

# Dissolution rates of five inorganic mine ore inorganic elements in synthetic lung fluid

Inhalation of dust generated in the mining process exposes workers to many health hazards. The inorganic elements nickel, copper, arsenic, cadmium, and lead have been found in some mine ore and have suspected relationships to adverse health effects. Dissolution rates for copper, arsenic, lead, cadmium, and nickel in respirable sized particles of a selected mine ore were determined in synthetic lung fluid at two different pH levels.

Synthetic lung fluid with a pH of 7.2 was used to simulate extracellular lung fluid and synthetic lung fluid with a pH of 4.5 was used to simulate intracellular lung fluid. The synthetic lung fluid samples and quality assurance and quality control samples were continuously agitated for a 25-day period. A ten-milliliter sample was removed from each solution on days 0, 1, 2, 3, 4, 5, 6, 7, 10, 14, 18, 21, and 25. Each sample was analyzed for dissolved nickel, copper, arsenic, cadmium, and lead concentrations using inductively coupled plasma mass spectrometry.

Analytical results show that all inorganic elements investigated dissolved at a higher rate in the 4.5 pH synthetic lung fluid than in the 7.2 pH synthetic lung fluid throughout the 25-day sampling period. In summary, it was observed that the dissolution rates for all inorganic elements in synthetic lung fluid were significantly different in the solutions at the two different pH levels. Maximum concentration of each inorganic element was higher in the 4.5 pH synthetic lung fluid solution.

Results of this study show the five inorganic elements investigated are more likely to dissolve in intracellular lung fluid than in extracellular lung fluid.

**By David S. Adams, Jordan C. Koyle, Leon F. Pahler, Matthew S. Thiese, Rodney R. Larson**

## INTRODUCTION

Exposure to dust generated during various mining processes has been reported to result in acute and chronic

*David S. Adams is affiliated with the University of Utah, United States.*

*Jordan C. Koyle is affiliated with the University of Utah, United States.*

*Leon F. Pahler, PhD, MPH, CAIH is affiliated with the University of Utah, United States (Tel.: 801 585 1032; fax: 801 581 7224; e-mail: [leon.pahler@hsc.utah.edu](mailto:leon.pahler@hsc.utah.edu)).*

*Matthew S. Thiese, PhD, MSPH is affiliated with the University of Utah, United States.*

*Rodney R. Larson, PhD, CIH is affiliated with the University of Utah, United States.*

health related issues, both systemic and localized. Examples of some of the suspected health effects include; lung cancer, respiratory sensitization, and neurological effects.<sup>1</sup> Dissolution of soluble inorganic particles is hypothesized to be necessary for development of some health problems in humans. As such, particle dissolution rates must be sufficient to generate concentrations that activate the body's immune response, and must remain in solution for sufficient time to maintain the development of adverse health effects. Synthetic lung fluid (SLF) procedures have been used to evaluate human exposure to inorganic parameters from various emission sources. The SLF procedure has been used to simulate different conditions in the lung with a solution having a pH of 7.2 to simulate extracellular lung fluid and a pH of 4.5 to simulate macrophage lysosomal fluid (intracellular fluid).<sup>2</sup>

## Examples of other dissolution studies

An investigation to measure dissolution rates and residence times of

silicon dioxide (SiO<sub>2</sub>) particles in SLF within the intracellular or extracellular lung spaces was conducted using SLF solutions having a pH 6.0, pH 6.5, and pH 7.5. This study reported that the optimum SiO<sub>2</sub> dissolution rate occurred at a pH of 7.5 and a particle size of 5 μm and decreased with decreasing pH and increasing particle size.<sup>3</sup> A number of studies have investigated the dissolution rates of beryllium in ores and particles using SLF procedures. One such investigation provided the dissolution rates for beryllium contained in several types of beryllium ores such as bertrandite (Be<sub>4</sub>Si<sub>2</sub>O<sub>7</sub>(OH)<sub>2</sub>). It was concluded that the beryllium in ore materials were more soluble in SLF at a pH 7.2 and 4.5 than beryllium oxide (BeO). This investigation also reported that beryllium hydroxide was more soluble than BeO at both SLF pH levels.<sup>4-7</sup>

