

Comparative Solubility of Nanoparticles and Bulk Oxides of Magnesium in Water and Lung Simulant Fluids

Gunjan Gakhar¹, John A. Pickrell¹, Sigrifido D. Castro², Kenneth J. Klabunde³, Emily Hayden¹, Frederick W. Oehme¹, Larry E. Erickson²
¹Comparative Toxicology Laboratories, ²Chemical Engineering, and ³Chemistry, Kansas State University, Manhattan, KS 66506-5705 USA

ABSTRACT

Nanoparticles, < 100 nanometers, can clear airborne smoke particles from the air. Small particles inhaled can deposit in the deep lung, evade phagocytosis and move to the interstitial space of the lung. If insoluble, nanoparticles can remain in the interstitial lung space as a chronic source of irritation and potential injury. Because nanoparticles have greater amounts of their mass on the surface, we hypothesized that dissolution of particles of nanomaterials would be more rapid than conventional dust particles. We investigated the solubility and the rate of dissolution of oxides of magnesium (MgO). We compared the relative solubility of magnesium (nanoactive™ MgO (NATM™MgO) and nanoactive™ MgO plus (NATM™ MgO plus) (NanoScale Materials Inc, Manhattan, KS) to that of conventional macrocrystalline MgO (MC MgO). These materials were added to three 1 liter acid washed glass beakers and the contents continuously stirred by magnetic teflon stirring bars. Solvents were deionized water, Hank's Balanced Salt Solution (HBSS; Sigma-Aldrich) and Dulbecco's Modified Eagle's Medium (DMEM) with low glucose (DMEM, Invitrogen). Dissolved magnesium was measured using ICP-AES; Accuris-141, Fisons Instruments, Beverly, MA). Short-term (20 minute) solubility of all 3 oxides of magnesium was correlated to the bicarbonate concentration of simulant fluids (p < 0.001): DMEM >> HBSS > Distilled water. The results suggest that the dissolution would be relatively rapid for the MgO particles deposited in deep lung that completely avoided macrophage phagocytosis and moved to the interstitial portion of the lung. Risks of health effects would be minimal. Nanomaterials of MgO dissolved in only slightly greater amounts than did conventional MgO. Supported by the Department of Defense, US Marine Corps, Quantico, VA through subcontract from M2 Technologies.

INTRODUCTION

Nanoparticles less than 100 nanometers, used to clear airborne smoke, can deposit in the deep lung, evade phagocytosis and move to the interstitial space of the lung. If insoluble, nanoparticles can remain in the interstitial lung space as a chronic source of irritation and potential injury.

A comprehensive review of the literature revealed important properties of inhaled nanoparticles relating them to health effects to be small microcrystalline size, very small particle size, and biopersistence.

Single- and multiple-walled carbon nanotubes (CNT) have all of these characteristics and cause inflammation and fibrosis.

Ultrafine particles of titanium dioxide (TiO₂) have small microcrystalline structure (21 nm) and bio-persistence (insolubility). These particles cause inflammation and fibrosis in lung minces vs. TiO₂ with larger crystalline structures of the same chemical that have minimal effects.

Urban operations non-lethal weapon techniques do not use CNT or ultrafine titanium dioxide because of these health implications

NanoActive® MgO has only micro-crystalline size, This MgO lacks the very small particle size (Aerodynamic Diameter [AD] ~15,000 nm)

Thus, these MgO nanoparticles, although they are active have minimal potential for health effects unless this study reveals significant biopersistence.

HYPOTHESIS

Because nanoparticles have greater amounts of their mass on the surface, investigators hypothesized that

- dissolution of particles of nanomaterials would be more rapid than conventional dust particles, AND
- dissolution of particles would be more rapid in fluids with higher bicarbonate contents.

This result would reduce their potential for health effects still further because clearance would be rapid and persistence in lungs minimal

METHODS

We investigated the solubility and the rate of dissolution of 25 – 100 mg/100 ml of oxides of magnesium (MgO).

We compared the relative solubility of magnesium (nanoactive™ MgO (NATM™MgO) and nanoactive™ MgO plus (NATM™ MgO plus) (NanoScale Materials Inc, Manhattan, KS) to that of conventional macrocrystalline MgO (MC MgO).

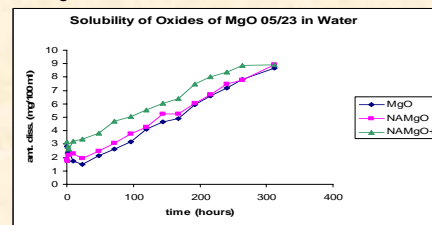
These materials were added to three 1 liter acid washed glass beakers and the contents continuously stirred by magnetic teflon stirring bars.

Solvents were deionized water, Hank's Balanced Salt Solution (HBSS; Sigma-Aldrich) and Dulbecco's Modified Eagle's Medium with low glucose (DMEM, Invitrogen).

Dissolved magnesium was measured using Ion Coupled Plasma Atomic Emission Spectroscopy (ICP-AES); Accuris-141, Fisons Instruments, Beverly, MA).

