

Book review

Drug delivery and targeting

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The first one notices on the front cover when picking up this pleasing looking book is that the text is written for pharmacists and pharmaceutical scientists which to me indicates a specialist book for well educated professionals. It is only when one reads the preface that it becomes evident that this book is a textbook primarily written for undergraduate and graduate students taking courses in relevant aspects of biological sciences. This fact should have featured more prominently on the front cover (or at least the back cover) of the book.

The editors have set out to produce a textbook that covers all aspects of advanced drug delivery and targeting (appropriate for undergraduate courses and continuing education courses) which is indeed a daunting and ambitious (if not impossible) goal. The book numbers 475 pages that are divided into three major sections: (1) Introduction to Advanced Drug delivery and Targeting; (2) Routes of Drug Delivery and Targeting and (3) Future Directions of Drug Delivery and Targeting. Of these sections the second section is by far the largest with eight chapters dealing with oral, oral mucosal, transdermal, nasal, pulmonary, vaginal, ophthalmic and CNS delivery.

Chapter 1 sets out to introduce the reader to the basic concepts of drug delivery. In 47 pages the authors tries to cover everything from the concept of bioavailability, epithelial barriers, drug transport mechanisms and factors affecting the transport, pharmacokinetic processes, timing for optimal delivery, peptide and protein delivery and gene therapy. The section on pharmacokinetic processes describing the ADME concept are placed in the middle of the chapter. This concept

should have been introduced in the very start of the book since 'absorption' is an important part of this concept. It is unavoidable that this introductory chapter can only give rather superficial information on the various topics covered. The reader, if only relying on the text, will in many cases be ill informed and in some cases miss-informed or miss-guided. For example, the chapter describes in 15 lines (on page 11) the paracellular route of transport and uses most of the space to warn against the use of penetration enhancers for opening tight junctions due to possible damage, whereas no warning is given on this topic when describing transcellular enhancement. Most (pure) paracellular transport enhancers act transiently and reversibly and safely whereas in general the transcellular enhancers such as surfactants and bile salts damages (permanently in some cases) the mucosal membrane. The author describes (page 35) the advantages of zero-order release oral dosage forms but fails to note that such formulations only work if the drug is well absorbed throughout the whole of the gastrointestinal tract and/or has a reasonable long plasma half-life. The section on peptide and protein delivery concentrates almost exclusively on degradation, which is important in the gastrointestinal tract, but not so important using other routes of delivery. The section on nucleic acid therapy only briefly describes gene therapy and leaves the reader to wonder about the difference between gene and oligonucleotide therapy. It would, all in all, have been better to concentrate in this introductory chapter on a more detailed description of the basic concepts for drug delivery (ADME) and leave drug formulation problems and problems with specific drug molecules to the individual chapters.

Chapter 2 deals with 'Drug Delivery: Market perspectives', which one can assume, is included to wet the appetite of prospective workers in drug delivery. What is not so clear is the author's definition of the difference between the terms 'drug delivery systems', 'novel drug delivery systems' and 'advanced drug delivery systems'. All drugs delivered to the body uses drug delivery systems albeit some a simple injectable solution or a simple tablet. Hence, when the author mentions that the market for all advanced drug delivery products was around \$16 billion in 1997 what does this include? The example given of the nasal calcitonin product (from Novartis) which is basically a simple solution formulation, can one really call this 'advanced drug delivery'? It also bothers me that the author in the 'analysis by mode of administration' lists oral, inhalation, transdermal, mucosal and parental routes of administration. Mucosal delivery includes oral and inhalation (pulmonary) and in reality the vaginal membrane is not a mucosal membrane. The three companies mentioned as working in 'mucosal delivery' are Theratech (now Watson) who works on buccal delivery systems, 3M who works mostly on local lung delivery and transdermal delivery and Nomen which I do not know, unless it is a mistake and should have been Noven (who works in transdermal and buccal delivery). Where are the mentions of the other better-known mucosal drug delivery companies?

