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Historical perspective

Effects of nanoparticles on the mechanical functioning of the lung

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ABSTRACT

Nanotechnology is a rapidly expanding field that has very promising applications that will improve industry, medicine, and consumer products. However, despite the growing widespread use of engineered nanoparticles in these areas, very little has been done to assess the potential health risks they may pose to high-risk areas of the body, particularly the lungs. In this review we first briefly discuss the structure of the lungs and establish that the pulmonary surfactant (PS), given its vulnerability and huge contribution to healthy lung function, is a mechanism of great concern when evaluating potential nanoparticle interactions within the lung. To warrant that these interactions can occur, studies on the transport of nanoaerols are reviewed to highlight that a plethora of factors contribute to a nanoparticle's ability to travel to the deep regions of the lung where PS resides. The focus of this review is to determine the extent that physicochemical characteristics of nanoparticles such as size, hydrophobicity, and surface charge effect PS function. Numerous nanoparticle types are taken into consideration in order to effectively evaluate observed consistencies across numerous nanoparticle types and develop general trends that exist among the physicochemical characteristics of interest. Biological responses from other mechanisms/components of the lung are briefly discussed to provide further insights on how the toxicology of different nanoparticles is determined. We conclude by discussing general trends that summarize consistencies observed among the studies in regard to physicochemical properties and their effects on monolayer function, addressing current gaps in our understanding, and discussing the future outlook of this field of research.

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1. Introduction

Characterized as any form of particulate matter whose size falls between 1 and 100 nm, nanoparticles (NPs) possess many unique properties and characteristics that often cannot be exploited at the macroscopic level. For this reason, these particles continue to attract great

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interest from science and industry who have already begun engineering them for countless applications. In light of these emerging nanotechnologies, NPs are rapidly becoming more and more prevalent and this has sparked concerns regarding the potential health implications they may pose. This is because despite their growing, widespread use in industrial processes and consumer products, to date, the health risks associated with nanoparticle (NP) exposure have not been thoroughly investigated. This lack of understanding is cited as one of the top ten critical topic areas of the Centers for Disease Control and Prevention (CDC) of the U. S. Department of Health and Human Services regarding nanotechnology [1]. Due to the very small size of NPs, they are often prone to being swept up into the air and dispersed as an environmental pollutant, which puts the lungs at high risk of potential exposure as a site for NP interactions. Studies on the transport of NPs in the lungs have demonstrated that NPs are capable of dispersing to the deepest regions of the lung, to vital mechanisms such as the PS. Given the complexity and crucial function of PS in regulating healthy lung function, there is a great need to better understand the potential interactions between PS and various types of NPs. Work that has been done in this area so far suggests that NP characteristics such as size, surface charge, and hydrophobicity are critical factors regarding the extent of PS impairment. The focus of this paper is primarily on these physicochemical qualities as we seek to evaluate both how and to what extent key NP properties affect PS.

2. Structure of the respiratory system

The human respiratory system, tasked with supplying oxygen to blood, is comprised of the nasal cavity, pharynx, trachea, bronchi, bronchioles, alveolar ducts, and alveolar sacs [2]. Each component of the overall system is equipped with characteristic cells and mechanisms highly specialized to make a unique contribution to the overall system. The trachea, bronchi and bronchioles make up the "human airway" comprised of an estimated 23 to 32 generations or branches that culminate in the alveoli [2]. While the surface area of the inner lung "peripheral region" spans more than 100 m^2, the human airway consists of only a few square meters but is lined with many different cell types such as epithelial, goblet, secretary, ciliated, and basal cells each adapted to carry out a specific function for their given compartment [2]. From the bronchi of the upper airway through the bronchioles, epithelial cells form a gradually receding lining along the walls of the airway while goblet and secretary cells coat this lining in a protective viscous mucus layer whose thickness also recedes with increasing airway depth [2]. Comprised of proteins, glycoproteins, inorganic salts, lipids and water, the produced mucus filters matter from the conducted air and is transported up the airway to the pharynx by ciliated cells for disposal [2]. Bronchioles gradually narrow to become terminal/respiratory bronchioles marking the beginning of the respiratory zone [2]. The "respiratory zone" is also referred to as the alveolar region where both the alveolar ducts and sacs, are lined with alveoli that supply oxygen to the blood as the alveolar sacs fill with conducted air [2]. The alveoli that coat the surface of the alveolar region are blanketed in a thin layer of PS which serves to reduce the surrounding surface tension and provide a physical boundary to protect alveoli from collapse and particle interaction. Unlike the upper airways, the alveolar region is void of ciliated cells and is instead patrolled by macrophages that phagocytize any insoluble particles that deposit (Fig. 1) [2].