## Potential health hazards for inorganic elements evaluated in this study

Cadmium is considered a Group 1 carcinogen by the International Agency

for Research on Cancer. This is due to it causing genotoxic effects in a variety of types of eukaryotic cells, including human cells.<sup>8</sup> The critical health effect of cadmium is renal tubular damage, and the absorption of cadmium in the lungs is 10–50%, while the absorption in the gastrointestinal tract is only a few percent.<sup>9</sup>

Arsenic is also classified by American Conference of Governmental Industrial Hygienists (ACGIH) as an A1 carcinogen and is associated with cancers of the skin, lung, upper respiratory tract and liver.<sup>10</sup> ACGIH also stated that multiple studies linked respiratory arsenic exposure to significantly increased respiratory cancer risk.<sup>10</sup> Dermatological, developmental, neurological, respiratory, cardiovascular, immunological, and endocrine effects have also been associated with arsenic exposure.<sup>10</sup>

Exposure to airborne lead particulates was found to reduce enzyme activity related to heme synthesis as reported in a study by Griffin et al.<sup>11</sup> ACGIH reported that lead has significant toxic effects on many body systems including neural, reproductive and hematological systems.<sup>12</sup>

Exposure to copper dust was determined by ACGIH to be able to cause nasal irritation and can result in perforation of the nasal septum.<sup>13</sup>

Chronic exposure to several airborne nickel compounds has been determined by ACGIH to cause pulmonary inflammation and fibrosis as well as damage to the olfactory epithelium.<sup>14</sup> Several nickel compounds are also listed as an A1 carcinogen (confirmed human carcinogens) by ACGIH.<sup>14</sup>

## METHODS

This study was designed to evaluate the dissolution of nickel, copper, arsenic, cadmium, and lead. The solubility of these inorganic elements was determined in SLF solutions that simulate both the extracellular and intracellular lung fluids. A SLF at a pH of 7.2 has been shown to be representative of extracellular lung fluid and at a pH of 4.5 simulates the intracellular lung fluid, with the exception of enzymes. Control samples used for quality assurance and quality control (QA/QC) purposes for this study included SLF with no added ore and adjusted to each of two pH levels. In addition, samples of the Milli-Q equivalent (deionized and distilled) water, which was used in the preparation of the SLF but without any additives, was also analyzed for QA/QC purposes.

A bulk volume of SLF was prepared using research grade components and separated into three portions; one adjusted to a pH of 4.5, one adjusted to a pH of 7.2, and the third portion left unadjusted. The first two groups of SLF were then used to analyze the dissolution of inorganic elements in the mine ore. The composition of the SLF is shown in Table 1.

The SLF was prepared by combining 2.49 g of ammonium chloride (Fisher Scientific, #A687-500, Pittsburgh, PA), 1.29 g of sodium dihydrogen phosphate monohydrate (Fisher Scientific, #S369-500, Pittsburgh, PA), 0.26 g of sodium citrate (Fisher Scientific, #S279-500, Pittsburgh, PA), 33.9 g of sodium chloride (Mallinckrodt Baker, Inc., #7581, Phillipsburg, NJ), 8.85 g of sodium bicarbonate (Fisher Scientific,

#BP328-500, Pittsburgh, PA), 3.145 g of sodium carbonate (Acros Organics, #419480010, Morris Plains, NJ), 1.8 g of glycine (Fisher Scientific, #BP381-500, Pittsburgh, PA), and 0.126 g of calcium chloride dehydrate (Fisher Scientific, #C69-500, Pittsburgh, PA) to 3 L of Milli-Q equivalent water. The solution was gently agitated until all solids had been dissolved and 12.5 mL of formaldehyde (Fisher Scientific, #BP531-25, Pittsburgh, PA) was added. Milli-Q equivalent water was then added until the total solution volume was 4 L. Carbon dioxide was bubbled through the mixture for approximately 10 min, to produce a mixture mimicking the fluid environment of the lungs. The SLF was then pH adjusted with a 1 M sulfuric acid (H<sub>2</sub>SO<sub>4</sub>) solution (Fisher Scientific, #A300-500, Pittsburgh, PA) or a 1 M sodium hydroxide (NaOH) solution (Mallinckrodt Baker, Inc., #7708-10, Phillipsburg, NJ) to obtain a pH of 4.5 and 7.2. The pH was measured using a pH bench meter (Oakton Instruments 1100, Vernon Hills, IL) that was triple point calibrated using buffer solutions at 4.0, 7.0, and 10.0 (Ricca Chemical Company, Arlington, TX).

