

TEM study of ret lung intratracheally instilled of metal oxide nanoparticles

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Industrial applications of nanoparticles were increasing in many fields recently. Particles less than 100nm with one of three dimensions were defined as nanomaterials. However, the toxicity of these nanoparticles for the human was not clear, so the toxicity study of nanoparticles is important. In this paper, intratracheal instillation studies of metal oxide nanoparticles using rats, and TEM observations of lung tissues were performed. The NiO, TiO₂, CeO₂, and ZnO nanoparticles were examined as metal oxide nanoparticles. The nanoparticles were suspended with 0.4 ml distilled water, and 0.2 mg (0.8 mg/kg) or 1 mg (4 mg/kg) of each metal oxide nanoparticles was intratracheally instilled once to rats (Fisher 344 male rats, 12 weeks old). The negative control groups received distilled water. Animals were dissected at 3 days, 1 week, 1 month, 3 months, 6 months, and 12 months after the instillation. Lung tissues after the instillation tests were observed by TEM. The lung tissues were fixed using a perfusion system using a 4% [paraformaldehyde](#) solution, and were then post-fixed using a 1% osmium tetroxide solution. They were subsequently dehydrated in ethanol, followed by embedding in epoxy resin. Ultrathin sections were cut with a diamond knife using microtomy. Thin sectioning specimens were stained with a 2% uranyl acetate solution and a mixed solution of 0.3% lead nitrate and 0.3% lead acetate, all at room temperature. TEM observation was performed at an accelerating voltage of 80kV.

In TEM images of lung tissue in high dose instillation groups of all metal nanoparticles 3 days later, large mounts of black particle aggregates are observed in macrophage. NiO, TiO₂, CeO₂, and ZnO particles are taken up as larger aggregates in phagosomes. NiO, TiO₂, and CeO₂ particles are observed in macrophage 3 months later, however, ZnO particles are not observed in macrophage. Water solubility of ZnO particle is high, so it seems that ZnO particles are dissolved and elements are translocated. After 6 months, accumulation of alveolar macrophage taken up nano-particles is observed in NiO and CeO₂ instillation groups. In TiO₂ instillation group, a small amount of TiO₂ is observed in the alveolar macrophages, however most of the alveolar macrophages are not containing TiO₂. We think that clearance of instilled NiO and TiO₂ particles is occurred. As NiO is observed more frequently in macrophages compared with TiO₂ after 6 months, it seems that clearance of NiO is more delayed than that of TiO₂. Retention on nanoparticle in lung tissue is toxic potential, so we think the intratracheal instillation test is useful as a toxicological assessment of nanoparticles.