CEFIC-LRI N1 Project: ORAL TOXICITY OF A SYNTHETIC AMORPHOUS SILICA (SAS) IN RATS

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Background

The systemic availability of nanoparticles after oral uptake is often discussed as an additional, nanospecific toxic potential. As NM-200 is an amorphous silica regularly used in the food sector it was decided to investigate the oral exposure path in addition to inhalation as the most relevant exposure at workplaces.

Objectives

- To evaluate the possible toxicity of Synthetic Amorphous Silica (NM-200) after oral administration (gavage) in rats for 28 days (+ additional 14-day recovery period)
- To investigate the biokinetics of NM-200 by determination of the silicon ion concentration in various organs following oral uptake.

Methods

- *Test item:* NM-200, a precipitated synthetic amorphous silica used in the food sector and delivered by the EU JRC repository of nanomaterials (for details of properties see poster board 459)
- *Animals:* Male Wistar rats [strain: Crl: WI(WU)], approx. 8 weeks old at study start
- *Conduct of study:* According to OECD Guideline 407: Repeated Dose 28-day Oral Toxicity Study in Rodents (October 03, 2008)
- *Test item formulation:* A suspension of NM-200 in 0.5 % methylhydroxypropylcellulose/ deionised water was prepared fresh daily.
- *Administration of test item:* Oral gavage of 7.5 ml/kg/day over 28 days

Endpoints

- Hematology & Clinical Chemistry
- Gross Pathology and Histopathology
- Locomotor Activity & Functional Observational Battery (FOB)
- Silica concentration was determined by chemical analytics in liver, kidney, and blood (ICP-MS).
- Silica particles were analysed in liver, kidney, and mesenterial lymph nodes (spot checks with transmission electron microscopy - TEM)

Table 1 Study Design (according to OECD 407)

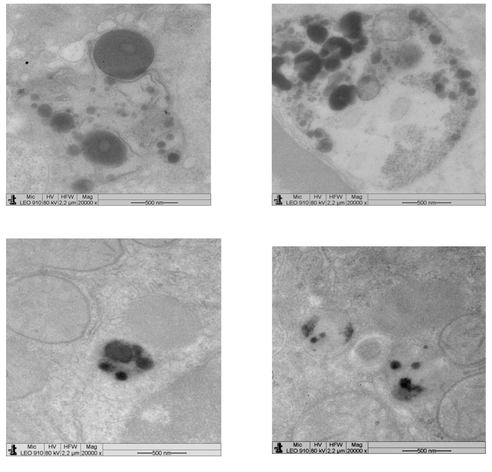
Group	Daily Treatment Amorphous Silica mg/kg bw
1 Control (vehicle)	-
2 NM-200 low	100
3 NM-200 mid	300
4 NM-200 high	1000
5 Control (vehicle) recovery	-
6 NM-200 high recovery	1000

Results

Table 2 Study results for various endpoints investigated

Endpoint	NM-200 Low 100 mg/kg b.w.	NM-200 Mid 300 mg/kg b.w.	NM-200 High 1000 mg/kg b.w.
Body weights	-	-	-
Food consumption	-	-	-
Organ weights	-	-	-
Haematology & Clinical chemistry	-	-	-
Histopathology	-	-	-
OECD Guideline 407			NOAEL
Toxicokinetics	Chemical analysis: No treatment-related changes Ion concentrations in kidney, liver and blood were comparable (control vs. NM-200 high dose)		
TEM	TEM: Granular structures detectable in cytoplasm		
OECD 407 + additional parameters			NOAEL

- No significant effects detected



Figures 1-4: TEM photographs from mesenterial lymph nodes (top) and liver (bottom), each taken from control (left) or NM-200 high dose group (right)

The granular structures measured only few nanometer. However, these structures did not have the shape or appearance of amorphous material such as amorphous silica.

Conclusions

→ **Synthetic Amorphous Silica did not cause any substance-related effects in doses of up to 1000 mg/kg b.w. after oral exposure for 28 days in male Wistar (WU) rats.**

→ **The highest dose tested (1000 mg/kg BW) was determined as the NOAEL in this study.**

→ **Translocation of particulate NM-200 from the GI tract or systemic availability of dissolved NM-200 was not detected.**

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