Hard rock mine ore originating from a location in the western United States was selected as the source material for use in this study. The mine ore sample was first sent to the ALS Minerals Laboratory located at 4977 Energy Way, Reno Nevada where the ore was ground to 75 microns in size. The 75 micron size ore was further prepared by grinding the ore with a Krupus coffee grinder (KRUPUS Type F203 electric spice and coffee grinder with stainless steel blades, made in China) and a porcelain mortar and pestle (500 mL Cole-Parmer WU-6100-60, Cole-Palmer North America, 625 East Bunker Court, Vernon Hills, Illinois, USA). The resulting ground ore was then sieved through a stainless steel 25 micron and 10 micron U. S. Standard Sieve assembly (Dual Manufacturing Company, Chicago, IL, USA) using a Meinzer II sieve shaker (Meinzer II Sieve Shaker, Humboldt Manufacturing Company). A particle size (diameter) of 10 microns or less was preferred due to the capability of smaller sized particles to reach the alveoli of the lungs when inhaled.

**Table 1. Composition of synthetic lung fluid (SLF) millimolar (mM).**

Chemical species	Concentration (mM)
Na <sup>+</sup>	150.7
Ca <sup>+</sup>	0.197
NH <sub>4</sub> <sup>+</sup>	10
H <sub>2</sub> CNH <sub>2</sub> H (glycine)	5.99
H <sub>2</sub> CO (formaldehyde) methanol solution	67
Cl <sup>-</sup>	126.4
HCO <sub>3</sub> <sup>-</sup>	27
HPO <sub>4</sub> <sup>2-</sup> , H <sub>2</sub> PO <sub>4</sub> <sup>-</sup>	1.2
COH(CH <sub>2</sub> ) <sub>2</sub> (COO) <sub>3</sub> <sup>3-</sup> (citrate)	0.2

After collection of the sieved ore, a particle size distribution was conducted on the resulting mine ore particles using Zeta Phase Analysis Light Scattering (PALS) particle sizing instrument (Brookhaven Instruments Corporation, Holtsville, NY) at the University of Utah's Geology and Geophysics laboratory. A sample of the micronized mine ore was sent to University of Utah's Geology and Geophysics laboratory for aqua regia digestion and analysis by inductively coupled plasma mass spectrometry (ICP-MS) (Agilent 7500ce with a quartz double pass spray chamber, PTFE nebulizer, quartz injector, and Ni cones) to determine the element content. Nickel, copper, arsenic, cadmium, and lead were selected for this investigation due to their presence in the mine ore and known correlation to adverse health effects.

A mass of mine ore of 400 mg with an average effective particle size of 1.1 micron to 1.8 microns was added to six separate containers (500 mL HDPE bottles) containing 500 mL of SLF, 3 of the containers having a pH of 7.2 and 3 containers having a pH of 4.5. 1 container of 500 mL SLF with no mine ore and 1 container of Milli-Q equivalent water were used as QA/QC samples. Resulting sample solutions and QA/QC samples were constantly agitated for 25 days at a constant rate of 100 rotations/min on an open air orbital shaker (Lab Companion SK 600, GMI, INC. Ramsey, MN). The solution temperature was maintained at 22 °C. During the 25 day study, the pH of the sample solutions were measured and adjusted immediately preceding sampling using either a 1 M sulfuric acid solution or a 1 M sodium hydroxide solution to maintain a pH of 7.2 and a pH of 4.5, respectively in order to simulate the pH of human extracellular and intracellular lung fluids. On the following days; 0, 1, 2, 3, 4, 5, 6, 7, 10, 14, 18, 21, and 25 with day 0 being the day the ore was added to the SLF; ten (10) mL aliquot samples were removed from the sample solutions that were stirred using a magnetic stirring bar and stirring platform and from QC samples. Samples were then filtered through a 0.22 µm membrane syringe filter (Fisher Scientific, #09-719-2B,

