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DIBLOCK COPOLYMERS INTERACTION WITH LIPOSOMES AND ANTIMICROBIAL ACTIVITY

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Abstract: Polymers can be used to prepare antifouling surfaces, antimicrobial agents and decontamination systems [1,2]. The interaction of poly (methyl methacrylate) (PMMA), poly[(dimethylamino ethyl) methacrylate] (PDMAEMA) and their diblock copolymers, prepared at different $PMMA_m$/$PDMAEMA_n$ ratios (m/n): $PMMA_{50}$, $PDMAEMA_{265}$, $PMMA_{94}$-*b*-$PDMAEMA_{88}$, $PMMA_{50}$-*b*-$PDMAEMA_{269}$, and $PMMA_{48}$-*b*-$PDMAEMA_{324}$, with Large Unilamellar Vesicles (LUVs), Giant Vesicles, GUVs, was studied and their antimicrobial potential was evaluated. We compared these polymers to proteins and verify its potential as antimicrobial compounds. LUVs of phosphatidylcholine (PC) and phosphatidylglycerol (PG) were prepared by extrusion. The effects of polymer type, concentration, pH, and PG:PC ratios on vesicle-incorporated 5,6-carboxyfluorescein (CF) leakage, were analyzed by fluorescence spectroscopy. NMR, Dynamic Light Scattering, Zeta Potential, and microscopy were employed as characterization methods. Antimicrobial activity was measured with *Escherichia coli* (*E.c.*) and *Bacillus subtilis* (*B.s.*). Positively charged polymers binds to anionic LUVs producing polymer/LUVs aggregates and CF leakage. PC:PG interactions with the cationic polymers were demonstrated by NMR and analysis of GUVs stability. Maximum vesicle leakage was obtained with $PMMA_m$:$PDMAEMA_n$ copolymers. The interaction with PC:PG LUVs was greater at pHs where the cationic polymers were partially neutralized while, at pH near 10, no interaction was observed. These results were confirmed by NMR, DLS, and zeta potential analyses. The cationic polymers inhibited the *E.c.* and *B.s.* growth while PMMA had no effect. The cationic polymers permeabilized LUVs with different PC:PG ratios varying with pH, polymer/lipid and PMMA/PDMAEMA ratios. The copolymers with higher PDMAEMA molar fractions were more efficient for permeabilizing LUVs, while PMMA had no effect. These polymers can be used to prevent bacterial growth on surfaces, are good models to understand protein/membrane interactions.

Key-words: Copolymers; Liposomes; antimicrobial

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