127. Acute Toxicity of Boron Nitride Nanotubes In-Vitro and In-Vivo

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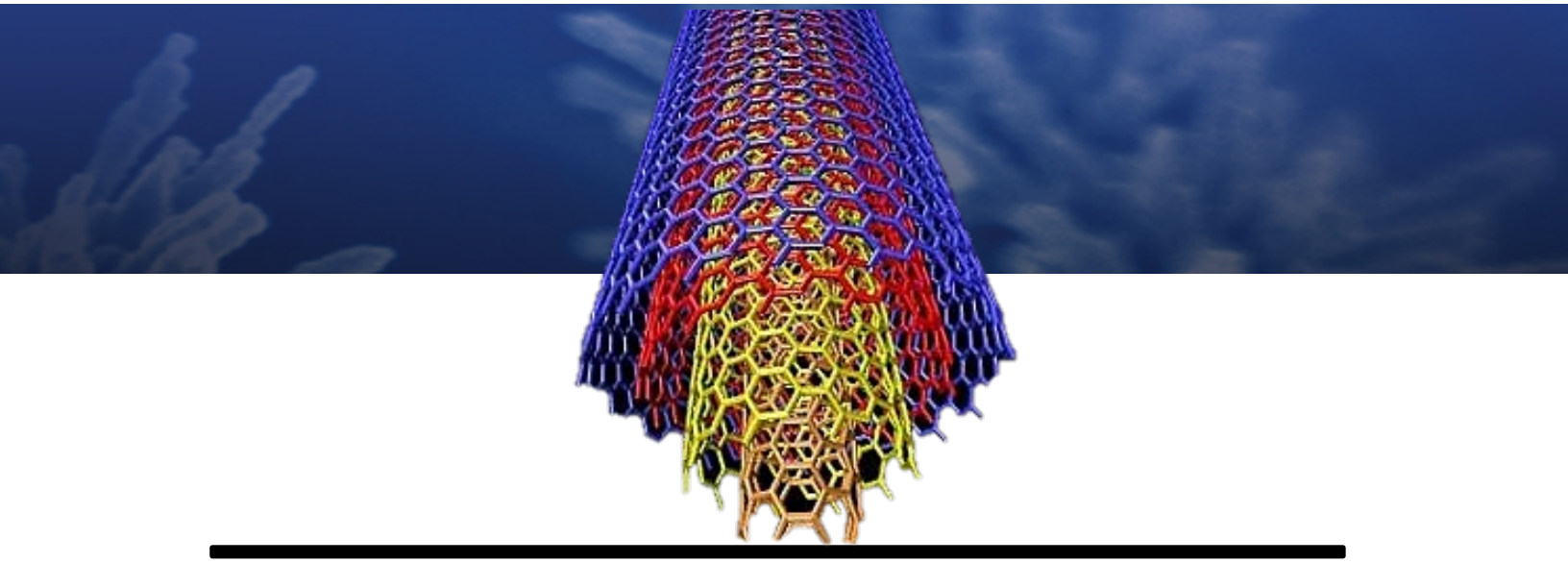
Boron nitride nanotubes (BNNTs) are an emerging engineered nanomaterial that has attracted significant attention due to its superior electrical, chemical, and thermal properties. As the number of applications grow, occupational exposures will likely increase. Since its toxicity is largely unknown, we performed acute in-vitro and in-vivo exposure studies with 13-23 nm diameter x 0.6-1.6 μm length BNNTs. THP-1 wild-type and NLRP3 knockout human monocytic cells were exposed to 0-100 μg/ml and male C57BL/6 mice were exposed by pharyngeal aspiration to 4 or 40 μg BNNTs and sacrificed 4 and 24 h post-exposure. The multi-walled carbon nanotube-7 (MWCNT-7) served as a particle control. In-vitro, BNNT induced a dose-dependent increase in cytotoxicity. This was confirmed in vivo by increased bronchoalveolar lavage levels of lactate dehydrogenase, a measure of lung cytotoxicity. In vitro, lysosomal destabilization, likely a result of particle uptake, was evident by acridine orange staining. Subsequent NLRP3 inflammasome activation was demonstrated by a dose dependent increase in IL-1β protein as well as cathepsin B and caspase 1 activity. Toxicity, and IL-1β production were attenuated in exposed NLRP3 knockout THP-1 cells. In-vivo, elevated pulmonary IL-1β confirmed in vitro findings. Consistent with suspected BNNT-induced inflammation, pulmonary neutrophil influx and inflammatory markers (Il6, Ccl2, Ccl22, Cxcl2) increased in a dose-dependent manner. In general, toxicity induced by BNNTs was less in comparison to MWCNT-7. Taken together, these results demonstrate that BNNTs induce inflammation in vitro and in vivo in part due to NLRP3 inflammasome activation and sub-chronic in vivo studies are warranted.

Keywords: Emerging nanomaterials



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