Pittsburgh, PA) into 20 mL high-density polyethylene storage vials for transport to the analytical laboratory and 5 µL of concentrated nitric acid (Fisher Scientific, #A509-P212, Pittsburgh, PA) was added to each sample for preservation prior to transport to the laboratory for analysis. Sampling began within 5 min of ore addition and occurred at the same time each sampling day. Each filtered sample and QC sample was analyzed three times using ICP-MS for detection and quantification of nickel, copper, arsenic, cadmium, and lead. A 2.0 mL SLF sample was diluted using a 1–10 ratio with Milli-Q equivalent water before ICP-MS analysis was performed for each analysis. Resulting analytical concentrations for nickel, copper, arsenic, cadmium, and lead were then compared to the calibration standards to determine the concentration in milligram/Liter (mg/L). The ICP-MS analytical detection limits for each element in the SLF used in this study are shown in Table 2. The resulting three concentrations from the ICP-MS analyses for each element were averaged according to pH and sampling day. Where concentrations were below detection limit, a quantity of half of the detection limit was used for statistical analysis purposes. This method for adjustments when analytical results are below detection limits is recommended in the literature by Croghan et al.<sup>15</sup> The average concentration results were plotted on graphs and dissolution rates were determined

based on these average results and the time between analyses.

Quality Control (QC) samples for this study included blank samples, certified standard solutions, and SLF with mine ore at different pH levels. Sample results were blank corrected and negative values after blank correction were dropped (2% of total results). Each sample collected was analyzed by ICP-MS in triplicate. Blank samples included the Milli-Q equivalent water used, Milli-Q equivalent water and nitric acid, and SLFs with no added ore, which were analyzed for concentrations of inorganic parameters. All blank samples were analyzed to determine the initial concentration of the inorganic chemicals present to determine if corrections to results were necessary. This was also done to determine if the Milli-Q equivalent water and other materials used in the study may have become contaminated and needed to be replaced. Laboratory ICP-MS control samples included certified standard solutions of inorganic elements at differing concentrations, which were used to prepare ICP-MS instrument calibration curves.

An average dissolution rate was determined for each element in each pH solution in time ranges from day 0 to day 7 and from day 7 to day 25. Day 7 was selected as the cut point because it appeared that the slope began to decrease significantly for most inorganic elements on that day. The dissolution rate was calculated by the sum of the changes in concentration over the time

**Table 2. ICP-MS lower detection limits for individual inorganic elements.**

Nickel	Copper	Arsenic	Cadmium	Lead
0.0003 mg/L	0.0008 mg/L	0.001 mg/L	0.00006 mg/L	0.00006 mg/L

**Table 3. Element concentrations in the 1.7 micron particle size mine ore.**

Nickel	Copper	Arsenic	Cadmium	Lead
105 mg/kg	27,000 mg/kg	10,400 mg/kg	66 mg/kg	1800 mg/kg

**Table 4. Average results for SLF blanks in mg/L (n = 39).**

Nickel	Copper	Arsenic	Cadmium	Lead
0.0007 mg/L	0.0021 mg/L	0.0064 mg/L	<0.00006 mg/L	0.0003 mg/L

