DRUG DELIVERY SYSTEMS: FUNDAMENTALS AND TECHNIQUES

Edited by P. Johnson and J.G. Lloyd-Jones

Ellis Horwood Series in Biomedicine ISSN 0930-3367. Published jointly by Ellis Horwood Ltd., Chichester, England and VCH Verlagsgesellschaft mbH, Weinheim, Federal Republic of Germany, 1987. Price (UK) £57.00.

The editors should be congratulated on coordinating the production of this excellent volume. They present a realistic view of the progress and potential of a wide range of delivery systems. There are several overviews on the subject together with chapters describing a range of delivery systems, for instance, liposomes, slow release polymers, mucoadhesives and implantable pumps. Aspects of parenteral oral, transdermal, intranasasl and ocular administration are covered in a readable comprehensive manner. Most chapters are well referenced and consequently the publication gives access to key works associated with all the branches in the field.

Site-specific drug delivery, a subject prone to overly optimistic concepts, is covered in several chapters. Fortunately, this book adopts as realistic approach to the subject and discusses in detail, the limitations presented by the various endothelial barriers, the problems associated with the introduction of liposomes into the blood supply and those associated with the conjugation of drugs to immunoglobulins. Nevertheless, the articles are forward-looking and future directions are clearly indicated. Oral administration is always going to be the major route for drug delivery and this is recognised in the book by the inclusion of chapters describing gastrointestinal transit times and recent technological advances in oral drug delivery. One problem with the more complicated delivery systems is the low drug load associated with such preparations. However, this need not always be so as exemplified by the example of slow release tablets consisting of virtually 100% drug. As as chemist, the reviewer would have been happier if more information at the molecular level was presented. In particular, a chapter on lipid/surfactant chemistry, including emulsions, would not have been out of place. In contrast to lipids, polymer chemistry is well

covered, with three chapters describing the properties of macromolecular drug carriers, biodegradable systems for controlled release and mucoadhesive polymers. The increasingly important problem of peptide delivery is discussed throughout the book. Again, a realistic view is presented. A general overview of the present situation is supplemented by two excellent chapters on implantable systems and separate presentations describing colon, transdermal and nasal peptide delivery.

The spirit of the book is encapsulated by two extracts taken from the final chapter.

"Although neither medicinal chemistry nor formulations is yet an exact science, it is time for medicinal chemists and formulation scientists to collaborate more closely".

"It is tempting to think, and perhaps true, that the problems of oral, nasal and topical delivery are soluble. The problems of implants and implanted devises are within the reach of the technology of this century. The problems of targeting seem so immense that we should be honest about it and define the problems that beset us".

Recommended reading for all medicinal chemists and pharmaceutics personnel involved with research.

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Introduction to Drug Metabolism
G. Gordon Gibson and Paul Skett
Chapman and Hall Ltd., London, 1986, pp 293.
Price – hardback £25.00, paperback £12.95.

"Drug metabolism", as the authors point out in the preface to this text, is considered to cover the absorption, distribution, biotransformation and excretion of drugs. However, in its strictest sense it should be restricted to the biotransformation of drugs and it is this aspect that is primarily covered in this book.

Chapter 1, in typical pharmacological fashion, catalogues most of the biotransformations that drugs might undergo, illustrating the reactions with thirty-eight different drugs or xenobiotics, followed by examples of similar reactions that occur with endogenous compounds. The second chapter looks at these reactions in more detail and considers the enzymes involved in the biotransformations. The overall impression given in these two chapters, which is reinforced in the preface, is that the enzyme mediated processes are primarily designed to metabolize drugs and that endogenous compounds can also act as substrates! Whilst the high affinity of drugs for the particular enzymes involved in their biotransformation and the fact that a number of drugs are able to induce cells to synthesize increasing amounts of the enzymes concerned (chapter 3), might be presented as evidence in favour of purely 'drug metabolizing enzymes', the observations, so eloquently presented by Jacob and Monod in their classic paper on the regulation of enzyme synthesis, that isopropylthiogalactoside (IPTG) was the most potent inducer of galactosidase, transacetylase and, as shown later, of permease, although it was not itself a substrate for the galactosidase, would not support that idea.

Other factors affecting drug metabolism are covered in the next two chapters, the fourth chapter concentrating on internal factors and the fifth on external factors. Numerous examples are provided to illustrate the fact that the biotransformation of drugs can be modified by the external environment and also the status of the internal *milieu*, and the possible interaction between various factors alluded to in the final paragraph.

The discussion of the pharmacological and toxicological aspects of drug metabolism in chapter 6 would have provided an ideal introductory chapter since the range of metabolic reactions outlined in chapter 1 are repeated using 22 different drugs or xenobiotics as examples.

Pharmacokinetics is introduced with a minimum of mathematical treatment although this was sufficient to explain and provide an understanding of the concepts involved.

The final chapter describes a number of experiments that demonstrate drug metabolism *in vitro* and *in vivo*. These procedures are supported by explanatory notes in many cases and references to the original literature are also provided. The choice of some techniques might be questioned, for instance the protein estimation by the method of Lowry et al. – a technically difficult assay to carry out reproducibly and which suffers from the disadvantage that the relationship between absorbance at 750nm and concentration of protein deviates from linearity above an absorbance of about 0.3. In view of the large quantity of microsomal protein derived from rat liver by the technique described in the text, a less sensitive, more reproducible and technically easier technique might have been chosen.

In view of the very large number of drugs, xenobiotics and endogenous compounds chosen as examples for the different metabolic processes described in the text, relatively few errors in chemical structure are evident. The referencing of each chapter leads to a degree of duplication that could be avoided by a single bibliography at the end of the text.

As an introduction to drug metabolism the text would be enhanced by a preliminary chapter outlining some of the historical milestones in drug metabolism, e.g. Knoop and Dakin's isolation of hippuric acid during their investigations into β-oxidation, together with some evidence for the oxidative and reductive transformation of drugs and the involvement of the mixed function oxidase complex. Despite these comments this volume does provide a useful catalogue of concisely presented information on the metabolic reactions of many drugs.

Reviewed by I.Ab.I. Davies
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