Assessing the environmental effects of nanomaterials – dose metrics considerations

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“Bridging nanoEHS Research Efforts”

Questions to be addressed in Session 3

- What metrics are most scientifically accurate when relating dose to response in toxicity assessments?
- How are dose-response data best extended to determining environmental concern concentrations?
- Dose metrics are commonly reported as mass dose
- However, other dose metrics such as surface area dose or particle number dose have also been mentioned...

Physicochemical characteristics and biological reactivity

Nanomaterial source (manufacture, use, disposal, accidental release...)

Fate of NM in the environment
Interactions with other constituents and effects on bioavailability

Approaches

- What species?
- Endpoint – (mode of action?)
- Reported units – mass, surface area, particle number, ...
- Acute/chronic
- Media composition – fresh/salt water; pH, OM, etc...
- Exposure conditions – temperature, light, shaking,...
- Feeding/not feeding
- Bioaccumulation
- Population studies
- Food chain studies

same mass concentration (1 ppm)
Types of approaches

Surface area and surface atoms

Smaller particles have larger surface area per equivalent mass

<table>
<thead>
<tr>
<th>Diameter</th>
<th>Surface area</th>
<th>% atoms at surface</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 µm</td>
<td>0.03 m²/g</td>
<td>0.001 %</td>
</tr>
<tr>
<td>10 nm</td>
<td>286 m²/g</td>
<td>10.5 %</td>
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</table>

Surface area and inflammation

For relatively low toxicity particles (TiO₂ etc) there is a straight line relationship between surface area and lung inflammation. Highly pathogenic particles with a highly reactive surface (eg quartz), are more inflammmogenic in this model.

Surface area and inflammation

Relating the inflammatory effects to the particle characteristics: organic content, primary particle size, or specific surface area demonstrates the most obvious dose response for particle surface area. This study suggests that the surface area measurement developed by Brunauer, Emmett, and Teller (BET) is a valuable reference unit for the assessment of causative health effects for carbonaceous NPs.

Surface area and inflammation

Mortality of mass dose in 96h acute tests with micro and nano sized particles of carbon black (top) and silver (bottom)

Stoeger et al. 2006. Instillation of Six Different Ultrafine Carbon Particles Indicates a Surface Area Threshold Dose for Acute Lung Inflammation in Mice. EHP 114; 328-333.

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Particles used in these experiments

CB: micro (260 nm) and nano-sized (14 nm)
(8m$^2$/g) (254m$^2$/g)

Ag: micro (0.6-1.6 µm) and nano-sized (35 nm)
(1.2m$^2$/g) (50m$^2$/g)

Mortality as a function of surface area dose

Cumulative moulting as a function of surface area dose

Conclusion from this study?

Assessing toxicity – comparing mass dose with surface area dose...

Pseudokirchneriella subcapitata exposed to silica particles (12.5, 27 nm and < 62 um) for 72 hrs


EC$_{20}$ sig. different when treatments are compared as mass concentration
PARTICLE TYPE DEPENDENT

EC$_{20}$ NOT sig. different when treatments are compared as surface area concentration
SURFACE AREA DEPENDENT

Assessing toxicity – comparing mass dose with surface area dose...

Daphnia magna exposed to CeO$_2$ particles (14, 20 nm, 29 nm and bulk) for 21 days

Van Hoecke et al (2009)

• Pattern was different for the different particles when assessed as mass concentration.
• No differences between the different particles found when surface area concentration was used
Summary

- A range of physico-chemical characteristics influence nanomaterial toxicity
- The receiving environment affects fate, bioavailability and effects
- Assay preparation and conditions, as well as reporting of any observed effects need to be considered carefully
- Surface area and particle number dose metrics may be provide an interesting perspective when interpreting and reporting results from hazard studies
- A major issue to consider is how to measure accurately surface area and particle number in environmental matrices

**Important question**

- What reliable measures exist for the accurate measurement of surface area and/or particle number in environmental matrices?

**Challenges**

- BET is a method developed by Brunauer, Emmett and Teller for measurement of specific surface area and pore sizes of dry powders by gas sorption under high vacuum conditions
- BET measurements may not be accurate even in dry samples given that results depend on displacement of gas and their reproducibility will depend on assay conditions; BET is more appropriate for materials with homogeneous surfaces
- ESA (Envelope Surface Area Analyzer)? The BET technique gives total surface area including that within the particles (if porous), while the ESA gives the surface area on the exterior of the particles, which is used to calculate the average particle size.
- Visual images can be used to estimate surface area
- The specific surface area (SSA) measured by BET in a dry sample may not coincide with the apparent SSA in aqueous dispersion, especially for aggregating particles (Waychunas et al. 2005), although other methods for aqueous SSA may be used such as coulometric titrations and nuclear magnetic resonance (NMR) measurements (Washton et al. 2008; Yukselen and Kaya 2006). The calculation of SSA is further complicated by the effect of shape and porosity on the SSA calculation.

In: Ju-Nam et al (submitted to Nanotoxicology).

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