**Table 5. Average element concentrations in synthetic lung fluid at pH 7.2 (n = 9 unless otherwise stated).**

Day	Ni (mg/L)	Cu (mg/L)	As (mg/L)	Cd (mg/L)	Pb (mg/L)
0	0.0066 (0.00038) <sup>a</sup>	0.0033 (0.0025)	0.64 (0.13)	$6.8 \times 10^{-5}$ ( $1.8 \times 10^{-5}$ )	0.0073 (0.00098)
1	0.008 (0.0043)	0.0055 (0.0016)	0.71 (0.0016)	$6.1 \times 10^{-5}$ ( $2.0 \times 10^{-5}$ )	0.00052 (0.00051) <i>n</i> = 6
2	0.0090 (0.00024)	0.0078 (0.00062)	0.67 (0.011)	$6.9 \times 10^{-5}$ ( $2.3 \times 10^{-5}$ )	$4.2 \times 10^{-4}$ ( $1.9 \times 10^{-5}$ ) <i>n</i> = 3
3	0.0099 (0.0086)	0.018 (0.0062)	0.68 (0.011)	$5.7 \times 10^{-5}$ ( $2.1 \times 10^{-5}$ )	0.00039 ( $8.9 \times 10^{-5}$ ) <i>n</i> = 6
4	0.010 (0.00017)	0.017 (0.0053)	0.72 (0.018)	$6.1 \times 10^{-5}$ ( $2.4 \times 10^{-5}$ )	0.0010 ( $2.0 \times 10^{-5}$ ) <i>n</i> = 3
5	0.0085 (0.0049)	0.015 (0.0018)	0.66 (0.012)	$4.3 \times 10^{-5}$ ( $2.0 \times 10^{-5}$ )	0.00011 ( $6.6 \times 10^{-5}$ ) <i>n</i> = 6
6	0.0099 (0.00041)	0.018 (0.0013)	0.074 (0.024)	$3.4 \times 10^{-5}$ ( $1.3 \times 10^{-5}$ )	0.00029 (0.00027)
7	0.0096 (0.00029)	0.018 (0.00029)	0.78 (0.046)	$5.0 \times 10^{-5}$ ( $2.4 \times 10^{-5}$ )	0.00035 (0.00037) <i>n</i> = 6
10	0.0099 (0.00037)	0.022 (0.00037)	0.83 (0.038)	$5.7 \times 10^{-5}$ ( $2.1 \times 10^{-5}$ )	0.0016 (0.0043)
14	0.0104 (0.00052)	0.028 (0.00045)	0.87 (0.046)	$8.2 \times 10^{-5}$ ( $1.2 \times 10^{-5}$ )	0.00053 (0.00039)
18	0.0102 (0.0004)	0.030 (0.0014)	0.89 (0.0014)	$7.9 \times 10^{-5}$ ( $6.8 \times 10^{-6}$ )	0.00024 (0.0002)
21	0.0106 (.0003)	0.036 (.0034)	0.99 (.024)	$1.1 \times 10^{-4}$ ( $1.9 \times 10^{-5}$ )	0.0010 (.00037)
25	0.0102 (0.00045)	0.032 (0.0013)	1.0 (0.072)	$5.6 \times 10^{-5}$ ( $2.0 \times 10^{-5}$ )	0.00078 (0.00045)

<sup>a</sup> Standard deviation.**Table 6. Average element concentrations (mg/L) in synthetic lung fluid at pH 4.5 (n = 9 unless otherwise stated).**

Day	Ni (mg/L)	Cu (mg/L)	As (mg/L)	Cd (mg/L)	Pb (mg/L)
0	0.0039 (0.0016) <sup>a</sup>	0.0067 (0.0078) <i>n</i> = 6	1.2 (.35)	0.000409 ( $5.3 \times 10^{-5}$ )	0.0059 (0.0045) <i>n</i> = 6
1	0.0057 (0.00096)	0.0026 (0.0014)	2.0 (0.80)	0.000507 ( $6.3 \times 10^{-5}$ )	0.00087 (0.00039)
2	0.0084 (0.00066)	0.0070 (0.0011)	2.7 (0.70)	0.000625 ( $2.7 \times 10^{-5}$ )	0.00083 ( $4.4 \times 10^{-5}$ )
3	0.010 (0.00043)	0.014 (0.0029)	3.7 (0.33)	0.000659 ( $1.6 \times 10^{-5}$ )	0.0015 (0.00054)
4	0.011 (0.00080)	0.022 (0.0034)	4.3 (0.23)	0.000663 ( $2.2 \times 10^{-5}$ )	0.0042 (0.00092)
5	0.010 (0.00021)	0.025 (0.0030)	4.0 (0.12)	0.000661 ( $3.0 \times 10^{-5}$ )	0.0044 (0.00041)
6	0.012 (0.00013)	0.037 (0.0039)	4.4 (0.073)	0.000730 ( $1.8 \times 10^{-5}$ )	0.0059 (0.0019)
7	0.012 (0.00030)	0.041 (0.0034)	4.6 (0.022)	0.000759 ( $2.0 \times 10^{-5}$ )	0.010 (0.0036)
10	0.012 (0.00014)	0.040 (0.0020)	4.5 (0.11)	0.000767 ( $2.4 \times 10^{-5}$ )	0.0073 (0.00038)
13	0.013 (0.00033)	0.044 (0.0024)	4.6 (0.095)	0.000804 ( $3.7 \times 10^{-5}$ )	0.0084 (0.0015)
18	0.013 (0.00026)	0.046 (0.0025)	4.6 (0.099)	0.000827 ( $4.2 \times 10^{-5}$ )	0.010 (0.0021)
21	0.013 (0.00041)	0.049 (0.0032)	4.8 (0.13)	0.000863 ( $6.2 \times 10^{-5}$ )	0.014 (0.0046)
25	0.012 (0.00010)	0.048 (0.0032)	4.7 (0.021)	0.000869 ( $5.5 \times 10^{-5}$ )	0.016 (0.0049)

