

The proposal to select MWCNT as the Poison of the Month came from the Working Group on Inhalation Toxicology

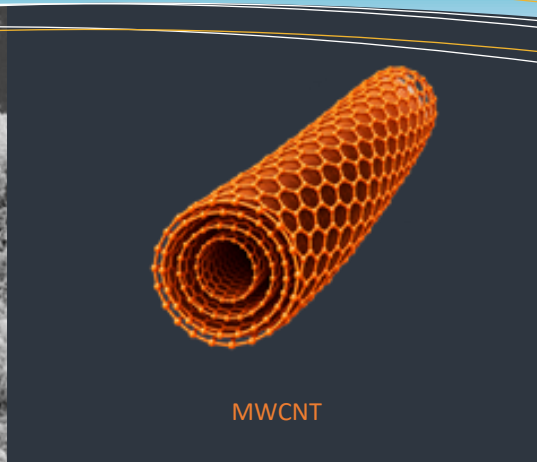
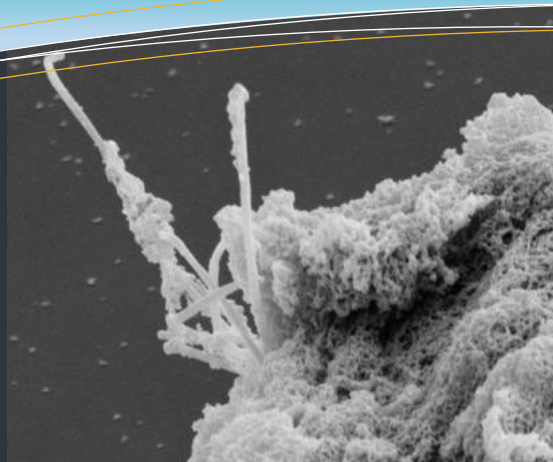
... because MWCNT clearly show that the toxicity of fibrous substances is not determined by chemical composition alone.

CNT and carbon fibers

Despite their similar names, CNT and conventional carbon fibers used in composites differ considerably in their dimensions and properties. Industrially produced carbon fibers typically have diameters of several micrometers (10^{-6} m) and are not per se respirable in their original form. CNT, in contrast, are in the nanometer range (10^{-9} m) and, due to their small diameter, may penetrate deep into the lung.

Under certain conditions, however, carbon fibers may also release relevant fiber fragments. Under mechanical or thermal stress, certain pitch-based fibers in particular may split longitudinally. This can generate thin, respirable fragments with critical fiber dimensions, which at higher concentrations also appear to have weak carcinogenic effects.

For assessment, a distinction must therefore be made between the original carbon fiber and released respirable fragments. Their hazard, however, is very likely considerably lower than that of MWCNT.



MWCNT

MWCNT – when shape determines hazard

Carbon nanotubes (CNT) are tubular carbon structures with diameters in the nanometer range. Depending on their structure, they consist of a single wall (single-walled CNT, SWCNT) or several concentric walls (multi-walled CNT, MWCNT). Their high mechanical strength at low weight and their electrical and thermal conductivity make them useful in batteries, electronics and composites. Their broad technical use raises the question of whether CNT may be released and inhaled during manufacture, processing or recycling. This is particularly relevant for biopersistent CNT, which may remain in tissue for extended periods after uptake.

Toxicological studies consistently show that CNT can exert asbestos-like effects due to their fibrous shape. Very thin fibers may penetrate deep into the lung. Above a certain length, complete uptake by macrophages may fail. This “frustrated phagocytosis” promotes persistent inflammatory responses and is considered a key mechanism of fiber toxicity. Rigidity and biopersistence are also critical, i.e. prolonged tissue residence when such fibers can neither be degraded nor cleared.

