

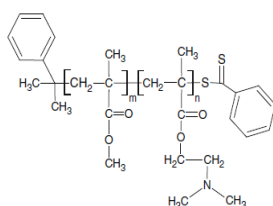
Study of the effect of copolymer structure on the permeability of phospholipid vesicles

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Introduction: Polymers are organic or inorganic macromolecules with high molar mass consisting of repeated units linked usually by covalent bonds. Copolymers are polymers that have more than one kind of monomer. In this study poly (methyl metacrylate)-*block*-poly (N, N-dimetilaminoethyl metacrylate), PMMA_n-*b*-PDMAEMA_m, (diblock copolymer) with different compositions and molar masses (Scheme 1) were studied concerning its ability to increase the permeability of large unilamellar vesicles (LUVs) prepared with phospholipids mixtures. Amphipathic diblock copolymers can aggregate like surfactants, exhibiting, however, different chemical behavior and biocompatibility. The PMMA_n-*b*-DMAEMA_m diblock copolymers were synthesized by RAFT polymerization of methyl metacrylate, MMA, (hydrophobic) and dimetilaminoethyl metacrylate, DMAEMA (polar). Physical-chemical characteristics of the PMMA_n-*b*-DMAEMA_m, copolymers were studied as well as its interaction with LUVs.



Scheme 1- Structure of PMMA-b-PDMAEMA

Material and Methods: LUVs, of egg-phosphatidyl choline (PC) and egg-phosphatidyl glycerol (PG) mixtures were prepared by extrusion through membranes containing pores with 100 nm diameter. LUVs were loaded with 50 mM of carboxyfluorescein (CF). Non-entrapped CF was removed by a Sephadex-G25 column.

Results and Discussion: The CF release by the copolymers was followed as a function of time using LUVs with different composition, at several copolymers concentrations. The interaction of the copolymers with LUV's was studied also as a function of pH. The percentage of CF leakage (%Leakage) caused by the copolymer depended of the percentage of PG (%PG) and pH. Increasing %PG resulted in higher leakage rate at pH 8 while at pH 10 the leakage rate was low. Increasing pH a higher percentage of PG was required to achieve maximum leakage, which is consistent with a more negative LUV surface. Varying the pH, a maximum of %Leakage is observed between pHs 8.5 and pH 9, suggesting that the pKa of the copolymers amino groups are between these pHs.

Keywords: diblock copolymer, membrane, vesicles.

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