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Effect of Anionic Lipid on Zeta Potential Values and Physical Stability of Liposomal Amikacin

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Abstract : A surface charge of the nanoparticle is a very important consideration in pulmonal drug delivery system. The zeta potential (ZP) is related to the surface charge which can predict stability of nanoparticles as nebules of liposomal amikacin. Anionic lipid such as 1,2-dipalmitoyl-sn-glycero-3-phosphatidylglycerol (DPPG) is expected to contribute to the physical stability of liposomal amikacin and the optimal ZP value. Suitable ZP can improve drug release profiles at specific sites in alveoli as well as their stability in dosage form. This study aimed to analyze the effect of DPPG on ZP values and physical stability of liposomal amikacin. Liposomes were prepared by using the reserved phase evaporation method. Liposomes consisting of DPPG, 1,2-dipalmitoyl-sn-glycero-3-phosphatidylcholine (DPPC), cholesterol and amikacin were formulated in five different compositions 0/150/5/100, 10//150/5/100, 20/150/5/100, 30/150/5/100 and 40/150/5/100 (w/v) respectively. A chloroform/methanol mixture in the ratio of 1 : 1 (v/v) was used as solvent to dissolve lipids. These systems were adjusted in the phosphate buffer at pH 7.4. Nebules of liposomal amikacin were produced by using the vibrating nebulizer and then characterized by the X-ray diffraction, differential scanning calorimetry, particle size and zeta potential analyzer, and scanning electron microscope. Amikacin concentration from liposome leakage was determined by the immunoassay method. The study revealed that presence of DPPG could increase the ZP value. The addition of 10 mg DPPG in the composition resulted in increasing of ZP value to 3.70 mV (negatively charged). The optimum ZP value was reached at -28.780 ± 0.70 mV and particle size of nebules 461.70 ± 21.79 nm. Nebulizing process altered parameters such as particle size, conformation of lipid components and the amount of surface charges of nanoparticles which could influence the ZP value. These parameters might have profound effects on the application of nebules in the alveoli; however, negatively charge nanoparticles were unexpected to have a high ZP value in this system due to increased macrophage uptake and pulmonal clearance. Therefore, the ratio of liposome 20/150/5/100 (w/v) resulted in the most stable colloidal system and might be applicable to pulmonal drug delivery system.

Keywords : anionic lipid, dipalmitoylphosphatidylglycerol, liposomal amikacin, stability, zeta potential
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