This applies to MWCNT that are long, straight or needle-like, and rigid. In a two-year rat study, four MWCNT types were examined against amosite asbestos after a single intraperitoneal injection. All MWCNT types induced mesotheliomas, i.e. malignant tumors of the pleural serosa, which so far have been observed exclusively after asbestos exposure. Tumors occurred early and frequently with straight MWCNT of mean diameters 62 and 85 nm (10^{-9} m), whereas more curved and thinner MWCNT produced weaker or delayed effects. In some MWCNT groups, tumor incidence exceeded that in the asbestos control group. However, carcinogenic potency cannot be compared directly because substantially higher numbers of MWCNT fibers were administered.

To better characterize carcinogenic potential, follow-up long-term studies examined whether the asbestos-like effect is lost with decreasing diameter and rigidity. Earlier studies had shown that very thin, flexible CNT are more



Why the inflammation does not resolve

To investigate in more detail how MWCNT may contribute to long-term lung damage, a total of 41 cell types and states, including alveolar and airway epithelial cells, macrophages, monocytes and fibroblasts, were analyzed for changes in gene activity following exposure to different carbon-based nanomaterials. Single-cell RNA sequencing showed that rigid MWCNT induced a characteristic pattern of epithelial and macrophage damage as early as twelve hours after exposure. So-called alarmins were released, i.e. endogenous danger signals from damaged cells that trigger inflammatory responses. These included the interleukins IL-33 and IL-1 α , important signaling proteins of the immune system. Fibroblasts were also involved early in the inflammatory network. In additional longitudinal studies, the inflammatory response persisted until day 28 after MWCNT exposure. At the same time, the pool of alveolar macrophages remained reduced and was not fully restored by recruited monocytes. This suggests a possible transition from acute cell damage to persistent inflammation.

readily taken up by macrophages and transported onward through pulmonary clearance.

MWCNT with mean diameters of about 10 and 20 nm showed no clear carcinogenic effect. At about 30 nm, there were indications of weak carcinogenic potential. The findings suggest a transition range between 20 and 30 nm, without defining a generally applicable threshold.

The lower effect of very thin MWCNT may be related to their lower flexural rigidity and thus easier uptake by macrophages. Yet diameter alone is not decisive. To test whether extremely thin, flexible fibers, figuratively more like spaghetti than rigid needles, are less critical, SWCNT were also examined. Surprisingly, these very thin individual fibers formed rope-like bundles that became more rigid as a unit and showed a weak carcinogenic signal.

These findings underline the complexity of CNT hazard assessment and demonstrate that the interplay of exposure, length, morphology, diameter, rigidity, biopersistence and bundle formation is decisive for their toxicological effects. For effective health protection, these material-specific properties must therefore be considered in the risk assessment of CNT-containing products and applications, together with the question of whether respirable fibers may be released under realistic conditions.

By Ute Haßmann

Literature and links:

- [The carcinogenic effect of various multi-walled carbon nanotubes \(MWCNTs\) after intraperitoneal injection in rats - PMC](#)
- [Impact of carbon-based fibers morphologies on their carcinogenic potential | Particle and Fibre Toxicology | Springer Nature Link](#)
- [Toward a ToxAtlas of Carbon-Based Nanomaterials: Single-Cell RNA Sequencing Reveals Initiating Cell Circuits in Pulmonary Inflammation | ACS Nano | ACS Publications](#)
- [Cell circuits underlying nanomaterial specific respiratory toxicology | bioRxiv](#)
- [BAuA - Aufsätze - Investigation of the Tendency of Carbon Fibers to Disintegrate into Respirable Fiber-Shaped Fragments - Bundesanstalt für Arbeitsschutz und Arbeitsmedizin](#)
- [Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study | Nature Nanotechnology](#)
- Abbildung: Elektronenmikroskopische Aufnahme „frustrane Phagozytose“ des MWCNT NM-401 durch NR8383 Rattenalveolarmakrophagen. im Rahmen des Projekts FP 474 der Deutschen Gesetzlichen Unfallversicherung e.V. (DGUV) als Kooperation des „Chemistry and Center for Nanointegration Duisburg-Essen (CeNIDE), University of Duisburg-Essen“ und dem Institut für Prävention und Arbeitsmedizin der DGUV Institut der Ruhr-Universität Bochum (IPA).

