Adsorption of Nanocarriers to Pulmonary Mucus Membrane

Gokce Alp*, Nihal Aydogan

Department of Chemical Engineering, Hacettepe University, Ankara, Turkey

*gdilli@hacettepe.edu.tr

Drug delivery through the lungs is considered to be a very advantageous route due to the large surface area and low catabolic enzymatic activity. Mucus layer, which covers the pulmonary airways, provides a natural defence to immune system towards exogenous particles by its clearance mechanism. However, this natural barrier also hinders the penetration and diffusion of the therapeutics through the mucus layer, especially in case of lung diseases due to the increasing thickness and viscosity of the mucus. This hindrance occurs as a result of several interactions between the mucus and the drug delivery system. In most of the studies, polymeric particles with 100-500 nm of diameter are used and their diffusion behaviour are tried to be enhanced by modifying the surface of the particles with different functional groups. Stealth design is also used in order to avoid the macrophages [1]. However, more detailed investigation of the interactions between the mucus and the drug carriers should be performed in order to increase the efficiency of the penetration through the mucus barrier.

In this study, solid lipid nanoparticles (SLN) are used as model drug delivery vehicles. They are chosen due to their high biocompatibility and stability. Three different SLNs with different size and zeta potentials are used and their interactions with mucus membrane are investigated by using different techniques. Mucin, which is the key glycoprotein of mucus, is used in order to mimic the mucus structure. First of all, the initial size and zeta potential values of the SLNs are determined by using Dynamic Light Scattering and Zeta Sizer. Then, the same measurements are carried out after the SLNs are incubated in mucin solution. The change at the size and zeta potentials of the particles provided us to detect if the particles are interacting with mucin, or not. Moreover, by using Langmuir trough, mucin layer is formed at the air/NaCl solution interface and particles are injected to the subphase of the mucin membrane. The adsorption and the penetration of the particles to previously formed mucin layers are examined by measuring the variation at the surface pressure with time. Also, the pre-formed mucin layers are compressed to selected pressures and therefore, the adsorption behaviours and the diffusion of the particles are also investigated for different mucin thicknesses. The resulting interfaces are also transferred to substrates and visualized with Atomic Force Microscopy (AFM).

From the variation at the size and the zeta potential values of the particles, it is determined that particles nearly show no interaction with mucin, even though at high mucin concentrations. The results are also supported by the AFM images. From both the surface pressure-time isotherms and AFM measurements, it is obtained that SLNs have successfully adsorbed and diffused through the mucin layer towards the interface even at high mucin thickness. The best result is obtained with the SLN, of which the zeta potential is the closest to zero. The results of this study are promising for obtaining a drug delivery system that is able to adsorb and penetrate through the mucus layer that covers the pulmonary airways.