<sup>a</sup> Standard deviation.

period and dividing by the length of time considered. Dissolution graphs were created using SAS 9.4 (SAS Incorporated, Cary, NC) to generate a spline with a knot or separation at day 7. A spline is a curve that is generated using a separate equation for each segment with a smooth joint at the knot (in this case day 7).

## RESULTS

The particle size distribution of the ground and sieved mine ore as determined by Zeta PALS particle sizing instrument indicated an average effective particle size of 1.7 micron (geometric mean) with a standard deviation of 1.3. Concentrations of nickel, copper, arsenic, cadmium, and lead in the Milli-Q water samples were below the lower limit of detection (see Table 2 for lower limits of detection).

The ICP-MS instrument inorganic element concentrations reported from the aqua regia digestion of the 1.7 micron particle size mine ore are recorded in Table 3.

The ICP-MS instrument analytical results for the SLF blanks in mg/L ( $n = 39$ ) were averaged and are listed in Table 4. The average cadmium results were below the lower limit of detection.

The average nickel, copper, arsenic, cadmium, and lead analytical results for SLF pH 7.2 and 4.5 over the 26 day sampling period with standard deviation values in parentheses are displayed in Tables 5 and 6 and in graph format (element concentration - y axis and time period - x axis) in Figures 1-5. These results were used to determine the average dissolution rates for nickel, copper, arsenic, cadmium, and lead contained in the hard rock mine ore for days 0 to 7 and 7 to 25. The calculated dissolution rates for each element and time period are displayed in Table 7. Dissolution of nickel, copper, arsenic, cadmium, and lead in micronized mine ore in pH 7.2 and pH 4.5 SLFs over a 25 day time period had the following results. The dissolved nickel average maximum concentration was 23% higher in the 4.5 pH SLF than the maximum concentration in 7.2 pH. The 4.5 pH SLF average maximum concentra-

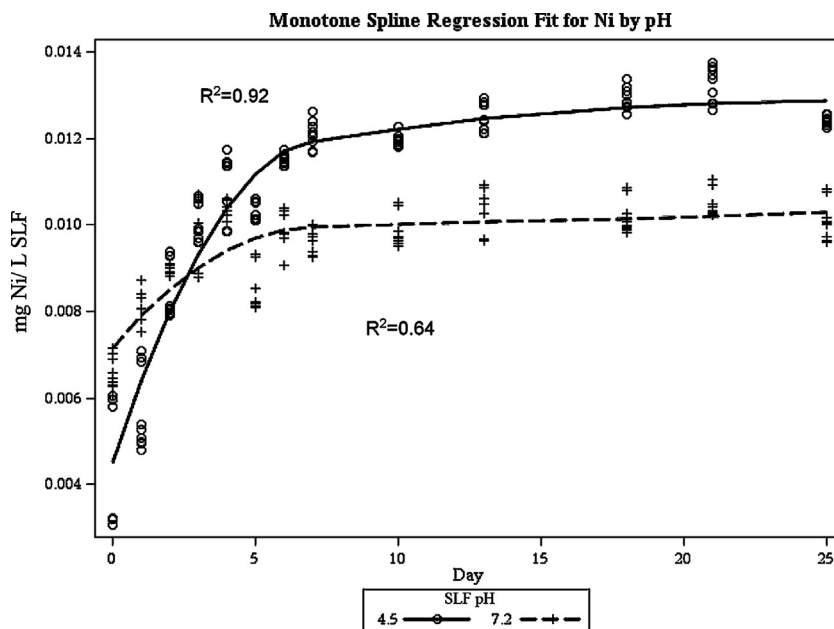


Figure 1. Synthetic lung fluid dissolution results for nickel at pH 4.5 and 7.2.

