

Synthesis of biocompatible amphiphilic block copolymers for the use as drug carrier system

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Summary.

In this PhD study amphiphilic block copolymers from polylactic acid (PLA) and polyethylene oxide (PEO) were synthesized by anionic polymerisation. Polymers were characterized by GPC, MALDI-TOF-MS and NMR. The block length ratio of the hydrophilic PEO-block and the hydrophobic PLA-block was chosen to yield polymers forming vesicles in water. Both blocks are known for good biocompatibility and are approved by the FDA for use in pharmaceuticals. Due to their biocompatibility, vesicles from such block copolymers could potentially be suitable for use as drug carrier systems.

Sequential anionic polymerisation of ethylene oxide and lactide (D3) led to block copolymers with narrow size distributions and well defined block lengths. To be able to study vesicle properties large vesicles with a diameter of 1 - 10 μm were synthesised. Especially for encapsulation experiments, vesicles were examined by light- and fluorescence microscopy as well as confocal laser scanning microscopy. By encapsulating a hydrophobic fluorescent dye into the vesicles double layer it was possible to gain three dimensional images of the vesicles by confocal laser scanning microscopy.

Additionally the Encapsulation of fluorescent CdSe/CdS/ZnS nanocrystals into the vesicles was investigated. New insights about the position of nanocrystals in the vesicles and the mechanism of encapsulation were gained.

For most potential applications, small vesicles in the nanometre regime are beneficial. With modified preparation methods PLA-PEO vesicles with a diameter of about 200 nm were prepared and examined by cryo-electron-microscopy. A very important issue for potential drug carrier systems is the carrier surface and its functional group, which in this case is represented by the end group function of the PEO blocks. Block copolymers with acetal-, allyl, and for the first time with a tyramine functional group were synthesised. These functional groups facilitate coupling reactions to ligands or peptides, which can be used for targeted drug delivery. As proof of the vesicles' surface functionality, fluorescent dyes were coupled to the surface and analysed by fluorescence microscopy.

Furthermore new synthetic strategies for the preparation of amphiphilic block copolymers from polydimethylsiloxane (PDMS) and polyethylene oxide (PEO) were explored. A series of block copolymers prepared by sequential synthesis and by stepwise synthesis of the blocks followed by a coupling reaction, were investigated.