Abstract

In liposome-mediated delivery of therapeutic molecules, it is required to design responsive liposomes (or vesicles) capable of changing their properties in a controlled way under external stimuli, such as pH, salt concentration, cholesterol, temperature, light etc. This requires either integration of responsive functionality near the polar head-group of the bilayer forming amphiphile or incorporation of an amphiphilic molecule which bears the responsive functionality. The rationale for designing pH-sensitive vesicles is to exploit the acidic environment of tumors or damaged tissues to trigger release of entrapped guest/drug molecules through destabilization of bilayer membranes. In this work, preparation of non-phospholipid stable vesicles based on the mixture of two oppositely charged single-chain surfactants has been discussed. An amino acid-based carboxylate surfactant has been employed to impart pH-responsive character to the vesicles. The cationic surfactant is a commercial one. These so-called catanionic mixtures were observed to have very low critical micelle concentration in comparison to pure components and a strong synergistic interaction was observed. They were found to exhibit vesicle formation in a wide range of concentration and composition. The vesicles formed under different conditions have been characterized by a number of techniques, including surface tension, conductivity, fluorescence probe, dynamic light scattering, and microscopy. The prepared unilamellar vesicles of sizes in the range 100-200 nm were found to be stable under biological conditions (pH 7.4, [NaCl] = 150 mM and temperature 37 ^{o}C) for months. The influence of additives, such as cholesterol, salt, and alcohol on the membrane rigidity was investigated. Both cholesterol and salt were found to enhance rigidity of the bilayer membrane of the vesicles. However, addition of increasing concentration of ethanol disrupted the vesicles to small micellar structures. The effects of pH and temperature on vesicle stability were also studied. Finally, encapsulation and subsequent pH-triggered release of calcein, a fluorescent dye from the aqueous core of the vesicles was demonstrated. The biocompatibility of the vesicles was established by cytotoxicity and hemolytic studies under physiological conditions. The vesicles were observed to be compatible to RBCs and also nontoxic to mammalian cells.

Keywords: Catanionic mixture, Surface activity, Synergistic interactions, Vesicles, Fluorescence, Microscopy, Light scattering, Cytotoxicity, Drug delivery.