Book Reviews

Heparin-Binding Proteins. By H. Edward Conrad. Academic Press, San Diego, CA, and London. 1998. xvi + 527 pp. 16 x 23.5 cm. ISBN 0-12-186060-4. $89.95.

Heparin, the hallmark "mucopolysaccharide" of mast cells, has been used for decades in the clinic to prevent and treat thrombosis. Its blood anticoagulant activity is due to the specific interaction of the polymer with the protease inhibitor antithrombin. The mechanism behind this interaction has been unraveled, along with the growing realization that many cell types produce related polysaccharides, heparan sulfates, that exert their diverse biological functions by interacting with a multitude of proteins. Heparan sulfate has gradually been recognized as being a key player in cell and developmental biology, much to the frustration of scientists who realize that carbohydrate chemistry may be a major and unavoidable ingredient in their chosen area of research. The ambition of the expert author of this volume has been to smooth the steep learning curve that faces newcomers to the "heparinoid" (an ambiguous term, in my opinion) field.

Beginning with chapters on basic definitions, structural properties of the polysaccharide chains, biosynthetic pathways, and proteoglycan forms, the author provides comprehensive overviews on methods to determine the carbohydrate structures and to modify these structures by controlled chemical reactions. The cellular metabolism of heparan sulfate proteoglycans is discussed, with emphasis on core proteins as well as polysaccharide chains. General aspects of "heparinoid"/protein interactions are considered, along with a more detailed exposure of antithrombin, the "prototypic heparin-binding protein". The remainder of the volume is devoted to interactions between heparin and/or heparan sulfate and selected proteins, including components of the hemostatic mechanism, members of the fibroblast growth factor family and their receptors, extracellular superoxide dismutase, and heparin-binding proteins in lipoprotein metabolism. The extensive reference list (1700 references) at the end of the book essentially covers the period up to 1996, more recent references being added at the end of each chapter. The subject index is useful but somewhat incomplete (for instance, entries under I−K are missing).

Most previous (not so recent) books on heparin/heparan sulfate have been proceedings of symposia, contributed by several authors. The present volume, a remarkable achievement, has the unmistakable quality of a monograph, with continuous development of several parallel, often intertwined, themes (e.g., the structural variability of "heparinoids", its control in biosynthesis, and the concept of specificity in polysaccharide/protein interactions). The preface states that while "the book is not intended primarily for those who are already converted, the latter may also find some value here". Indeed, I found reading this book to be highly rewarding, particularly because it reflects the personal outlook of a single authority. Some flaws in the presentation (unnecessary repetitions, poor quality of many of the illustrations, errors in layout and proof-reading) are noticeable, but they do not significantly detract from the overall positive reading experience. Likewise, a certain degree of personal bias is inevitable, and acceptable, in a presentation of this kind. For example, the discussion on polysaccharide biosynthesis features some rather novel (and interesting) interpretations of data in the literature. Moreover, certain proposed mechanisms of growth factor action tend to be favored at the expense of other, equally plausible suggestions. With these caveats in mind, I find the book highly valuable as an introduction to various aspects of heparin/heparan sulfate chemistry and biology. More than a source for selected reading, however, I appreciate the book for its broad survey of a complex, rapidly developing, and fascinating research field at the intersection of biology and carbohydrate biochemistry. I warmly recommend reading the entire volume.

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JM980683H

10.1021/jm980683h

Comparative QSAR. Edited by James Devillers. Taylor and Francis, Washington, DC. 1998. ix + 371 pp. 16 × 24 cm. ISBN 1-56032-716-2. $135.00.

This book provides reviews that use the information contained in multiple QSAR models to gain insights into mechanisms of actions of chemicals on biological systems, to probe reasons for interenzyme or interspecies specificity, and to better understand the relationships between different approaches to QSAR. The eight reviews, by experts with diverse experiences and interests, provide new understandings of the systems investigated and also insights into how experts analyze the relationships between different QSARs and how they glean new insights from multiple QSARs. Devillers et al., Schultz et al., Compadre et al., and Magee provide biological data on hundreds of compounds.

Devillers, Domine, Bintein, and Karcher compare fish bioconcentration models from various authors and show that bioconcentration is nonlinear in log P with an optimum of −6. Their analysis of residuals from the various equations illustrates the power of this strategy. Schultz, Sinks, and Bearden compare QSARs of aquatic toxicity as derived from different assays in three species. The QSARs for these endpoints are dependent only on hydrophobicity for neutral organic nonpolar narcotics, amine narcotics, ester narcotics, and weak respiratory uncouplers. However, for direct-acting electrophiles and proelectrophiles, the QSARs differ between testing protocols and suggest that extrapolation of results to other systems be approached with caution. Compadre, Byrd, and Compadre study the mutagenicity of nitroaromatic compounds. Classic QSAR suggests that an

optimum log *P* of −5 and electron affinity are the most important determinants of mutagenicity, whereas the best CoMFA model, derived from 257 compounds, includes only the standard steric and electrostatic fields, not log *P*. The approaches agree that electronic factors are important in mutagenicity and suggest that log *P* and steric fields may reflect the same SAR in this dataset. Magee models transdermal penetration and reactivity with epidermal proteins using different techniques to model the penetration of the molecules into the epidermis; activation of the molecules, if necessary, and reaction with proteins; and the overall sensitization process. For electrophilic haptens these models have been proven to be as accurate as clinical testing. Zakarya and Chastrette consider the SAR of musk odor and provide a comprehensive and critical review of all known QSARs using descriptions as varied as size and shape or autocorrelation vectors. They find that the relationship between molecular properties and musk odor is nonlinear and that most studies lead to similar conclusions. Reddy, Dyan, and Duke develope QSARs for several different classes of protoporphyrinogen oxidase inhibitors. They discover, contrary to findings in other chapters in the book, that the equations are specific to the class from which they were developed. Selassie and Klein compare the QSAR for inhibition of dihydrofolate reductase from mammals, birds, and bacteria by triazines, 2,4-diamino(X-benzyl)pyrimidines, 2,4-diaminoquinazolines, pyrimethamine analogues, and piritrexim analogues. From the 63 equations presented, they show that species selectivity is a subtle property of each type of inhibitor. Hansch, Gao, and Hoekman summarize their database system that includes 10 000 QSARs from physical organic chemistry (6500) and biological systems (3500) and allows easy comparison between the two universes. They present many examples of the information that can be gained by comparing different QSARs, for example: multiple physical organic systems, physical organic versus biological systems, toxicity as related to log *P*, and multiple dose QSARs that include the same compound. The utility of this computer system has just started to be explored.

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JM9806953

10.1021/jm9806953