Poly(substituted-lactides): Novel functionalized PLA for Drug Delivery

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Keywords: functionalized poly(lactides), biodegradable polymers, controlled drug delivery

In the last 30 years biodegradable polymers, such as polyesters, polyamides, -amines, -amines, chitosans, alginate, saccarides and other natural polymers have been developed and improved for important pharmaceutical and medical applications. Many successful developed and marketed devices are based on polyesters such as poly(ε-caprolactone) or poly(lactide). For most applications the properties of the simple homopolymers need to be modified. Syntheses of block or random copolymers were one of the most obvious and promising strategies to meet the requirements of individual applications. Surface modifications by different methods or incorporation of diverse auxiliaries, e.g. salts or plasticizers are other investigated and applied possibilities. Material properties could be adjusted due to increased stability needs or in contrast to better degradation profiles for new drug delivery systems. Next to these two basic but opposite physical properties of a polymeric matrix for the controlled drug release in the human body many other contrary factors are of importance too. Especially the hydrophobicity / hydrophilicity parameter of the system has a major impact and is to be pointed out. In case of drug delivery devices the drug needs to be incorporeable and stable under the different conditions during the administration. The delivery system should reach its site of action without prior degradation or being eliminated by the body's natural protection systems and finally the release of the drug should be controlled over time and of a defined rate. An application will only be feasible if the system shows biocompatibility, in particular non-toxicity, also in regard to the degradation products. For all this our strategy is to synthesize novel functionalized poly(lactides), which will be a) easily available, b) easy in its synthesis and purification c) with well-defined polymer structures and molecular weight. They are d) considered as safe and show e) controlled degradation and controlled drug release, f) the degradation products are safe and biocompatible and g) sterilization of the system should be possible without changing the properties, e.g. γ-irradiation with minimal effect on the polymer properties. Moreover functionalities for drug targeting and transfection efficiency can be added via addition onto the functional end groups of the polymers.

To obtain new poly(lactide) based materials with the above mentioned requirements we are preparing in a two-step one-pot synthesis various new mono- and di-substituted lactides. Followed by their ring-opening polymerization hydrophilic and hydrophobic, respectively PLA-based polymers with good controlled molecular weights and narrow polydispersities are obtained.\(^\text{1,2}\)

![Scheme 1: Monomer and new functionalized PLA Synthesis](image)

References:


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