METADATA

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Abstract

The book includes the current trends in the design of new pharmaceutical substances. Starting from the early stages of design to discover new lead-compounds with specific target receptor affinity, it extends to the role of ADME (Absorption, Distribution, Metabolism, Excretion) and physicochemical properties so as to achieve an appropriate pharmacokinetic profile, in the context that the fate of the drug in the organism should be investigated in parallel with its affinity to the target receptor. The in silico techniques comprising structure-based drug design, ligand-based drug design and fragment-based drug design are presented and discussed. The main statistical techniques are analyzed as tools for the development of prediction models in the frame of quantitative structure-activity relationships. The physicochemical and molecular properties - lipophilicity, electronic, steric - that influence the binding of molecules to macromolecules and the permeability of biological barriers are discussed. Particular emphasis is placed on the partition or distribution coefficient in the octanol/water system, the measure of lipophilicity which is the primary property in drug action. Techniques for determining and calculating the partition/distribution coefficient are presented. Optimal lipophilicity values for the permeability of biological barriers will be reported, while the principle of minimal lipophilicity will be emphasized. The concept of drug-likeness is introduced and the corresponding metric rules will be presented. The role of stereochemistry, chelates and prodrugs in biological action will also be presented. In addition, the strategy of multi-targeting is discussed. Finally, the main drug anti-targets and the techniques for controlling the binding of candidate pharmacomolecules to them is mentioned. In summary, the book demonstrates the complexity in research for the development of new drugs and highlights the drug as a high-tech product.

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