tion of copper was 36% higher than the maximum concentration in 7.2 pH. The average maximum concentration of arsenic was 380% higher in the 4.5 pH SLF than the maximum concentration in 7.2 pH. In addition, the dissolution concentration of arsenic in the pH 4.5 SLF at day seven was the highest of all

the inorganic elements. Cadmium reached an average maximum concentration of 690% higher in the 4.5 pH SLF than the maximum concentration in 7.2 pH. Finally the lead average maximum concentration was 120% higher in the 4.5 pH SLF than the maximum concentration in 7.2 pH SLF.

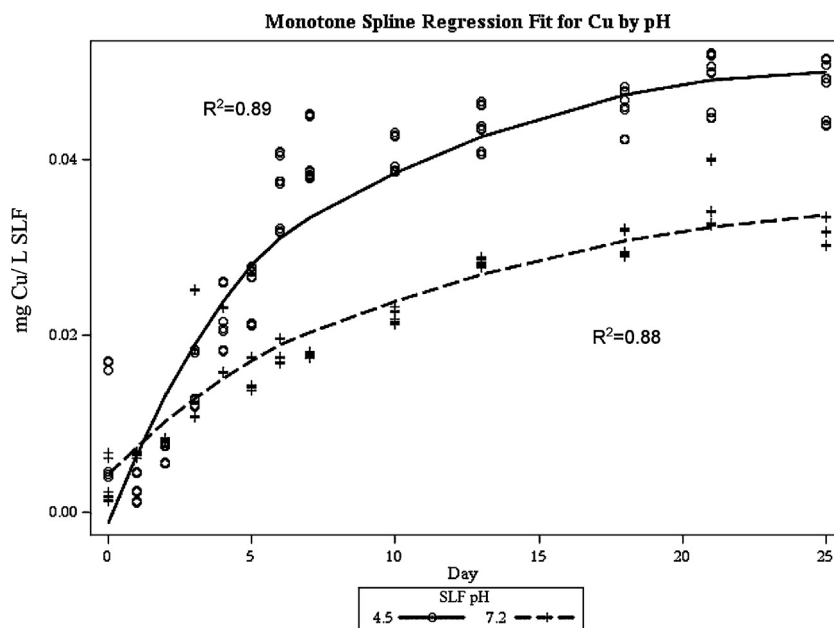
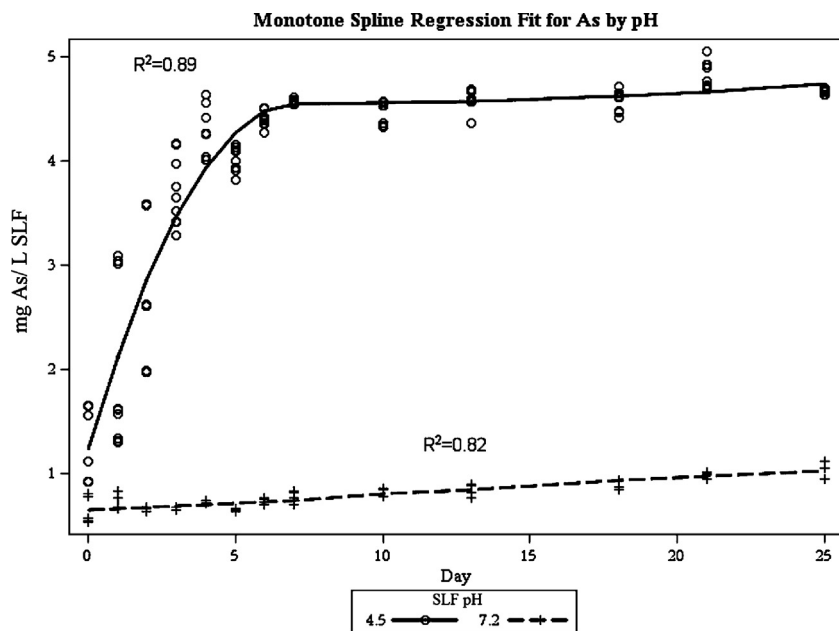


Figure 2. Synthetic lung fluid dissolution results for copper at pH 4.5 and 7.2.

