Nanotoxicology: The Effect of Nanoparticles to Health & Environment

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• **Exposure assessment:** Dose-Metric  Number, Surface area, Mass?

• **Health effects in humans:** Cardiovascular/autonomic response

• **Health effects in experimental systems:** Cardiovascular effects of nanomaterials

• **Safe by Design:** Surface Modification affects uptake of materials into cells and inflammatory response
Exposure assessment

Dose-metrics for exposure to nanoparticles
Workplace exposure to alumina nanoparticles

Fig. 5 Temporal variations in total particle concentration at the packaging location: (a) number concentration (NC) and surface area concentration (SAC); (b) mass concentration (MC).
Table 6  Correlations between mass-, number- and surface concentrations for all samples (n = 878) \(^a\)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Respirable MC(_{100–1000}) nm</th>
<th>NC(_{20–1000}) nm</th>
<th>Active SAC(_{10–1000}) nm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respirable MC(_{100–1000}) nm (mg m(^{-3}))</td>
<td>1.000</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>NC(_{20–1000}) nm (10(^5) cm(^{-3}))</td>
<td>0.361(^b)</td>
<td>1.000</td>
<td>—</td>
</tr>
<tr>
<td>Active SAC(_{10–1000}) nm (μm(^2) cm(^{-3}))</td>
<td>0.666(^b)</td>
<td>0.823(^b)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

\(^a\) NC: number concentration; MC: mass concentration; SAC: surface area concentration. \(^b\) \(p < 0.01\).
Minglan Xishowedng .Meibian Zhang et al. concluded

- Number Concentration and Surface Area Concentration metrics may be distinct from Mass Concentration

- Number Concentration and Surface Area Concentration metrics might be more appropriate for characterizing exposure to airborne nanoparticles.
Health effects in humans

Cardiovascular or autonomic nervous effects of nano-scaled titanium dioxide particles in humans
Heart rate variability (HRV)

- The time- and frequency- domains of HRV are widely used noninvasive and quantitative markers for characterization of the sympathetic and parasympathetic components of the cardiac autonomic nervous system (Zareba et al. 2001)
Previous epidemiological studies have shown the association of declines in HRV with ambient particulate air pollution exposure (Luttmann-Gibson et al. 2010; Park et al. 2005) and occupational particulate exposure (Magari et al. 2001).
Health effects in experimental systems
Possibility of effects of nanomaterials on cardiovascular system

PM2.5 • • • Almost particles are deposited in the respiratory area and phagocytosed by macrophages.

Nanoparticles • • • Particles of less than 34 nm can pass through the blood-air barrier.

ZnO nanoparticles enhanced the migration capacity of monocytes into the media.

Effects of nanoparticles on modified LDL uptake in macrophages

ZnO nanoparticles increased modified LDL uptake in THP-1 monocytes/macrophages.

Safe by Design
SiO₂ NPs

- 25 nm SiO₂ NPs
- Fluorescent (Rhodamine labeled) – red NPs
  - Excitation: max at 550 nm
  - Emission: max at 580 nm

Neutral surface charge
–OH functionalization

Positive surface charge
–NH₂ functionalization

Negative surface charge
–COOH functionalization

Neutral surface charge
–NH₂ functionalization

Excitation and emission wavelengths of Rhodamine-SiO₂ NPs
Mice exposure

8 weeks old mice (C57BL6J) NPs dispersed in water Pharyngeal aspiration 24h 0, 40, 200 μg per mouse

BALF recuperation Collection of organs

Total/differential cell count Protein level Cytokine secretion
Surface modification affects
• Uptake of nanomaterials into cells
• Inflammatory response

→ Knowledge about the relationship between surface property and inflammatory response would be useful to design "safer" nanomaterials.
Summary

• Number concentration/surface area correlates well and might be a good metric for nanoparticle exposure.

• Heat rate variability might be useful to reveal cardiovascular/autonomic effects of nanoparticles in humans.

• In vitro system with monocyte is useful to evaluate cardiovascular effects of nanomaterials. (Zinc oxide /migration capacity of monocytes, uptake of modified LDL into monocytes/macrophages. Single/double carbonnanotubes /adhesion ability of monocytes to endothelial cells)

• Surface modification of silica nanoparticles affects uptake of particles into macrophages and neutrophils and thereby migration of neutrophils.
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