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Book Review

Stability and Characterization of Protein and Peptide Drugs. Case Histories
(Pharmaceutical Biotechnology Volume 5)
Edited by Y. John Wang and Rodney Pearlman
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Although there are over two hundred peptides in current clinical trials, the therapeutic potential offered by the current understanding of the pathophysiological role of such molecules is, as yet, largely unrealized. Despite major advances in disparate medical disciplines, the use of peptides as medicinal agents is restricted by, for example, the large, polar nature of these molecules, which limit membrane transport and thus disposition to target tissues, while their frequent physical, chemical and enzymatic instability provides a major obstacle to pharmaceutical development and use. There is, thus, an established need to develop delivery systems suitable for the large, polar and unstable products of molecular biology. This requirement will become more intense as other potential therapies, such as antisense oligonucleotides, are evaluated and developed. The appearance of the series to which the volume under review belongs has been prompted by a desire to facilitate the formulation and delivery of these new agents.

Earlier volumes in the series have established the principles determining the biological barriers to peptide delivery and their stability and pharmacokinetic profiles. The present volume extends this approach by presenting a series of in-depth case studies of important or novel peptides of actual or potential medicinal value. In all, eleven peptides are presented. These range from the old (insulin, ACTH) to the new (interleukin-1β, interleukin-2), from the large (muromonab-CD3, 150 kDa) to the small (leuprolide, 1·2 kDa), from the synthetic (leuprolide) to the recombinant (α_1-antitrypsin) and from the hormonal (human and bovine growth hormones) to the enzymatic (alteplase, fibrolase). Each chapter is written by authors intimately associated with the development of the peptide and, to illustrate the practical and industrial relevance of the volume, all but three of the twenty seven contributing authors are from the pharmaceutical industry.

In addition to providing a detailed description of the properties of the drugs under consideration, the volume also serves as a generic preformulation primer. In this role, it illustrates those studies essential for the assessment of the parameters necessary to allow rational formulation development. This is particularly important for peptides where small sample availabilities combine with adverse physicochemical properties to make such studies complex and expensive. A feature of this approach is that it shows the breadth of study needed and nicely illustrates how the integration of many techniques is necessary for the successful formulation and delivery of peptide drugs. Studies include the typical preformulation concerns of analysis, solubility and stablity where chromatography, pH profiles and degradation mechanisms (particularly of the facile deamidation reactions of glutamine and asparagine residues) are discussed. Thermal analytical methods are introduced and particular mention is made of freeze-drying. This is of concern because peptide activity frequently depends upon physical (tertiary and quaternary structure) as well as chemical stability, so that the simple removal of water may not be sufficient to ensure long-term stability. These procedures are combined with analytical spectroscopy (NMR, mass spectrometry, circular dichroism) to provide structure elucidation where appropriate. Of special interest is the way in which the techniques of molecular biology are now moving into the pharmaceutics laboratory. Thus, various electrophoretic and blotting methods complement the more traditional approaches.

Although there is an interesting section on the physicochemical basis for the nasal delivery of leuprolide, the volume generally has little to say on specific formulations, their performance or assessment. The coverage in each chapter is variable, for example, the sections on insulin and ACTH concentrate mainly on stability, and the volume might be a little more user-friendly if chapters had, as far as possible, used the same section headings. Additional standardization could be envisaged in, for example, the presentation of summary information where the tabulation of data showing such properties as the number of residues, molecular weight, isoelectric point and elimination half-life would be useful. These small complaints do not, however, significantly detract from the value of this volume which presents a wealth of factual and illustrative material. Indeed, with the explosive interest in this field it may even be the forerunner of a series concerned with the pharmaceutical profiles of peptide drugs. It is recommended both as a source of specific information on the peptides included and also as a general guide to the design and interpretation of preformulation studies on peptide drug candidates.

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