

## Coincidental study of inhalation and intratracheal instillation for hazard assessment of nanoparticles

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For assessing the inhalation toxicity of nanoparticles, inhalation study and intratracheal instillation study were generally performed. Although inhalation study is gold standard as we all known, it takes much time and effort. Instead, many intratracheal instillation studies were performed which has advantage of being able to assess several materials in a short time. However there are not enough evidences that the data in the intratracheal instillation studies reflect the harmful effect of chemicals. Therefore, in this research, we performed an intratracheal instillation study and an inhalation study of the same material, nickel oxide nanoparticle, at almost the same dose to rat lung and compared the results of the two methods.

Inhalation study: Male Fisher 344 rats were exposed to NiO nanoparticles at 3 concentrations, 0,  $1.65 \pm 0.20$  and  $0.32 \pm 0.07$  mg/m<sup>3</sup> for 4 weeks. At 3 days, 1, 3 months after the inhalation, each 10 rats of both groups were dissected.

Intratracheal instillation study: 0, 0.2 mg, 1 mg of NiO nanoparticle suspended in 0.4 ml distilled water were intratracheally instilled into Fischer 344 male rat's lung. At 3 days, 1 week, 1, 3, 6, 12 months after the instillation, each 10 rats were dissected.

After collecting broncho-alveolar lavage, dissected lungs from each 5 rats of all groups were used for determination of NiO amounts in lungs. Lungs were acid-digested with microwave and the Ni concentration in completely digested solution was determined by ICP-AES. And some part of bronchoalveolar lavage fluid (BALF) was used for NiO determination. And the number of PMN was also counted in BALF.

The determined amounts of NiO in rat lungs of all groups at 3 days after the treatment are shown in Table. The amounts of NiO in lung at 3 days after the inhalation were almost the same with that at 3 days after 0.2 mg instillation.

Lung weight and the number of PMN in BALF are also shown in Figure 1 and 2. Lung weights and the PMN number of two inhalation groups and two instillation groups increased compared with control groups. Lung weight and PMN in BALF of both high concentration-inhalation group and 0.2 mg instillation group, in which NiO amounts in lung are the same, increased similarly although the time difference exists.

Our results suggested that both inhalation study and instillation study show the similar inflammation at almost same lung dose. Further research is continued.

Table NiO amounts in rat lung

	NiO amount in lung ( $\mu$ g)
Inhalation:	
Low concentration	$40 \pm 2.4$
High concentration	$132 \pm 9.9$
Intratracheal instillation	
0.2 mg instillation	$136 \pm 6.5$
1 mg instillation	$738 \pm 50$

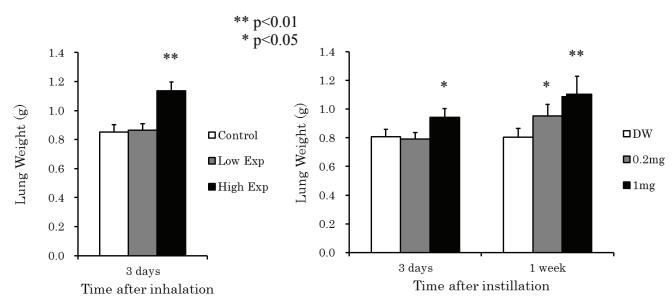


Figure 1. Lung weight of the two methods.

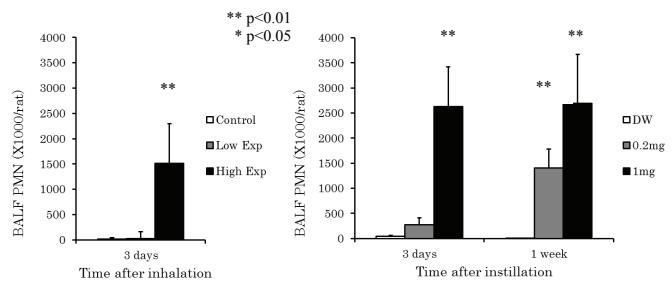


Figure 2. PMN in BALF of the two methods.

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