

## Biophysical Analysis of the Interaction of Polymeric Nanoparticles with Biomimetic Models of the Lung Surfactant

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**Abstract :** The human body offers many avenues that could be used for drug delivery. The pulmonary route, which is delivered through the lungs, presents many advantages that have sparked interested in the field. These advantages include; 1) direct access to the lungs and the large surface area it provides, and 2) close proximity to the blood circulation. The air-blood barrier of the alveoli is about 500 nm thick. The air-blood barrier consist of a monolayer of lipids and few proteins called the lung surfactant and cells. This monolayer consists of ~90% lipids and ~10% proteins that are produced by the alveolar epithelial cells. The two major lipid classes constitutes of various saturation and chain length of phosphatidylcholine (PC) and phosphatidylglycerol (PG) representing 80% of total lipid component. The major role of the lung surfactant monolayer is to reduce surface tension experienced during breathing cycles in order to prevent lung collapse. In terms of the pulmonary drug delivery route, drugs pass through various parts of the respiratory system before reaching the alveoli. It is at this location that the lung surfactant functions as the air-blood barrier for drugs. As the field of nanomedicine advances, the use of nanoparticles (NPs) as drug delivery vehicles is becoming very important. This is due to the advantages NPs provide with their large surface area and potential specific targeting. Therefore, studying the interaction of NPs with lung surfactant and whether they affect its stability becomes very essential. The aim of this research is to develop a biomimetic model of the human lung surfactant followed by a biophysical analysis of the interaction of polymeric NPs. This biomimetic model will function as a fast initial mode of testing for whether NPs affect the stability of the human lung surfactant. The model developed thus far is an 8-component lipid system that contains major PC and PG lipids. Recently, a custom made 16:0/16:1 PC and PG lipids were added to the model system. In the human lung surfactant, these lipids constitute 16% of the total lipid component. According to the author's knowledge, there is not much monolayer data on the biophysical analysis of the 16:0/16:1 lipids, therefore more analysis will be discussed here. Biophysical techniques such as the Langmuir Trough is used for stability measurements which monitors changes to a monolayer's surface pressure upon NP interaction. Furthermore, Brewster Angle Microscopy (BAM) employed to visualize changes to the lateral domain organization. Results show preferential interactions of NPs with different lipid groups that is also dependent on the monolayer fluidity. Furthermore, results show that the film stability upon compression is unaffected, but there are significant changes in the lateral domain organization of the lung surfactant upon NP addition. This research is significant in the field of pulmonary drug delivery. It is shown that NPs within a certain size range are safe for the pulmonary route, but little is known about the mode of interaction of those polymeric NPs. Moreover, this work will provide additional information about the nanotoxicology of NPs tested.

**Keywords :** Brewster angle microscopy, lipids, lung surfactant, nanoparticles

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