Preface

Since the introduction of the term "lectin" (from the latin *legere*, to pick out, choose) by Boyd and Shapleigh (1954) to describe a class of proteins of plant origin which agglutinate cells and exhibit antibody-like sugar binding specificity, the subsequent discovery of many similar substances in both animal as well as plant tissue has prompted several attempts to reach common agreement as to how to define a lectin (Goldstein *et al.*, 1980; Kocourek and Horejsi, 1981; Franz *et al.*, 1982). We have chosen to define a lectin simply as a carbohydrate-binding protein of nonimmune origin that agglutinates cells or precipitates polysaccharides or glycoconjugates (Goldstein *et al.*, 1980), a definition adopted by the Nomenclature Committee of the International Union of Biochemistry (Dixon, 1981). This definition implies that lectins are multivalent, that is, they possess at least two sugar binding sites which enable them to agglutinate animal and plant cells and/or to precipitate polysaccharides, glycoproteins, peptidoglycans, teichoic acids, glycolipids, etc. The sugar specificity of lectins is usually defined in terms of the monosaccharide(s) that inhibits lectin-induced agglutination or precipitation reactions. The emphasis on "nonimmune origin" is included in the definition in order to distinguish lectins from anti-carbohydrate antibodies which may act as cell agglutinins. Furthermore, many lectins are found in plants and bacteria that do not synthesize immunoglobulins. Also, in contrast to antibodies which are structurally similar to each other, lectins are structurally diverse and are known to vary in molecular size, amino acid composition, metal requirement, and three-dimensional structure. In this regard, as well as with respect to specificity, lectins are more akin to enzymes.

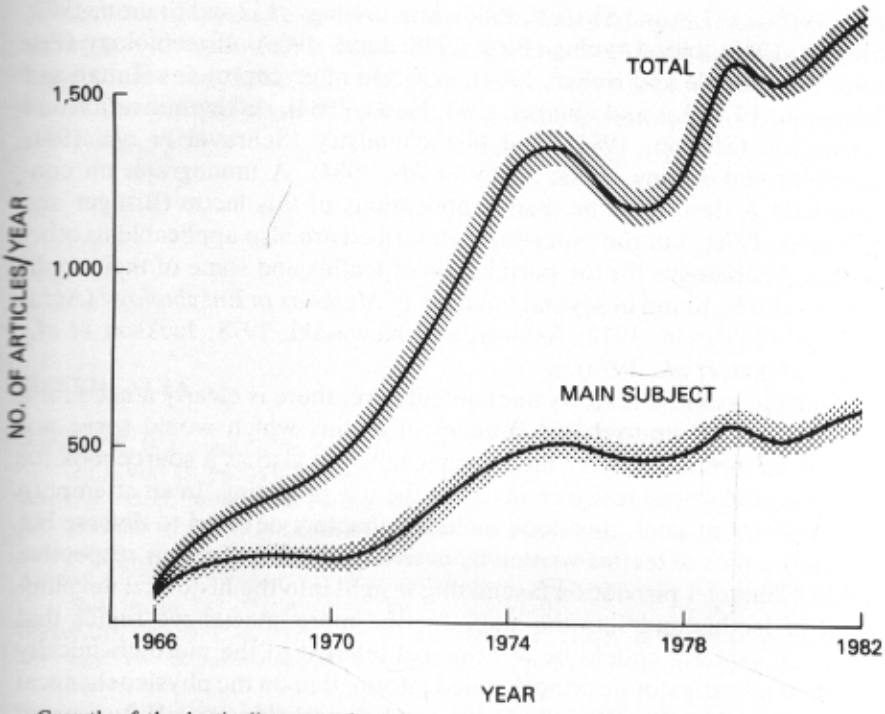
The definition of lectins as used here is an operational one (i.e., evidence of agglutination or precipitation) which requires the presence of more than one sugar binding site. Accordingly, this definition would exclude a wide variety of other sugar-binding proteins such as sugar-specific enzymes [i.e., glycosidases, glycosyltransferases, glycosylkinases, glyco-

sylpermeases, glycosylepimerases, sugar transport proteins, hormones (e.g., thyroid-stimulating hormone), chemotaxis receptors, bacterial toxins, and interferons]. Perhaps the most controversial aspect of this definition is the fact that, if rigorously applied, it would exclude such toxic plant proteins as ricin, abrin, and modeccin. These are proteins which may be found in the same plant in which "true" lectins are found and closely resemble the latter in terms of amino acid composition and possibly primary structure. However, they are poor agglutinins, if at all, and for this reason were once thought to lack multiple sugar binding sites. More recently, however, ricin has been shown to possess two carbohydrate binding sites (Houston and Dooley, 1982).

