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Symposium on Polymer Grafts in Biochemistry

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SYMPOSIUM ON POLYMER GRAFTS IN BIOCHEMISTRY

INTRODUCTION TO SECTION II--BIOACTIVE MATERIALS

The first section in the symposium dealt with one important class of biologically active polymers, those used for affinity chromatography. This second section surveys a number of other highly significant and scientifically intriguing areas in the broad field of biologically active polymeric materials. These areas include:

1. Chemical modification and immobilization of enzymes, antigens, and hormones.

2. Localization and controlled release from polymeric compositions of bioactive agents such as drugs, hormones, or pesticides.

3. Synthesis of biopolymers such polypeptides through monomer sequence development on synthetic polymer substrates (e.g., the Merrifield-type preparation of polypeptides).

4. Synthesis of artificial cells or membranes which mimic natural biological systems.

5. Polymeric compositions which have a detoxifying function by sequestering or chelating toxic agents.

These papers in Section II touch upon many aspects of these areas and suggest new opportunities at the interface between polymer science and biological science. It was, in fact, a primary objective in structuring this symposium to expose the "traditional" polymer scientist to some of these exciting research opportunities and thereby provoke more attention to some of the key problems which now beg solution. By way of further introduction to this section, brief comments concerning each of the papers follow.

Immobilized Proteins and Peptides by Falb and Grode surveys the preparation and application of enzymes and other natural biopolymers when attached to insoluble polymeric substrates. There are numerous implications for the use of such materials in catalysis, therapy, analytical and diagnostic chemistry, production and purification of biological materials, and the fundamental understanding of biological functions. Production of these biomaterials, is of course, at the heart of the affinity chromatography techniques as well. Despite the considerable progress reported since the pioneering work of E. Katchalsky, one can judge that this facet of biomaterials research is yet in its infancy and developing rapidly.

The Controlled Release of Bioactive Compounds for Polymeric Systems by Allan, Friedhoff, McConnell, and Powell concerns a vitally important and burgeoning facet of the biomaterials field. Ability to localize and control the release of biologically active agents through chemical attachment or admixture with polymeric hosts affords opportunities for controlling the application of useful hazardous or toxic materials. In the case of pesticides which are so important to agricultural development, but often dangerous in widespread application, this approach to control will undoubtedly achieve a major step forward in the future utilization of pesticides. In fact, the microencapsulation of pesticides has recently won final approval from the EPA for commercial marketing. Pennwalt Corp. has introduced a product, Penncap-N, for use on cotton and alfalfa which utilizes a cross-linked polyamide to microencapsulate a methyl parathion insecticide for control of activity.

Another important example is the controlled release of drugs or hormones and the localization in the body of substances which are harmful when introduced systematically. The recent development by Alza Corp. of a contraceptive device (the "Progestasert" System) based on controlled release of contraceptive hormones from a plastic uterine insert is likely to become a widespread practical achievement in this field of research. FDA approval has been obtained recently for this system.

A treatment for glaucoma also developed by Alza Corp. is yet another current example of the possibilities inherent in precisely controlling the release of a biological agent from a polymeric composition. The system uses a laminated polymeric wafer containing pilocarpine. The FDA has also approved the marketing of this "Ocusert" material.

Enzymes Immobilized by Microencapsulation within Spherical Ultrathin Polymeric Membranes by Chang represents the first step toward the preparation of cellular structures which exhibit biological activity and which may function either in-vivo or in-vitro to achieve enzymatic or detoxifying functions or to introduce and localize hormonal or immunochemical activity. The preparation and the study of physical behavior of polymeric membranes which is inherent in this research is also, of course, of broad implication to the understanding of biological functions.

Solid Phase Peptide Synthesis by Stewart reviews the development and recent progress in the synthesis of polypeptides, particularly by the Merrifield technique, which has resulted in automated instrumentation for the synthesis of complex polypeptides. The achievement of such syntheses by Merrifield and co-workers has also demonstrated one crucially important point in clarifying property-structure relationships for biological materials. This is the fact that once the enzymatic polypeptide chain structure is achieved through synthesis, its molecular conformation, which is so important to its function, is a natural energetic consequence of its molecular structure. The opportunity afforded by the solid phase peptide synthesis technique to produce new polypeptides as well as duplicate natural polypeptide structures has opened up a new era in the field of biopolymers as well as in molecular biophysics and biochemistry. One possible defect of this technique, however, is the occasional "mistake" in sequence development. The use of a homogeneous solution attachment method which aboids this problem is under investigation by Patchornik and co-workers at the Weizmann Institute.

The reported isolation of polypeptides from the brain of animals after particular learning or stress situations by Unger at Baylor and Routtenberg, et al. at Northwestern creates the prospect, both intriguing and frightening, that there are chemical "codes" to behavior and that our ability to synthesize and measure biopolymers with greater facility today may produce a new behavioral science with a strong biophysical and biochemical basis.

Rigid Support Materials for the Immobilization of Enzymes by Royer, Green, and Sinha is devoted to a more detailed consideration of enzyme immobilization and serves to provide an insight into the complexity of the chemistry and physics associated with attaching a biologically active agent such as an enzyme to a polymeric substrate.

The last paper, Polymer-Drug Grafts for Iron Chelation by Ramirez and Andrade, looks at a specific system for detoxification; iron removal from the circulatory system. Although this paper focuses on a particular polymeric system for metal chelation detoxification, the broad ranging implications of this approach are obvious for the removal of other metallic as well as organic and metabolic toxic agents which occur by accidental ingestion or by biological malfunction.

Finally, some further comments are appropriate. Other important facets of the field embraced by the synthesis and properties of polymeric agents possessing biological activity which are not so clearly represented in this symposium include:

1. Development of "artificial organs" utilizing combinations of polymeric materials having selective surface and permeability characteristics with living cells as, for example, reported recently by Dr. Wolf of the New York Hospital-Cornell Medical Center with liver cells grown on hollow fibers or the work of Dr. Chick at Harvard using pancreas cells also grown on hollow fibers.

2. Synthesis and characterization of polymers which intervene in the body's natural immunochemistry to enhance resistance to viral attack, carcinogenesis, etc. This is an important future thrust in the field of bioactive polymers. An example is the study

of pyran polymers and polysaccharides which have been demonstrated to affect Interferon stimulation. Understanding Interferon induction and the study of property-molecular structure relationships in polymers which affect the human immunochemical system are clearly some of the more exciting areas for further study and progress.

This symposium specifically did not concern itself with polymeric Biocompatible Materials which represents a major area of investigation of both scientific and practical importance. Indeed, the issues of biocompatibility and bioactivity are necessarily intertwined in the design and development of materials having improved biological function as well as for the important prosthetic applications of polymers. The chemistry and physics of polymer biocompatibility is receiving rapidly increasing attention. Although not represented in this symposium because of other recent surveys of the field, biocompatibility deserves emphasis as one of the high priority areas of biopolymer research.

I am indebted to the authors for their fine contributions, their help and cooperation, and especially their patience in developing the symposium and this collection of expanded papers. Very special thanks are due Dr. Harry Hixson my cochairman in this adventure.

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