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Nutritional and Medical Consequences
ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY

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PROTEIN CROSSLINKING
Nutritional and Medical Consequences

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Western Regional Research Laboratory
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U.S. Department of Agriculture
Berkeley, California

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Proceedings of the second half of a Symposium on Protein Crosslinking held in San Francisco, California, August 30-September 3, 1976, with additional invited contributions

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The word crosslinking implies durable combination of usually large, distinct elements at specific places to create a new entity that has different properties as a result of the union. In the case of proteins, such crosslinking often results in important changes in chemical, physical, functional, nutritional, and biomedical properties, besides physical properties simply related to molecular size and shape. (Nucleic acids, carbohydrates, glycoproteins, and other biopolymers are correspondingly affected.) Since proteins are ubiquitous, the consequences of their crosslinking are widespread and often profound. Scientists from many disciplines including organic chemistry, biochemistry, protein chemistry, food science, nutrition, radiation biology, pharmacology, physiology, medicine, and dentistry are, therefore, very much interested in protein crosslinking reactions and their implications.

Because protein crosslinking encompasses so many disciplines, in organizing the Symposium on Nutritional and Biochemical Consequences of Protein Crosslinking sponsored by the Protein Subdivision of the Division of Agricultural and Food Chemistry of the American Chemical Society, I sought participants with the broadest possible range of interests, yet with a common concern for theoretical and practical aspects of protein crosslinking.

An important function of a symposium is to catalyze progress by bringing together ideas and experiences needed for interaction among different, yet related disciplines. To my pleasant surprise, nearly everyone invited came to San Francisco to participate. Furthermore, those that could not come usually agreed to contribute a paper for the Proceedings. Many participants told me privately that they had made a special effort to come to San Francisco to help celebrate the combined Centennial of the American Chemical Society and Bicentennial of the United States. I am grateful for this friendly gesture. To supplement the verbal presentations further, the Proceedings include several closely related, invited contributions. The distinguished international participation from at least nine countries increases the authority and usefulness of the Proceedings.
These papers are being published in two volumes in the series Advances in Experimental Medicine and Biology under the following titles: PROTEIN CROSSLINKING: BIOCHEMICAL AND MOLECULAR ASPECTS (Part A) and PROTEIN CROSSLINKING: NUTRITIONAL AND MEDICAL CONSEQUENCES (Part B). The two volumes are intended to be complementary, but their interests necessarily overlap.

Part A, the first volume, encompasses detailed discussions of natural crosslinks such as disulfide and peptide bonds, various artificial crosslinks formed by means of bifunctional reagents, radiation-induced crosslinks, and techniques to determine crosslinks.

Ultraviolet and gamma radiations are widely used to increase vitamin D content of foods, to sterilize food and drug products, and to treat diseases such as psoriasis and cancer. However, our knowledge about the molecular and nutritional consequences of irradiating food products and other proteins and biopolymers is still imperfect. Such consequences include crosslink formation. Several contributions report recent results in these areas. The results directly concern those interested in radiation biology and cancer therapy as well as food scientists and food technologists responsible for balancing good and bad effects of radiation.

Part B, the second volume, includes detailed discussions of crosslink formation in food proteins through lysinoalanine, isopeptide bonds, and products derived from protein-carbohydrate reactions. Such crosslinks not only lower the nutritional quality and digestibility of food products but sometimes introduce toxicity. This volume discusses nutritional and biological consequences of crosslink formation in food proteins, various factors that govern crosslink formation, effects of crosslinks on protein structure, reactivity, and digestibility, and ways to minimize crosslinking.

Part B also discusses structural and tissue proteins, such as collagen and elastin, which contain many natural crosslinks derived from lysine. Several papers report evidence that these crosslinks are important in aging and connective tissue disease. The chemistry and biochemistry of such natural crosslinks are thus important to anyone concerned with the relation of nutrition, health, and aging.

I want to emphasize considerations supporting the diversity of the subject matter presented in these volumes and of contributors backgrounds and interests. The widest possible interaction of viewpoints and ideas is needed to transcend present limitations in our knowledge as expeditiously as possible and to catalyze progress in the field of crosslinking. Scientists from related disciplines need one another's results; results with different biopolymers need to be compared; scientists and physicians
responsible for practical applications need to share experiences and problems with basic researchers. These volumes bring together many elements needed for such interactions. The range of material includes a great variety of specific and general topics. This scope should interest at least a similar range of readers, but it challenges all of us to think seriously about subjects beyond our primary interests. It is my hope, therefore, that the reader will look not only to those articles of primary interest to him but to others as well and so profit by a broad overview.

I am particularly grateful to all contributors and participants for excellent cooperation, to Dr. Wilfred H. Ward for constructive contributions to several manuscripts, to my son Alan David Friedman for his help with the preparation of the subject index, to Dawn M. Thorne for final typing of several manuscripts, to Roy Oliver of Pierce Chemical Company and Dr. Rao Makineni of Bachem Fine Chemicals for financial assistance, and to the Protein Subdivision of the Division of Agricultural and Food Chemistry of the American Chemical Society for sponsoring the symposium. I hope that PROTEIN CROSSLINKING will be a valuable record and resource for further progress in this very active interdisciplinary field.

Finally, I dedicate this work to the late Professor S. Morris Kupchan, with whom I had the privilege of spending a post-doctoral year at the University of Wisconsin. His untimely death deprives us of a very great scientific benefactor whose twenty-year global search for natural anti-tumour protein (enzyme) alkylating compounds is just now beginning to bear fruit.

Mendel Friedman
Moraga, California
March, 1977

GENESIS 44:30...because the father's (Jacob's) life is crosslinked to his son's (Benjamin's)...

SAMPLUEL 18:1...Jonathan's soul was crosslinked to David's...
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