Although known for nearly a century, it is only during the last decade or two that lectins have become the focus of intense interest. This is evidenced by the rapid growth of the literature on the subject which, since the 1960s, has increased nearly twentyfold. The total number of publications that deal with various aspects of lectins is fast approaching 2000 per year (see figure). There are many reasons for the current interest in lectins. Prominent among these is their usefulness in detecting and studying carbohydrates in solution and on cell surfaces. As a result, lectins have become indispensable tools in many areas of biological research. Another reason is that lectins are believed to serve as recognition determinants in a variety of biological systems in microorganisms, plants, and animals. Bacterial surface lectins mediate the sugar-specific adherence of bacteria to epithelial cells, which is an essential prerequisite for infection. Plant lectins, on the one hand, may act as protective agents against fungal phytopathogens and, on the other hand, may mediate the attachment of nitrogen-fixing bacteria to the roots of leguminous plants. In animals, membrane-associated lectins appear to function in the clearance of glycoproteins from the circulatory system and in the intracellular translocation and targeting of glycoproteins.

With the expansion of our knowledge about lectins, it became apparent that they deserve attention in their own right. Some of them exhibit unusual structural properties. They constitute a convenient source of well-defined plant glycoproteins, and are excellent models for studying protein–carbohydrate interactions. Furthermore, the availability of lectins from different species and tribes of the same family (e.g., of plants or bacteria) makes them suitable objects for taxonomic and phylogenetic studies as well as for evolutionary correlations (Goldstein and Etzler, 1983).

Contributing to the increasing popularity of lectins is not only the ease of their purification (mainly by affinity chromatography on immobilized carbohydrates) but also their increased availability from commercial



Growth of the lectin literature from 1966 to 1982, based on citations in the Medlars System. The decrease in the annual number of publications in the middle of the 1970s was due to a change in the data base. Data obtained from Dr. Elizabeth J. Van Lenten at the National Library of Medicine, National Institutes of Health, Bethesda, Maryland.

sources. Well over a hundred lectins have been purified to date, and more than forty of these are available from a large number of companies.

The voluminous literature generated by this interest in lectins has made it extremely difficult for the nonspecialist to keep abreast of the latest developments as they might impinge on the researcher's particular area of specialization. Numerous reviews and monographs dealing with selected aspects of lectins have appeared. Among these, mention should be made of reviews covering such specific topics as lectins from plants (Liener, 1976; Kauss, 1981; Lis and Sharon, 1981; Goldstein and Etzler, 1983), slime molds and animals (Barondes, 1981, 1984; Olden and Parent, 1986), invertebrates (Yeaton, 1982; Cohen, 1984), and membranes (Ashwell and Harford, 1982; Monsigny *et al.*, 1983). Other reviews deal with the possible role of lectins in nature (Sharon, 1979, 1984b; Schmidt, 1979; Schmidt and Bohlool, 1981; Sequeira, 1978; Dazzo and Sherwood, 1983) and the application of lectins to the study of glycoconjugates in solution and on

cells surfaces (Lis and Sharon, 1984), immunology (Lis and Sharon, 1977; Sharon, 1983), blood typing (Bird, 1978; Judd, 1980), microbiology (Pistole, 1981; Doyle and Keller, 1984), isolation of glycoproteins (Lotan and Nicolson, 1979; Lis and Sharon, 1984; Hedo, 1984), cell identification and separation (Sharon, 1983), and histochemistry (Schrevel *et al.*, 1981; Leathem and Atkins, 1983; Alroy *et al.*, 1984). A monograph on concanavalin A describes the many applications of this lectin (Bittiger and Schnebli, 1976), but the procedures described are also applicable to other lectins. Techniques for the purification of lectins and some of their applications can be found in several volumes of *Methods in Enzymology* (Agrawal and Goldstein, 1972; Ashwell and Kawasaki, 1978; Jackson *et al.*, 1982; Barker *et al.*, 1974).

Valuable as these reviews undoubtedly are, there is clearly a need for a comprehensive, up-to-date treatment of lectins which would serve not only as an introduction for the nonspecialist but also as a sourcebook for the specialist whose research involves the use of lectins. In an attempt to accomplish this goal, this book includes chapters devoted to diverse but selected topics of lectins written by active researchers in their respective fields. Chapter 1 provides a fascinating insight into the historical development of lectins and sets the stage for the more specialized topics that follow. Chapter 2 should be of principal interest to the more chemically oriented investigator desiring detailed information on the physicochemical properties of lectins, their isolation, and remarkable specificity toward sugars.* Chapter 3 should be of interest to those whose research deals with the molecular aspects of protein evolution, since the lectins provide an excellent example of a family of homologous proteins. One of the most interesting and important features of lectins is the diversity of their biological activities (Chapter 4) and how these properties have been utilized for the isolation and characterization of carbohydrate-containing compounds in solution and on cells (Chapter 5). Chapter 6 attempts to answer the ever-recurring question regarding the functions of the lectins in their natural milieu. Chapters 7, 8, and 9 serve to emphasize the importance of lectins in nonplant systems as exemplified by lectins that occur in vertebrates, slime molds, and bacteria respectively. Chapter 10 deals with an area which, until recently, has received scant attention, namely, the nutritional significance of the occurrence of lectins in plant foods such as legumes.

The literature pertaining to lectins continues to proliferate at a seemingly unabated rate. For this reason, a book such as this can at best portray only the current status of the field, but even so, many facets of the

* All sugars referred to in this book are of the D-configuration unless otherwise noted.

subject may not have received the attention that some may feel they deserve. Nevertheless, it is our hope that this book will serve as a reference source for those who choose, for whatever reason, to learn more about this unique class of proteins and their applications to biology and medicine.

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