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Inhalation of nanoplatelets – Theoretical deposition simulations

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Abstract

Primary objective of the contribution was the theoretical prediction of nanoplatelet deposition in the human respiratory tract. Modeling was founded on the hypothetical inhalation of graphene nanoplatelets (GNP) measuring 0.01 and 0.1 μm in thickness and adopting a projected area diameter of 1–30 μm. Particle uptake was assumed to take place with inhalation flow rates of 250, 500, 750, and 1000 cm^3 s^{-1}, respectively. For an appropriate description of pulmonary particle behavior, transport of GNP in a stochastic lung structure and deposition formulae based on analytical and numerical studies were presupposed. The results obtained from the theoretical approach clearly demonstrate that GNP with a thickness of 0.01 μm deposit in the respiratory tract by 20–50%, whereas GNP with a thickness of 0.1 μm exhibit a deposition of 20–90%. Larger platelets deposit with higher probability than small ones. Increase of inhalation flow rate is accompanied by decreased deposition in the case of thin GNP, whilst thicker GNP are preferably accumulated in the extrathoracic region. Generation-specific deposition ranges from 0.05 to 7% (0.01 μm) and from 0.05 to 9%, with maximum values being obtained in airway generation 20. In proximal airway generations (0–10), deposition is increased with inhalation flow rate, whereas in intermediate to distal generations a reverse effect may be observed. Health consequences of GNP deposition in different lung compartments are subjected to an intense debate.

Inhalation von Nanoplättchen – Theoretische Depositionssimulationen

Zusammenfassung

Primäres Ziel des Beitrages war die theoretische Prädiktion der Deposition von Nanoplättchen im menschlichen Respirationstrakt. Das zugehörige Modell gründete auf der hypothetischen Inhalation von Graphen-Nanoplättchen (GNP) mit einer Dicke von 0,01 und 0,1 μm und einem Durchmesser der projizierten Fläche von 1 bis 30 μm. Für die Teilchenaufnahme wurden jeweils inhalative Flussraten von 250, 500, 750 und 1000 cm^3 s^{-1} angenommen. Zur geeigneten Beschreibung des pulmonalen Teilchenverhaltens fanden eine stochastische Lungenstruktur sowie auf analytischen und numerischen Studien basierende Depositionsformeln ihre Anwendung. Die aus der theoretischen Näherung gewonnenen Resultate geben klar zu erkennen, dass GNP mit einer Dicke von 0,01 μm im Respirationstrakt zu 20 bis 50% abgelagert werden, GNP mit einer Dicke von 0,1 μm hingegen eine Deposition von 20 bis 90% aufweisen. Größere Plättchen zeigen eine höhere Depositionswahrscheinlichkeit als kleine. Eine Erhöhung der inhalativen Flussrate bewirkt eine Reduktion der Deposition von dünnen GNP, wohingegen dickere GNP zu vermehrter extrathorakaler Ablagerung tendieren. Für einzelne Luftwegsgenerationen prädizierte Depositionswerte schwanken zwischen 0,05 und 7% (0,01 μm)

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bzw. zwischen 0,05 und 9% (0,1 μm), wobei Maximalwerte jeweils in Generation 20 auftreten. In proximalen Luftwegsgenerationen (0-10) besteht eine positive Korrelation zwischen Deposition und inhalativer Flussrate, während in mittleren und distalen Generationen der umgekehrte Effekt zu beobachten ist. Gesundheitliche Auswirkungen der Ablagerung von GNP in verschiedenen Lungenregionen werden im Detail diskutiert.

Keywords: Graphene nanoplatelets, Deposition, Model simulation, Human respiratory tract, Stochastic lung structure, Clearance

Schlüsselwörter: Graphen-Nanoplättchen, Deposition, Modellsimulation, Menschlicher Respirationstrakt, Stochastische Lungenstruktur, Clearance

1 Introduction

Previous studies could demonstrate that carbon nanotubes (CNT), representing graphene sheets rolled up to cylinders of variable length, may be easily taken up into the human respiratory tract and may deposit in the bronchial and alveolar lung compartments [1–4]. Although no irrevocable proof with regard to health implications of inhaled CNT has rendered hitherto, these nanoscale particles are assumed to act as disease-causing agents that are among other responsible for inflammatory reactions and, in the worst case, the initiation of malignant transformations [5–8].

In material industry graphene sheets are not exclusively used for the production of CNT, but are also further processed to single- and multi-layer platelets with rigid or flexible shape. According to electron-microscopic investigations graphene nanoplatelets (GNP) usually adopt diameters ranging from 5 to 30 μm, whereas their thickness varies between several nanometers in the case of one-layer particles and 100 nm in the case of multi-layer particles (Fig. 1a, b) [9–11]. Although such highly specific nanomaterials usually remain limited to production areas, which are strictly isolated from the environment, they might be released accidentally and might come into contact with the population. However, any information on the inhalation toxicity of GNP may be evaluated as rather limited so far [9,10]. Sanchez and coworkers [9] computed the deposition fraction of GNP ranging from 0.001 to 100 μm in diameter in the nasopharyngeal, tracheobronchial, and alveolar region. The authors came to the conclusion that GNP bear the potential for a substantial deposition throughout the respiratory tract. Respective calculations carried out by Sturm [2–4,12,13] largely support these results, but additionally suggest that particle deposition is increasingly relocated to more distal lung compartments in case of enhanced inhalation flow rates.

Previous studies could demonstrate that long and thin fibers, which have penetrated to the distal lung, may escape clearance by macrophages, because the phagocytes fail to fully engulf the highly anisometric particles. This phenomenon commonly results in frustrated phagocytosis and inflammation [14,15]. According to *in vitro* examinations with variably sized GNP also platelet-shaped particles reaching the alveolar region due to their extreme thinness undergo an attempted uptake by macrophages. Similar to the fibrous materials frustrated phagocytosis, inflammation, and failed clearance may emerge resulting in enhanced translocation of GNP to the pleural space [10].

In the present contribution aerodynamic behavior and deposition of inhaled GNP are subject to a detailed description. It is to be shown that platelet-shaped particles partly behave differently with respect to spheres and fibers of similar size. Since theoretical studies on nanoplatelets are still rather scarce, the study may be regarded as one of the first investigations providing a detailed insight into this essential topic. Possible health consequences of GNP deposition will be submitted to a brief discussion.

2 Materials and methods

2.1 Theoretical approximation to GNP aerodynamics

As demonstrated by numerous previous studies with experimental and theoretical orientation, inhaled anisometric particles (i.e., particles with at least one dimension clearly exceeding the others) are characterized by an aerodynamic behavior within the tracheobronchial and alveolar structures which significantly differs from the aerodynamics of spheres [1–5,12,13,16]. Numerical simulations purporting the pulmonary transport of fibrous and tubular particles yielded evidence that inhaled air passing the bronchial tubes features a parabolic velocity profile (highest velocity in the center, lowest velocity at the margins) that results in specific fluiddynamic forces and torques exerting on the particular bodies. In consequence of that, extremely elongated particles undergo rotation enhancing their probability to hit the bronchial wall. In more distal airways, where air flow largely proceeds in laminar fashion ($Re \ll 1$) and fluid shearing becomes a subordinate effect, particles tend to align parallel to the streamlines [1–5,17]. Aerodynamic behavior of thin platelets presents as more complex than that of fibers insofar as fluiddynamic torque affects