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BIODEGRADABLE AND FUNCTIONAL ALIPHATIC CO-POLYESTERS

Tiziana Fuoco

TUTOR
Prof.ssa Daniela Pappalardo

CO-TUTORS
Prof.ssa Marina Lamberti
Prof.ssa Anna Finne-Wistrand

COORDINATORE
Prof. Gaetano Guerra

ABSTRACT

Over the past decades, aliphatic polyesters have found rapidly increasing interest. Linear aliphatic polyesters, such as poly(glycolide) (PGA), poly(lactide) (PLA), poly(ε–caprolactone) (PCL) and their copolymers have found a wide range of practical applications, from packaging to more sophisticated biomedical devices. This class of materials is biocompatible and biodegradable; the degradation products are excreted via the citric acid cycle.

The uniqueness of this class of polymers lies in its immense diversity and synthetic versatility. They can be prepared by a variety of monomers via different approaches. The ring-opening polymerization of cyclic esters and lactone is the best strategy.

There is still need for improvements to provide materials with enhanced features to address the new requirements of use. A precise control over properties, like hydrophilicity, glass transition, the presence of functional group is important to regulate the biodegradation rate, the thermomechanical properties and it relies on a controlled synthetic pathway.

This doctoral thesis was focused on the development of synthetic pathways to obtain aliphatic polyesters with different and controlled microstructures and functional groups by extending the expertise in the ring-opening polymerization of cyclic esters by dimethyl(salicylaldiminato)aluminum compounds.

Dimethyl(salicylaldiminato)aluminum compounds with a different steric hindrance at the ortho position of the phenolato ring were tested as catalysts in the ring-opening homo- and co-polymerization of GA, rac-LA and CL. These complexes resulted active for the production of PLGA copolymers with variable microstructure.

This copolymer is one of the most used in biomedical field as temporary scaffolds and as drug delivery device. The degradation profile of PLGA is strongly influenced by the microstructure.

The copolymerization of GA and LA were performed in bulk and in solution, by varying comonomers ratio, monomer/catalyst feed ratio, temperature, reaction time and solvent. By changing the reaction conditions, copolymers from random, to blocky, to di-block were obtained, demonstrating the versatility of such system in modulating the copolymers microstructure and the related thermal properties.

The same catalytic approach was extended to the copolymerization of GA with CL and to the terpolymerization of GA, CL and rac-LA. The formation of random copolymers was favored by the steric hindrance of the catalyst and transesterification reactions contributed to randomize the structure. All the terpolymer samples resulted random and amorphous, the incorporation of the monomers is in this case determined by the bulkiness of the catalyst and by the higher coordination ability of the cyclic esters.

While the physical properties can be tailored by copolymerization, the introduction of functional group extends the possible applications to new areas, especially in biomedical field where the binding of biological motifs could enable interactions with cells.

Due to the ubiquity of thiol groups in the biological environment and to the pliability of thiol chemistry, an ad hoc lactide-type monomer possessing a pendant thiol-protected group, the 3-methyl-6-(tritylthiomethyl)-1,4-dioxane-2,5-dione was designed and synthetized. Then, this molecule was used as a “building block” for the

preparation of functionalized aliphatic co-polyesters by copolymerization with LA and CL promoted by dimethyl(salicylaldiminato)aluminum compounds. After polymerization, the pendant groups incorporated along the chains were converted into pyridyl disulfide functionalities. This derivative was used to prepare porous scaffolds by salt-leaching method after blend with PCLA.

The pyridildisulphide groups, which are very reactive in the disulphide exchange reaction, embedded in the 3D porous scaffolds were exploited to graft a cysteine terminated RGD peptide demonstrating the potential of such prepared materials.

Finally, dimethyl(salicylaldiminato)aluminum compounds were employed as catalyst in the ring-opening polymerization of an unsaturated large lactone, the ω–6-hexadecenlactone (6HDL). Semicrystalline polyethylene-like unsaturated polyesters were obtained with a good control over the chain growth.

The double bonds along the polymeric backbones were used to carry out further modification, which occurred without any change in the degree of polymerization, however, modifying the thermal and structural polymer features.

Copolymerization of the 6HDL with the smaller ring size CL produced a true random semicrystalline copolymer. The pseudo-living behaviour of the catalytic system and the absence of transesterification reactions allowed also the preparation of linear block copolymers of 6HDL with CL and/or rac-LA by sequential addition of the monomers. These block copolymers were also semicrystalline.