

## Bis-Az lactone Based Biodegradable Poly(Ester Amide)s: Design, Synthesis and Study

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**Abstract :** Biodegradable biomaterials (BB) are of high interest for numerous applications in modern medicine as resorbable surgical materials and drug delivery systems. This kind of materials can be cleared from the body after the fulfillment of their function that excludes a surgical intervention for their removal. One of the most promising BB are amino acids based biodegradable poly(ester amide)s (PEAs) which are composed of naturally occurring ( $\alpha$ -amino acids) and non-toxic building blocks such as fatty diols and dicarboxylic acids. Key bis-nucleophilic monomers for synthesizing the PEAs are diamine-diester-di-p-toluenesulfonic acid salts of bis-( $\alpha$ -amino acid)-alkylenediester (TAADs) which form the PEAs after step-growth polymerization (polycondensation) with bis-electrophilic counter-partners - activated diesters of dicarboxylic acids. The PEAs combine all advantages of the 'parent polymers' - polyesters (PEs) and polyamides (PAs): Ability of biodegradation (PEs), a high affinity with tissues and a wide range of desired mechanical properties (PAs). The scopes of applications of the PEAs can substantially be expanded by their functionalization, e.g. through the incorporation of hydrophobic fragments into the polymeric backbones. Hydrophobically modified PEAs can form non-covalent adducts with various compounds that make them attractive as drug carriers. For hydrophobic modification of the PEAs, we selected so-called 'Az lactone Method' based on the application of p-phenylene-bis-oxazolinons (bis-az lactones, BALs) as active bis-electrophilic monomers in step-growth polymerization with TAADs. Interaction of BALs with TAADs resulted in the PEAs with low MWs (Mw 2,800-19,600 Da) and poor material properties. The high-molecular-weight PEAs (Mw up to 100,000) with desirable material properties were synthesized after replacement of a part of BALs with activated diester - di-p-nitrophenylsebacate, or a part of TAAD with alkylenediamine - 1,6-hexamethylenediamine. The new hydrophobically modified PEAs were characterized by FTIR, NMR, GPC, and DSC. It was shown that after the hydrophobic modification the PEAs retain the biodegradability (in vitro study catalyzed by  $\alpha$ -chymotrypsin and lipase), and are of interest for constructing resorbable surgical and pharmaceutical devices including drug delivering containers such as microspheres. The new PEAs are insoluble in hydrophobic organic solvents such as chloroform or dichloromethane (swell only) that allowed elaborating a new technology of fabricating microspheres.

**Keywords :** amino acids, biodegradable polymers, bis-az lactones, microspheres

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