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Synthesis of biodegradable amphiphilic copolymers and their application as drug carriers

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Abstract –Amphiphilic copolymers were synthesized from biodegradable polyester and poly(ethylene glycol). Micellar nanostructures (100-500 nm) were obtained by sol-gel processing of the biodegradable amphiphilic copolymers through self-organization in aqueous medium. The micelles formation was characterized by ^{1}H Nuclear Magnetic Resonance (^{1}H-NMR) and confirmed Scanning Electron Microscopy (SEM).

The use of drug carriers formed from amphiphilic block copolymers AB and ABA (di- and triblock) as encapsulating substance for hydrophilic (peptides and proteins) and hydrophobic drugs is a promising pharmaceutical technology [1]. The amphiphilic copolymers, compared to the polymer blends, has shown much more efficiency, because of the improvement of the miscibility due to the covalent bond between the dissimilar blocks, which limits the molecular diffusion and phase separation to short ranges 100-400 Å. In aqueous medium, amphiphilic block copolymers are thermodynamically driven to self assemble in micellar nanostructures [2]. Micelles of block copolymers of poly(ethylene glycol) (PEG) present a hydrophilic corona region composed by PEG, creating therapeutic advantages by reducing adverse autoimmune reaction, adding longer circulation time in the blood system [3] and introducing capability to transport drugs either lipophilic or hydrophilic within the core region of the micelle.

In this work, triblock block copolymers of PEG were prepared with polylactide (PLLA) and poly(3-hydroxybutyrate) (PHB) as the lipophilic segments, PLLA-PEG-PLLA and PHB-PEG-PHB, respectively. The block copolymers were synthesized, using PEG as macroinitiator, through coordination-insertion reaction from the lactide [4] and by molten transesterification of PHB. The chemical structures of the block copolymers were characterized by ^{1}H-NMR and ^{13}C-NMR spectroscopies. The micelles of the copolymers were prepared by their self-assemblage in aqueous medium, through the solvent diffusion method [4]. ^{1}H-NMR spectroscopy was able to differentiate the micellar structures comprised by hydrophilic corona and hydrophobic inner part, while the observation of their globular morphology was achieved by SEM (Figures 1 and 2), and particles from 50 nm to 1000 nm were observed, depending on the copolymer structure and micelle preparation process.

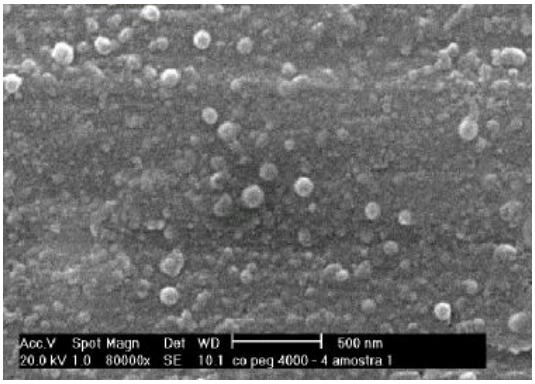

Figure 1: SEM of micellar structures, 80000 X.

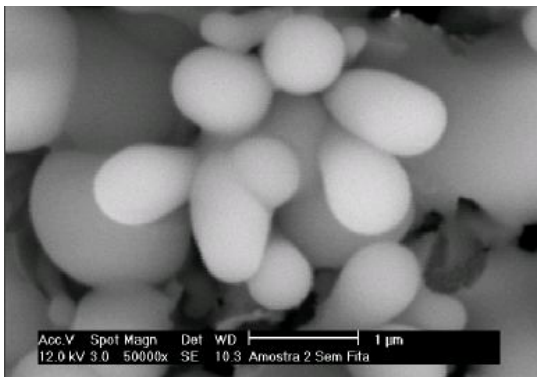

Figure 2: SEM of micellar structures, 50000 X

References

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