Complex Liposomes for Phototherapy: development and optimization

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Photodynamic Therapy (PDT) is currently a promising treatment methodology for several types of cancers [1]. Three main components are necessary for PDT: a light source, a photosensitizing molecule and oxygen [2]. Under these conditions, PDT leads to oxidative stress and, as consequence, cell death. However, drug solubility and its delivery to the target tissue are factors that can affect the treatment efficacy. To overpass these situations, it is possible to use nanocarriers such as liposomes. These lipid carriers are able to encapsulate both hydrophobic and hydrophilic molecules and are suitable for photodynamic applications [3]. This work focuses on the development and optimization of complex liposomes for drug delivery based on the zwitterionic lipid 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC), on the electrical negative lipids 1,2-dipalmitoyl-sn-glycero-3-phospho-(1′-rac-glycerol) (sodium salt) (DPPG) and 1,2-dioleoyl-sn-glycero-3-phospho-(1'-rac-glycerol) (sodium salt) (DOPG), and on cholesterol (CHOL), produced by sonication and extrusion methods. Lipid mixture was prepared with different composition in chloroform-methanol and liposomes were prepared by thin-film hydration method [4]. The suspensions were submitted to sonication or extrusion through a 200 nm polycarbonate membrane. Dynamic light scattering analysis was employed to compare size and polydispersity. Figure 1 shows the comparison between the two methods using 3 different lipid compositions namely, C1: DPPC+DPPG; C2: DPPC+DPPG+DOPG; C3: DPPC+DPPG+CHOL). While C2 and C3 liposomes produced by sonication show sizes around 150 nm, the ones prepared by extrusion present smaller sizes. However, C1 liposomes prepared through sonication present higher sizes (more than 1000 nm) while through extrusion C1 liposomes have diameter around 120 nm. Another major difference between the methods was the polydispersity indexes, above 0.3 and below 0.2 for sonication and extrusion, respectively. Therefore, sonication method produced small liposomes with DPPC and DPPG in presence of cholesterol or DOPG, but all the formulations present a moderate polydispersity index, which results in non-homogeneous liposomes size distribution. Extrusion through a 200 nm membrane enables the downsizing of all liposomes formulations, achieving a more homogeneous population of particles, which makes extrusion the selected method for further studies with the encapsulation of photosensitizer molecules in liposomes.

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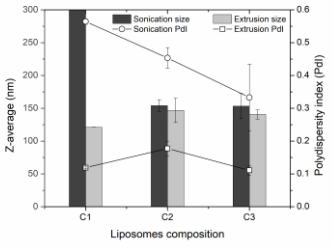

Figure 1: Comparison of size and polydispersity index (PdI) for different liposomes compositions produced through extrusion and sonication methods.