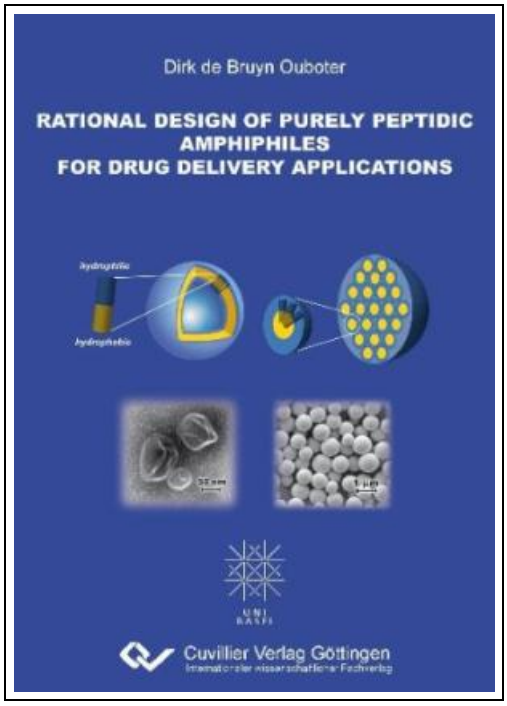
Rational Design of Purely Peptidic Amphiphiles for Drug Delivery Applications



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RATIONAL DESIGN OF PURELY PEPTIDIC AMPHIPHILES FOR DRUG DELIVERY APPLICATIONS

Cuvillier Verlag Jul 2011, 2011. Taschenbuch. Book Condition: Neu. 211x148x15 mm. Neuware - A broad range of new properties is emerging from supramolecular aggregates. Self-assembled structures of purely peptidic amphiphiles exploit these properties to produce biocompatible, biodegradable, smart materials for drug administration. This thesis explores the design, synthesis, purification, characterization of purely peptidic amphiphiles, and the evaluation of potential applications. The first chapter provides a general introduction to the field of self-assembly and drug delivery as compared to natureÆs delivery mechanisms. Further, the advantage of amino acid based molecules in producing smart materials for drug delivery applications is highlighted via biocompatibility and biodegradability considerations. Next, synthetic strategies and purification methods are discussed. Finally gramicidin A (gA) û a naturally occurring, short, hydrophobic, membrane-integrating peptide used to produce the amphiphilic peptides presented here û is introduced. Chapter two presents an initial approach to produce self-assembled structures by purely peptidic amphiphiles. The undecamer used features a repetitive L-tryptophan and D-leucine (LW-DL) motif representing the hydrophobic block, and an N-terminally attached hydrophilic (lysine or acetylated lysine) section. Besides solid-phase peptide synthesis and purification, the process that self-assembles micelles and spherical peptide particles, termed ôpeptide beadsö was characterized as a function of temperature and solvent composition by means of electron paramagnetic resonance (EPR), dynamic and static light scattering, fluorimetry and electron microscopy. An equilibrium process between single peptide molecules, micelles and peptide beads is then presented. Chapter three examines the structure of self-assembled peptide beads of diameters between 200 to 1500 nm. The beads were analyzed by electron and atomic force microscopy (AFM), static and dynamic light-, and small angle X-ray scattering. The beads are seen to result from hierarchical organization of micellar-like subunits and confirm the concept of multicompartment micelles. An improved understanding of the beadsÆ capacity to embed hydrophobic and hydrophilic payloads...

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