

# Polyhydroxyalkanoate (PHA) copolymers for drug delivery applications: a ring-opening polymerization of functional $\beta$ -lactones approach

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## Introduction

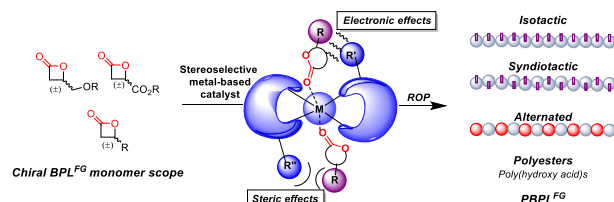
Polyhydroxyalkanoates (PHAs) are a unique class of natural or synthetic aliphatic polyesters which feature the same three-carbon backbone structure, only differing by their side-chain substituent. Introduction of a pendant functional group (FG) along the PHA backbone provides a handle to tune their properties, such as their thermal, mechanical and (bio)degradability signature. PHAs have attracted considerable interest as “green” engineering plastics. These biodegradable and biocompatible polymers represent a targeted choice as versatile green alternatives to single-use plastics especially for packaging, and for biomedical applications.

## Results and Discussion

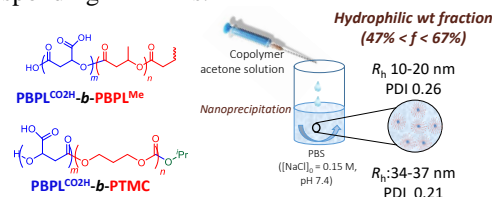
Recent highlights of research in our group have been achieved in the field of 1) tunable catalytic systems for the ring-opening (co)polymerization (ROP) of functional  $\beta$ -lactones (BPL<sup>FG</sup>) (e.g.  $\beta$ -butyrolactone (BPL<sup>Me</sup>),  $\beta$ -malolactonates (BPL<sup>CO<sub>2</sub>R</sup>; R = CH<sub>2</sub>Ph (Bn), (CH<sub>2</sub>)<sub>2</sub>=CH<sub>2</sub> (All)), or 4-alkoxymethylene- $\beta$ -propiolactones (BPL<sup>CH<sub>2</sub>OR</sup>; R = Me, Allyl, Bn)) into their corresponding PHAs (namely poly(3-hydroxybutyrate) (PBPL<sup>CH<sub>3</sub></sup>, aka. PHB), poly(alkyl  $\beta$ -malolactonate) (PBPL<sup>CO<sub>2</sub>R</sup>), or poly(alkoxy methylene- $\beta$ -propiolactones) (PBPL<sup>CH<sub>2</sub>OR</sup>), respectively), of 2) original sequence controlled PHAs featuring a high degree of control over molecular and microstructural characteristics (Figure 1)<sup>1-3</sup>, and of 3) PHA copolymers as promising drug delivery systems (Figure 2).<sup>5</sup>

## Conclusions

Our most significant achievements in the ROP of functional  $\beta$ -lactones include the development of catalytic strategies that enable the controlled synthesis of functional PHAs with tunable microstructure, alternated or block PHA-based copolymers, and the evidences of the relationship between the catalytic system, the chemical structure (especially the nature of the pendant functional



**Figure 1.** Stereoselective ROP of various chiral *racemic* 4-substituted- $\beta$ -propiolactones *rac*-BPL<sup>FG</sup>s (FG = Me, CO<sub>2</sub>R, CH<sub>2</sub>OR; R = Me, All, Bn) catalyzed by diamino- or amino-alkoxy-bis(phenolate) complexes, affording the corresponding PBPL<sup>FG</sup>s.<sup>1-3</sup>



**Figure 2.** Design of nanoparticles derived from PHA based copolymers.<sup>4</sup>

substituent along the PHA backbone imparted by the exocyclic  $\beta$ -lactone FG substituent) and the composition of the macromolecules. Amphiphilic PHAs also revealed as promising biobased and biocompatible drug delivery systems.

## References

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