3. Transport of nanoaerosols in the respiratory system

Using our current knowledge of respiratory structure, researchers have begun studying how various NPs are transported throughout the respiratory system as well as identifying the key factors involved. Transport of nanoaerosols plays a crucial role in determining specifically what respiratory system mechanisms are at risk of interaction with NPs, to what extent they will be exposed, and whether particles would be capable of translocating to other parts of the body. A more developed understanding of this process is a first step in providing researchers with answers to questions regarding the feasibility of NP interactions with different mechanisms such as PS and whether the extent of exposure warrants further investigation into the effects of these potential interactions. Research in this area, focused primarily on understanding regional

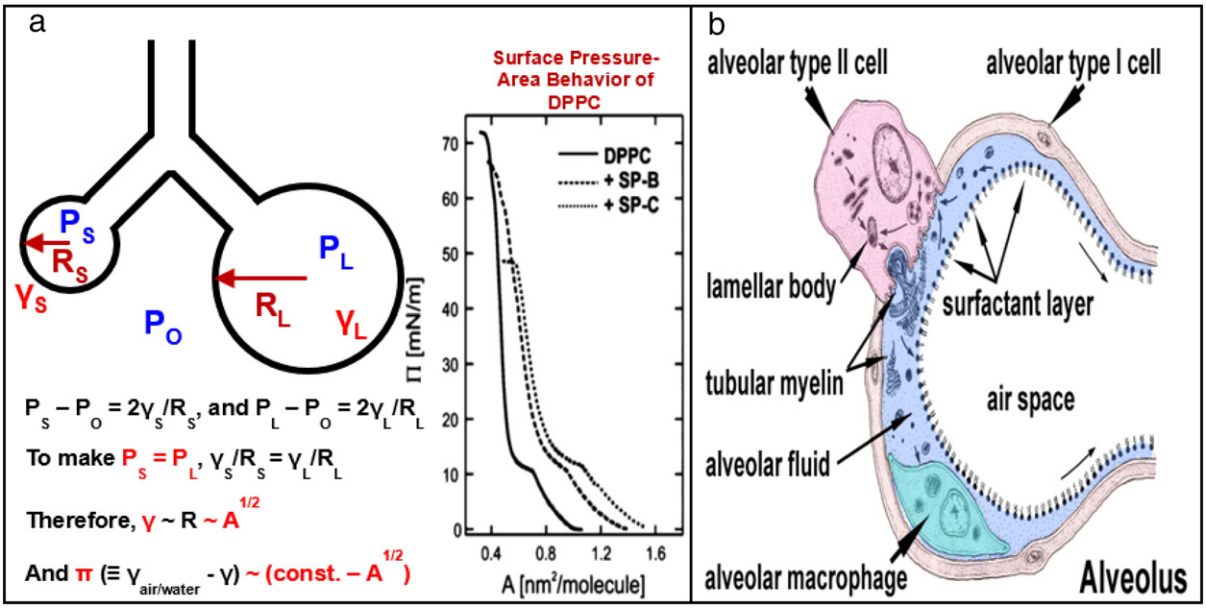

Fig. 1. Fig. 1a demonstrates the pulmonary surfactant function of maintaining low surface tension by describing its behavior using the Young–Laplace Equation (lines 1 & 2). From this equation we get the relationship that surface tension is proportional to the square root of the alveoli area (line 3). Line 4 demonstrates the common method of evaluating surface tension through the use of a new variable surface pressure (π) that can be plotted as a characteristic isotherm by taking the difference between the surface tension of a pure air/water interface (constant) and the square root of alveolar area. Isotherm taken from [9]. Fig. 1b is a useful diagram in visualizing the physiological structure of alveoli and the location of pulmonary surfactant (taken from Physiologynotes.com).