Book Review

Targeting of Drugs 2, Optimization Strategies, NATO ASI Series, Series A: Life Sciences, Vol. 199, Edited by Gregory Gregoriadis, Anthony C. Allison, and George Poste. Plenum Press, New York, 1990 vii + 185 pp. ISBN 0-306-43739-2.

This well-written text comprises the proceedings of the 5th NATO ASI "Targeting of Drugs: Optimization Strategies" held in Cape Sounion, Greece, between June 24 and July 5, 1989.

In keeping up with its great tradition, this volume in this outstanding series provides excellent coverage of a wide range of topics where significant advances in targeting of drugs have been made in recent years. As stated in the Preface, the text especially deals with "strategies by which milieu interference curtailing the function of drug carriers is circumvented or removed." The book comprises 16 chapters by 38 contributors who are well-qualified individuals from academia and the pharmaceutical industry.

The topics covered in reviews and research papers are diverse and include chapters on the design of site-specific therapeutic systems, modeling of cell membrane targeting, various ways of targeting liposomes, drug delivery to the brain, and polymeric delivery systems. Each of the 16 chapters is well introduced and the reader is carefully guided through a substantial amount of literature. In each case the reference is current through 1989, with some 1990 references included, and draws on work from the authors' laboratory and other laboratories. The papers on modeling of cell membrane targeting, antitumor effects of Six Ricin A-chain, tissue-specific serum opsonins, phagocytosis of liposomes, and stabilization of lipid microstructure are well organized and thoughtfully presented, with relevant references and a concise conclusion, thus providing the reader with a sense of future direction in the subject areas. Similarly the papers on targeting of liposomes, therapeutic systems, enhancement of hormone activity by monoclonal antibodies, drug delivery—industrial view, drug delivery to brain, and polymeric drug delivery systems are well written, with pertinent references. However, most of these topics have been extensively reviewed elsewhere.

I found this to be an excellent book which will be of interest to both students and research workers in several disciplines including pharmaceutics, pharmacology and experimental medicine and would be a welcome addition to libraries of colleges of pharmacy, the pharmaceutical industry, and organizations interested in targeted drug delivery.

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Letters to the Editor

The Influence of Molecular Volume and Hydrogen-Bonding on Peptide Transport Across Epithelial Membranes

Recent studies (1–3) conclude that peptide transport across Caco-2 cell monolayers is dictated primarily by the number of hydrogen bonds (N_H) which the peptide can form in aqueous solution. We suggest that this interpretation should also include the molecular volume (MV) in a model which is generally consistent with transcellular transport through diverse biomembranes.

We consider the permeability coefficient (P) through lipid lamellae in terms of the solutes's physicochemical properties (4,5),

$$P = K \cdot D/\delta \quad (1)$$

where K is the membrane–water partition coefficient, D is the diffusion coefficient in the membrane, and δ is the diffusion pathlength. The diffusivity is related to MV,

$$D = D_o \cdot \exp(-\beta \cdot MV) \quad (2)$$

where the constant β is inversely proportional to the average free-volume available for diffusion, and D_o is the diffusivity of a molecule with vanishingly small MV (6).

K can be estimated (7) from the solute's octanol–water partition coefficient (K_{oct}):

$$\log K = \alpha \cdot \log K_{oct} \quad (3)$$

where α is another constant. Combining these equations gives

$$\log P = \alpha \cdot \log K_{oct} - (\beta/2.3) \cdot MV + \log D_o/\delta \quad (4)$$

It has also been demonstrated that K is a function of the solute's MV and hydrogen-bond donor/acceptor activity (8) and can be related to the solute's MV and N_H by

$$\log K = a_1 \cdot MV + a_2 \cdot N_H \quad (5)$$

where all hydrogen bonds are considered equivalent. Combining Eqs. (1), (2), and (5) gives P in terms of MV and N_H,

$$\log P = (a_1 - \beta/2.3) \cdot MV + a_2 \cdot N_H + \log D_o/\delta \quad (6)$$

Conradi and co-workers (1–3) analyzed the permeability of a series of peptide analogues and found no correlation ($r^2 = 0.03$) between $\log P$ and $\log K_{oct}$ for compounds I–VI

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