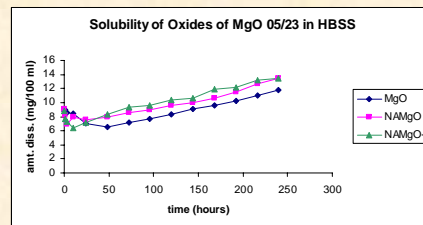
RESULTS

Effect of Time and Fluid simulating Lung Epithelial Fluid on MgO dissolution



Solubility of MgO in water – initial MgO concentration 100 mg/100 ml. Each line is an average of 3 trials. There was minimal difference in solubility in distilled water between conventional MgO and nanoactive MgO

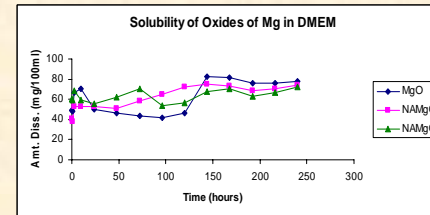
Early solubility was ~25% of final solubility. Atmospheric CO₂ may have contributed to the increasing dissolution with time



Solubility of MgO in Hank's Balanced Salt Solution (HBSS) – initial MgO concentration 100 mg/100 ml. Each line is an average of 3 trials. There was minimal difference in solubility in HBSS between conventional MgO and nanoactive MgO

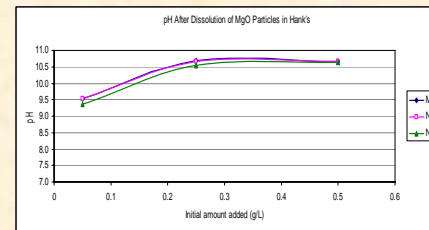
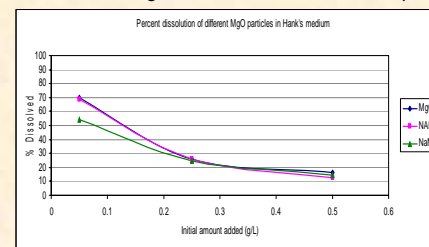
Early solubility was ~70% of the final solubility. This fluid models pulmonary epithelial lining fluid (ELF) at the end of inspiration.

HBSS dissolved ~20% of the MgO dissolved in DMEM, a lung simulant fluid with a higher bicarbonate concentration (35 vs 370 mg/100 ml bicarbonate).



Solubility of MgO in Dulbecco's Modified Eagle's Medium (DMEM) – initial MgO concentration 100 mg/100 ml. Each line is an average of 3 trials. There was minimal difference in DMEM between conventional MgO and nanoactive MgO. >90% of solubility of MgO in Dulbecco's minimal essential medium (DMEM) occurs in the first few minutes.

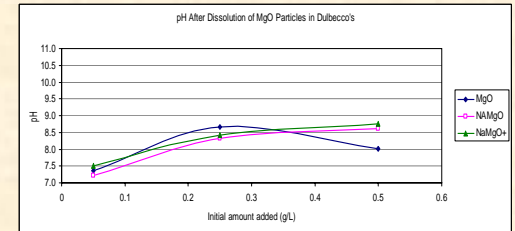
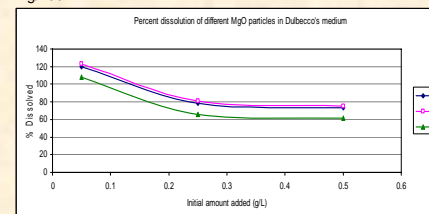
Peak short-term 10-20 minute solubility and pH of different concentrations of MgO in Hanks Balanced Salt Solution (HBSS)



Percent Solubility of MgO in HBSS increased to 50-70% at 5 mg/100 ml. At this concentration pH was 9.3 to 9.5. This increased to 10.5-10.6 at 25 and 50 mg /100 ml.

10-20 minute solubility and pH (next column) of different concentrations of MgO in Dulbecco's modified essential medium (DMEM)

Percent Solubility of MgO in HBSS increased to 50-70% at 5 mg/100 ml.



At 5 mg/100 ml MgO pH was 7.3 to 7.5. This increased to 8.0-8.7 at 25 and 500 mg /100 ml.

* Conventional macrocrystalline- MgO, nanoactive – MgO, nanoactive MgO Plus, NanoScale Materials, Manhattan, KS

These data do not support the hypothesis that micro-crystalline size is an important determinant of dissolution in these epithelial lining fluid (ELF) simulants.

Microcrystalline size was not as important as the bicarbonate concentration of the fluid simulating ELF.

Dissolution was rapid.

The decreasing initial concentration increases the percentage dissolved. All MgO was dissolved in 10-20 minutes with DMEM that simulates ELF at expiration.

DISCUSSION - SUMMARY

Our data do not support the hypothesis that micro-crystalline size is an important determinant of dissolution.

Short-term (10-20 minute) solubility of all three oxides of magnesium correlated well to the bicarbonate concentration of lung simulant fluids (p < 0.001)

These data support the hypothesis that clearance of NanoActive® MgO by dissolution was rapid and biopersistence minimal.

Maximum dissolution was 100% in the 5 mg MgO/100 ml DMEM fluid simulating lung absorption.

Bio-persistence was minimal for the MgO particles deposited in deep lung that completely avoided macrophage phagocytosis and moved to the interstitial portion of the lung.

Lung simulant fluids with 5 mg/100 ml of conventional or nanoactive MgO led to 50-70% solubility in HBSS simulating ELF at the end of inspiration and ≥ 100% in DMEM, simulating ELF at the end of expiration. This amount is nearer the expected deposition at field concentrations.

Possible Mechanism

At the end of inspiration the chemical form of Mg may shift between brucite (magnesium hydroxide) and hydromagnesite (tri magnesium carbonate magnesium hydroxide trihydrate) with solubilities of 1 to 40 mg Mg/100 ml H₂O AND

At the end of expiration this chemical form may shift between hydromagnesite and nesquehonite (magnesium carbonate trihydrate) with solubilities of 30 to 179 mg Mg/100 ml H₂O at expiration with dissolution modeled fluctuation between HBSS and DMEM.

Dissolution more near that at the end of expiration, because of the greater amount of dissolution when magnesium is in the carbonate form.