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TITLE: STRUCTURAL DEFECTS PLAY A MAJOR ROLE IN THE ACUTE LUNG TOXICITY OF MULTIWALL CARBON NANOTUBES: TOXICOLOGICAL ASPECTS

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ABSTRACT: Experimental studies indicate that carbon nanotubes (CNTs) have the potential to induce adverse pulmonary effects, including alveolitis, fibrosis, and genotoxicity in epithelial cells. Here, we explored the physicochemical determinants of these toxic responses with progressively and selectively modified CNTs: ground multiwall CNTs modified by heating at 600 degrees C (loss of oxygenated carbon functionalities and reduction of oxidized metals) or at 2400 degrees C (annealing of structural defects and elimination of metals) and by grinding the material that had been heated at 2400 degrees C before (introduction of structural defects in a metal-deprived framework). The CNTs were administered intratracheally (2 mg/rat) to Wistar rats to evaluate the short-term response (3 days) in bronchoalveolar lavage fluid (LDH, proteins, cellular infiltration, IL-1 beta, and TNF-alpha). The long-term (60 days) lung response was assessed biochemically by measuring the lung hydroxyproline content and histologically. In vitro experiments were also performed on rat lung epithelial cells to assess the genotoxic potential of the modified CNTs with the cytokinesis block micronucleus assay. The results show that the acute pulmonary toxicity and the genotoxicity of CNT were reduced upon heating but restored upon grinding, indicating that the intrinsic toxicity of CNT is mainly mediated by the presence of defective sites in their carbon framework.