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| **Effect of Hydrophobicity Alterations and Purification Nature on Poly(glycerol adipate) Self-Assembling Behaviors.** |
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| **Background:** Nowadays, biodegradable polymers are rendered as an appealing polymeric system for biomedical applications. In this regard, polyesters appear as one of the most promising platforms for these applications owing to their tendency to be hydrolyzed under physiological conditions. Although they have been used for many years for biomedical and pharmaceutical applications, due to their lack of biological and chemical clues, there is still need for improvements. For this reason, poly(glycerol adipate) (PGA) has been investigated as a bio-derived, biodegradable alternative and thanks to its intrinsic  amphiphilicity, it self-assemblies into nanoparticles (NPs) without the addition of any stabilizers. It has also been shown to be able to encapsulate small- and macro- active ingredients. The chemo- and regioselective enzymatic synthesis of PGA leaves the secondary hydroxyl group as an available pendant, useful for further functionalization and modifications. Hydrophobicity and its impact on this polymeric system is relatively underexplored. In addition, currently, in the literature, only a few studies investigate the effect of polymer purification upon polymer self-assembling and NPs properties.  |
| **Methods:** In this project we focused on the effect of the incorporation of a hydrophobic segment in different ratios compared to glycerol. Two polymers were synthesized according to previous studies; Poly(glycerol adipate) (PGA) and its hexanediol-functionalized variation; poly(glycerol adipate)-hexanediol (PGA-Hex). They were analyzed by 1H-NMR and Gel Permeation Chromatography (GPC) while the produced NPs, stability and surface charges were examined by DLS and zeta potential analysis. Purification of the polymers were performed by precipitation step.  |
| **Results:** To start with, 1H-NMR and GPC studies verified the successful synthesis and modifications. Moving forward, 3 different solvent systems; hexane, diethyl ether, and mix, have been used for the purification via precipitation process of the polymers. While 1H-NMR results showed that purification does not affect the polymer structure, GPC proved that although the Mw of the purified polymers remained almost the same, the purification step produced well-distributed peaks without any low molecular weight shoulders, and therefore absence of oligomers. The size of NPs before purification ranged between 170-210 nm and after purification 110-220nm. To investigate further the effect of hydrophobicity, we synthesized the PGA-Hex using different Gly:Hex ratios; 0,3:0,7/ 0,5:0,5/ 0,7:0,3. Altering the ratios enabled modifications in both physical and chemical behaviors.  |
| **Conclusions:** We successfully synthesized the polymers according to literature and we introduced new variations, the changing of the amphiphilic ratio and the purification step. Altering the hydrophobicity of the polymers is affecting their physiological properties and the NPs formation. However, further studies need to be considered in order to unveil whether these changes influence the use of polymers for biomedical applications. Additionally, the purification process, which has never been reported in literature, revealed that the purified polymers demonstrate variations in the physiological properties and NPs formation mainly due to the observation that purification step provided shorter chain entities upon self-assembling. Nevertheless, more studies are required to further highlight whether purification affects the stability of NPs.  |