New Biomimetic and Biodegradable Polymers for Clinical Use

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For recent decades, the most commonly biodegradable polymers used in clinical applications are aliphatic polyesters such as polyglycolide (PGA), polylactide (PLA), polycaprolactone (PCL) and their copolymers, mainly due to their excellent biocompatibility and biodegradability properties. However, the lack of functional groups on their backbone, which could otherwise be used for tuning physicochemical properties and/or for introducing bioactive units, limits their further biomedical applications.

Polymers with repeating phosphoester bonds in the backbone are structurally versatile and biodegradable through hydrolysis and possibly enzymatic digestion of phosphates linkages under physiological conditions. An advantage of polyphosphoesters (PPEs) compared to aliphatic polyesters is the possible functionalization of side chains due to the pentavalency of the phosphorous atom, allowing the introduction of bioactive molecules and extensive modification of the physical and chemical properties of polymer.

The Ring-Opening Polymerization (ROP) of cyclic esters is a well-established process to provide linear polyesters with predictable molecular weight, narrow polydispersity and well-defined end-groups. Up to now, metallic compounds are particularly used as initiators or polymerization catalysts to synthetize these materials but metallic derivatives are cytotoxic and a lack of residual metal contaminants is strongly required in view of biomedical applications. To tackle these drawbacks, we developed synthetic approaches that are metal-free (i.e., organocatalytic) using organocatalysis based on supramolecular recognition[1]. A variety of organocatalysts such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,5,7-triazabicyclo[4.4.0]undec-5-ene (TBD) and a bicomponent thiourea-tertiary amine catalyst were studied. Each of these catalysts is efficient to produce linear PPEs from cyclic phosphate monomers (CPMs) but with different sensitivity towards transesterification side reactions. Compared with polymerizations carried out with $Sn(Oct)_2$ as metal catalyst, the control of polymerization is much better so that it is possible to prepare PPEs with molecular weight close to 70.000 g/mol and polydispersity index below 1.10. The chain extension experiments through the use of hydroxy end-capped PPEs as macro-initiators confirm the controlled/living nature of organo-catalyzed ROP of CPMs and pave the way to the synthesis of block copolymers and others more complicated architectures based on polyphosphates[2].

Finally, these polymerizations procedures are expected to facilitate the synthesis of well-defined PPEs with various architectures and free of potentially toxic metal remnants for biomedical applications such as drug delivery and tissue engineering.

References

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