis by coupling with energy-yielding reactions has been suggested before.[4] The present hypothesis provides a mechanism which does not invoke structural alteration of the intermediates. Such a sequence is thus compatible with the action of proteases, and with aqueous systems. It furthermore relies upon a type of coupling reaction for which a pertinent experimental model exists.

An hypothesis of this type is also compatible with some salient biological facts. Citric acid and related acids occur in cellular metabolism.[11] These organic acids occur as products of carbohydrate metabolism, which spills the great reservoir of energy in organisms.[12] It is of interest that the cytological location of the tricarboxylic acid cycle (e.g., mitochondria)[13] also represents sites of protein synthesis.[14, 15] It should perhaps be emphasized that more than one mechanism of protein synthesis may actually operate. Whether or not this is true, at least one acid known to be present

in cells has, in glassware, effects which cannot justifiably be ignored in the biological balance sheet, regardless of the validity of the specific hypothesis presented. Since a theoretical means for provision of the calculated energy requirement for the joining of carboxylic and aminoid peptide fragments exists, rejection of the proteolysis reversal concept of protein synthesis is not warranted.

The formulation of this hypothesis has been aided by critical discussions with Drs. George S. Hammond and Joseph F. Foster.

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*AN ADENINE REQUIREMENT IN A STRAIN OF DROSOPHILA**

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With the improved growth now obtainable, the raising of *Drosophila melanogaster* upon a chemically defined medium under aseptic conditions,[1] renders possible more exacting studies of the nutritional requirements of genetically different strains. Thus a comparative study was made of a wild type (Oregon-R) and Inversion (2LR) 40d. The latter strain has been studied in detail in other respects[2, 3] and was found to possess a phenotype consisting of disarranged eye facets, mottled eye pigment, and