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Instillations of Different Carbonaceous Nanoparticles Indicate a Surface Area Threshold Dose for Acute Inflammation in Mice

Numerous epidemiological studies have demonstrated an association between elevated levels of ambient particles and morbidity and mortality. High levels of particulate matter seem to be especially harmful to susceptible subpopulations, such as the elderly, patients with preexisting cardiopulmonary diseases, and diabetics. However the toxicity of ambient particulate matter seems to be strongly dependent on specific properties of the contributing particles, in particular their size and chemical composition. Epidemiological and toxicological evidence suggests the sub-100-nm nanoparticles to be more harmful per unit mass than larger particles. Additionally, different PM sources, like vehicles, oil or coal combustion, and soil, differ in the level of noxious effects caused. Hence investigations relating mortality to source-specific PM concentrations have revealed significant associations between mortality and traffic or coal combustion, but not to oil combustion or solid factors.
Our study was aimed at a quantitative comparison of the acute adverse effects of different types of carbonaceous nanoparticles at a dose range that causes a moderate inflammatory response in lungs. Further on we related the inflammatory effects to physical/chemical particle properties.
Six different particle types with a primary particle size from 10 to 50nm and specific BET-surface areas of 30 to 800m^2/g were used: two pigment blacks of different size (PrintexG and Printex90), two flame soot particles with different organic content (SootL and SootH), one spark generated (ufCP) and the reference diesel exhaust particles, SRM1650a (DEP). To characterize the acute inflammatory events in the lungs, BALBc/J mice were instilled with 5, 20 and 50 µg of each particle type. Bronchoalveolar lavage was analyzed 24 hours after instillation for the influx of inflammatory cells and the level of several proinflammatory cytokines.
Within the investigated nanoparticles ufCP proved to be the most active species. Consequently ufCP instillation caused at a dose of 5µg/mouse the same grade of inflammatory response as 50µg PrintexG or DEP. At respective mass-doses, the investigated particles caused detrimental effects ranked in the following order: ufCP > SootL ≥ SootH > Printex90 > PrintexG ≥ DEP. Relating the inflammatory effects to the particle characteristics - organic content, primary particle size or specific surface area - demonstrates for particle surface area the most obvious dose response. Below a instilled particle surface area of 20 cm^2, no inflammatory reaction could be observed.
Our study suggests the BET surface area as a valuable reference unit for the assessment of causative detrimental health effects for carbonaceous nanoparticles. Additionally, our data show the existence of a threshold for the particle surface area at an instilled dose of about 20cm^2, below of which no acute proinflammatory responses could be detected in mice.

back to index