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Dense stable suspensions of medium-chain-length poly(3-hydroxyalkanoate) nanoparticles

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ABSTRACT

This is the first study to examine the formulation (selection of ionic and nonionic surfactants and their concentrations) and processing conditions (ultrasonication time and amplitude, and selection of solvent) to make dense suspensions (10 and 30% (w/v)) of medium-chain-length poly(3-hydroxyalkanoate) (mcl-PHA) with particles less than 300 nm. A two-stage emulsification-solvent evaporation process was used. Previous studies made suspensions at much lower solids content (up to 0.4% (w/v)). The dispersed phase was mcl-PHA initially dissolved in methylene chloride, while the continuous phase was water containing one or more surfactants. Water miscible solvents, such as acetone and tetrahydrofuran, could not make dense suspensions of PHA nanoparticles, while those with low water solubility were effective. Among the ionic surfactants, the anionic, sodium dodecyl sulfate (SDS), and the cationic, dodecyltrimethylammonium bromide, produced the smallest particle sizes (both ~100 nm). Nanoparticles were more stable when SDS was combined with any of the non-ionic surfactants tested. The zeta potential of nanoparticles stabilized with SDS and polyoxyethylene octyl phenyl ether (Triton X-100) or polyoxyethylene (20) sorbitan monooleate (Tween 80) increased slightly over 30 days, indicating that they may be more effective than the other non-ionic surfactants stabilizers where a decrease was observed. Using the same surfactant formulation, similar size mcl-PHA stable nanoparticle suspensions were produced using either an ultrasonic probe or a more scalable high-shear microfluidic device.

1. Introduction

Poly(3-hydroxyalkanoates) (PHAs) are aliphatic polyesters, produced as intracellular granules from renewable resources by many bacterial species [1]. PHAs are classified as short-chain-length (scl), containing 3–5 carbon subunits, or medium-chain-length (mcl), containing 6–14 carbon subunits. PHAs that contain both scl and mcl monomers are referred to as scl-mcl-PHA. Mcl-PHAs are elastomeric or tacky materials with low or no crystallinity and low or no melting point, whereas scl-PHAs are typically highly crystalline and stiff. PHAs are non-toxic, and biodegradable in most biotic environments. They have been intensely studied in the last several decades [2–4]. Mcl-PHAs attract increasing attention as they find applications in toners [5–7], drug delivery [8–10], coatings and paint formulations [11]. For example, mcl-PHAs can replace polyester toners incorporating bisphenol A [6] which has been banned in certain applications in Canada and Europe because it disrupts

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hormonal functions and is carcinogenic [12]. Many of these applications require mcl-PHA as a dense suspension of nanoparticles.

Nanoparticles are defined as solid, colloidal particles that are 10–500 nm. They have better stability against particle aggregation and gravitational separation than larger particles [13,14]. Small particle size reduces creaming and sedimentation, allows a more uniform deposition on substrates, and coalescence can be prevented using surfactants that minimize disruption of the liquid film between particles [14]. Polymer nanoparticles can be made by (i) high energy methods using mechanical devices, such as ultrasonicators or high pressure homogenizers, which disrupt interfaces to form small particles with the help of surfactants and co-surfactants or (ii) low energy methods in which small particles form spontaneously due to altered conditions such as phase inversion [13]. High energy methods require much less surfactant to achieve small particles than low energy methods. For example, formation of droplets smaller than 200 nm via microfluidization required a surfactant to oil ratio (SOR) < 0.1 but when spontaneous emulsification was used a SOR > 1 was necessary [15].

Few studies have used low energy methods to make PHA colloidal suspensions [16] but high energy methods, specifically emulsification followed by solvent evaporation, have been commonly used to make both scl- and scl-mcl-PHA suspensions [10,17–22]. This approach is popular because of its simplicity and suitability for scale-up [23]. Particle size and distribution dictate specific applications and also determine significant properties such as viscosity, surface area, and packing density [24].

In the emulsification-solvent evaporation method, PHA is solubilized in an organic solvent, added to water with vigorous mixing to make an oil-in-water emulsion before the solvent is removed by evaporation to leave the mcl-PHA as a suspension. A surfactant must be added to the aqueous phase to make a stable latex of scl-PHAs [18]. Although a surfactant or emulsifier is routinely added to stabilize latexes of scl-mcl-PHAs [10,21,25] and mcl-PHAs [26], it is not needed if the final solids content is less than 0.4% (w/v) [19,27,28]. The stability of mcl-PHA suspensions without a surfactant was attributed to steric stabilization due to the relatively longer side chains of mcl-PHA monomers compared to the methyl group in poly(3-hydroxybutyrate) (PHB) [27]. However, without a surfactant, mcl-PHA nanoparticles agglomerate above 0.4% solids [28]. The thermoelastomeric scl-PHAs, poly(4-hydroxybutyrate) and poly(4-hydroxybutyrate-co-3-hydroxybutyrate), have not been found to form stable nanoparticles even with a surfactant [27]. Studies with scl-mcl PHAs for drug delivery [10,21,25] or mcl-PHAs for paper coating [29] were made at a low final solids content of 0.01–0.25% (w/v). Certain applications such as xerographic toners require much higher final solids content of 25–30% (w/v) and particles sizes of 25–300 nm [6]. There are no reports on the processing conditions and surfactants needed to make stable mcl-PHA nanoparticles at such high solids content.

This study is the first to demonstrate the preparation of concentrated (i.e. 10–30% w/v) mcl-PHA nanoparticles in suspension. The emulsification-solvent evaporation method was used. The effect of processing parameters such as the ultrasonication time and amplitude, and its formulation such as the choice of surfactants, their concentration, and the choice of the organic solvent to solubilize mcl-PHA on particle size and stability were investigated. In addition, we show that mcl-PHA nanoparticles can also be fabricated using a high-shear microfluidic device.

2. Experimental

2.1. Materials and methods

2.1.1. Preparation of concentrated mcl-PHA suspension

Mcl-PHA was obtained by fed-batch fermentation of *Pseudomonas putida* KT2440 as described previously [30]. The polymer was composed of 60 mol% 3-hydroxydecanoate, 20 mol% 3-hydroxyoctanoate, and 20 mol% 3-hydroxyhexanoate. Distilled, deionized water was used to prepare solutions. All chemicals were analytical grade.

Mcl-PHA suspensions were prepared by the emulsification-solvent evaporation method in two stages [31,32]. In stage 1, the suspension was prepared by adding the appropriate amount of polymer solubilized in 10 mL methylene chloride (unless otherwise stated), to 9 mL of an aqueous surfactant solution at the specified concentration (Fig. 1). The pH was adjusted to

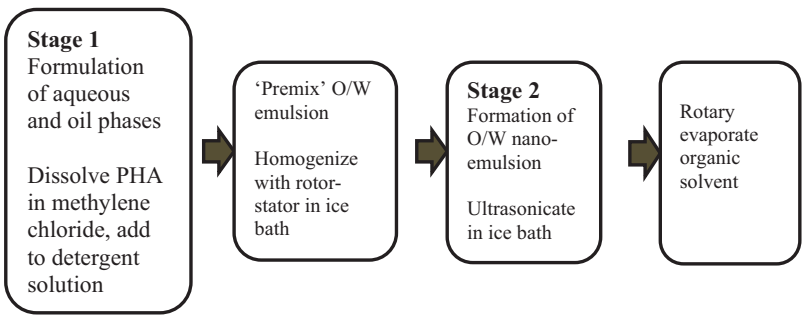

Fig. 1. Schematic diagram illustrating the two-stage process to make mcl-PHA nanoparticle suspensions.