The purpose of Chapter 3 is according to the authors to provide a general overview and describe some of the fundamentals of advanced drug delivery. A list of expressions (for drug delivery systems) used in the book is explained but the list could have been organised better, i.e. alphabetically? or in-groups?, since some of the expressions encompasses others. What the chapter does not give is a definition of the terms 'Drug Delivery Systems' and in particular 'Advanced Drug Delivery Systems'. However, further along under 3.4 (Dosage forms for advanced drug delivery and targeting) the author includes dosage forms such as nasal drops and ophthalmic drops which I do not believe can be said to be advanced. The summary of the various routes of delivery adds very little to the understanding of drug delivery in

general. Also, the section on 'Strategies to increase drug absorption' is somewhat lacking in detail and especially the section on penetration enhancers leaves a lot to be said about more novel concepts. This whole chapter could have been left out of the book and parts of it better incorporated in Chapter 1.

Chapter 4 deals with implantable systems. This is a well-written and informative chapter, but one is missing specific references to where the information is taken from and more can be read. Also, the authors should have mentioned the novel hGH PLGA microsphere implant system marketed by Genentech (Neutropin).

Chapter 5 gives a reasonable good overview of 'Parental Drug Targeting Systems'. However, I am missing in this chapter a better discussion of the concept 'steric stabilisation' and factors affecting the clearance of particulate systems from the blood circulation. I was also surprised to note that the concept of nanoparticles contra microparticles is not discussed nor is the literature concerning self-assembly of pegylated macromolecules such as PLA-PEG. Why are Chapters 4 and 5 not included in the main section of the book? Since these two chapters deal with specific routes of drug delivery.

Chapter 6 sets out as a very pleasing and informative chapter. However, some flaws appear when reading further in more detail. For example, the authors say on page 151 that 'in some cases residence of a drug moiety in the small intestine can be in the order of minutes ----'. This I assume is a mistake, the word 'upper' is surely missing in front of 'small intestine'. The transport through the small intestine is generally about 3 h in total. Unfortunately, the whole concept of gastrointestinal transit time has not been dealt with although plenty of literature is available on this subject. Another flaw in this chapter is the description of mucoadhesive delivery systems as very promising. As far as I am aware promising results have only been obtained in animal models but so far not in humans. Similarly, when discussing the success of microparticles for delivery of vaccines it should be clearly stated that this has only been shown to work in animal models, not in man. It is rather disturbing as well that in the same chapter dis-

cussing colonic drug delivery systems only three examples of systems are mentioned. Two of these, i.e. azopolymers and Pulsincap have been shown either to work by failure or to fail working most of the time. The section on hydrogels does not give the reader an explanation on how the colonic targeting is achieved. Also, no basic information on how colonic delivery in general can be achieved (time, pH) is given. It would have been useful in this chapter to discuss also some of the new ways of delivering peptides and proteins for example the Emisphere approach. And what about gastroretention?

Chapters 7 and 8 are both informative and well written.

Chapter 9 is concerned with nasal drug delivery. It gives the standard description of the nose and the physiological and physiochemical factors which can affect nasal absorption. One or two mishaps are apparent. For example the authors say on page 240 that particles greater than 10 μm applied to the nose are filtered out by the vibrissae at the nostrils. This would mean that most of the droplets from the nasal sprays (size range 25–50 μm) would not reach the nasal cavity. This is surely not the case! The paper does not deal with the exciting new area of nose-to-brain delivery. The section on new technologies in nasal delivery is not well formulated with misconceptions and lack of detail. Also, the references quoted for further reading is mostly 10 years or more old. Several newer reviews and books are available.

Chapter 10 concerned with pulmonary drug delivery is well written and informative. The only point of disappointment is the limited discussion

of the results obtained with the new pulmonary drug delivery systems such as the devices from Inhale and Aradigm.

Chapter 11 and 12 describing the vaginal and ophthalmic drug delivery are very informative chapters with good illustrative examples. The same can be said for the following two chapters dealing with CNS delivery and gene therapy.

The chapter entitled 'Integrating Drug Discovery and Delivery' is most interesting but probably a bit too 'high brow' for this textbook. If at all, the chapter should have been placed in the beginning of the book to give an introduction to how new drugs are discovered and tested.

The last chapter on 'New Generation Technologies' takes well care of the newest opportunities in drug delivery where chemistry and biology are integrated to provide intelligent drug delivery systems.

All in all, the book is of mixed quality. The contents of many of the chapters reflects the interest of the authors rather than the importance in the field of advanced drug delivery. The book needs thorough updating and correcting of most of the chapters before one would happily hand it to undergraduate students with limited knowledge in the field.

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