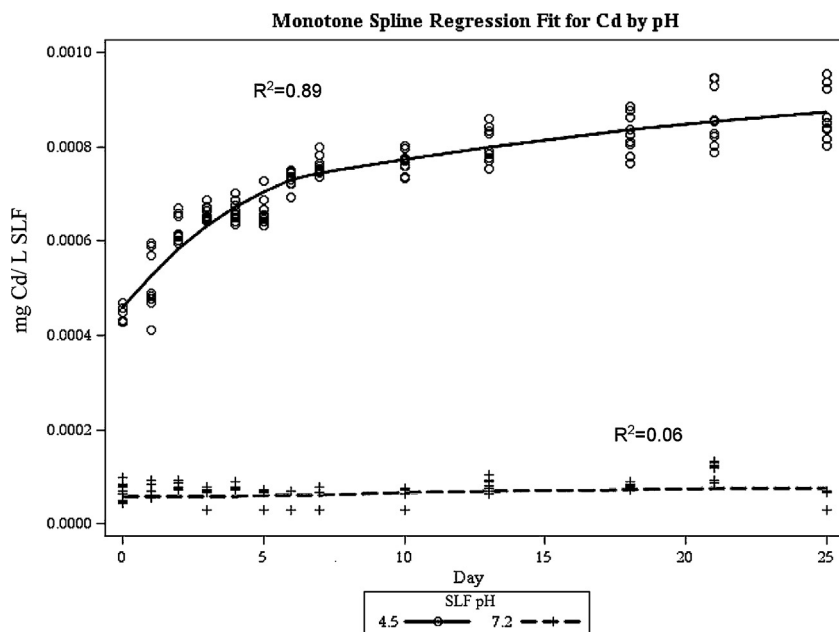


**Figure 3. Synthetic lung fluid dissolution results for arsenic at pH 4.5 and 7.2.**

## DISCUSSION

Croghan et al. found that when the relative number of values below the detection limit was small (below 10%) simple replacement techniques introduce little bias.<sup>15</sup> Thus simple replacement with half the detection limit

is adequate for this study because values below the limit of detection were approximately 2% of the total samples (1170 total samples). Because the number of values below detection in this study was well below 10% (approximately 2%), therefore the method for adjusting the data for use



**Figure 4. Synthetic lung fluid dissolution results for cadmium at pH 4.5 and 7.2.**

in statistical analyses recommended by Croghan et al. was applied as applicable to the data from this study.

The pH of the SLF solutions tended to increase over time. Because the human body would maintain internal conditions, the SLF was adjusted back to the target pH as the body would likely do to maintain conditions.

The results from this study demonstrate that all inorganic elements dissolve more rapidly and reach higher concentrations in the more acidic 4.5 pH SLF. These results suggest that these inorganic elements are more likely to dissolve more rapidly in intracellular lung fluid rather than in the extracellular lung fluid. Copper and nickel were found to be only slightly more soluble in the 4.5 pH SLF than the 7.2 pH SLF (35% and 26% higher concentrations). As presented in Table 7 the average rate of element dissolution was higher in the 4.5 pH SLF from days 0 to 7 than the 7.2 pH SLF. In the 7.2 pH SLF, lead and cadmium had a very low dissolution rates that that could be approximated by a slope of zero, see Figures 4 and 5. These results, when paired with the low concentration of lead and cadmium in 7.2 pH SLF, indicate very low solubility of these inorganic elements in these conditions. Negative rates were calculated for cadmium and lead at 7.2 pH, this was due to low dissolution of these inorganic elements in this environment. The dissolution concentrations fluctuated over time and the average rate was negative over the selected time periods. After day seven the dissolution of nickel, arsenic and cadmium slowed significantly as element concentrations approached equilibrium points. Copper demonstrated a more moderate decrease in dissolution rate after day 7. Lead concentrations at pH 4.5 continued to rise when the last sample was taken on day 25.

It is important to note that the dissolved lead and copper continued to rise throughout the study period. Therefore it is recommended that similar studies in the future involving lead and copper should be carried out for a longer period of time, such as 60 day, to determine a better overall rate and a point of equilibrium for this element.

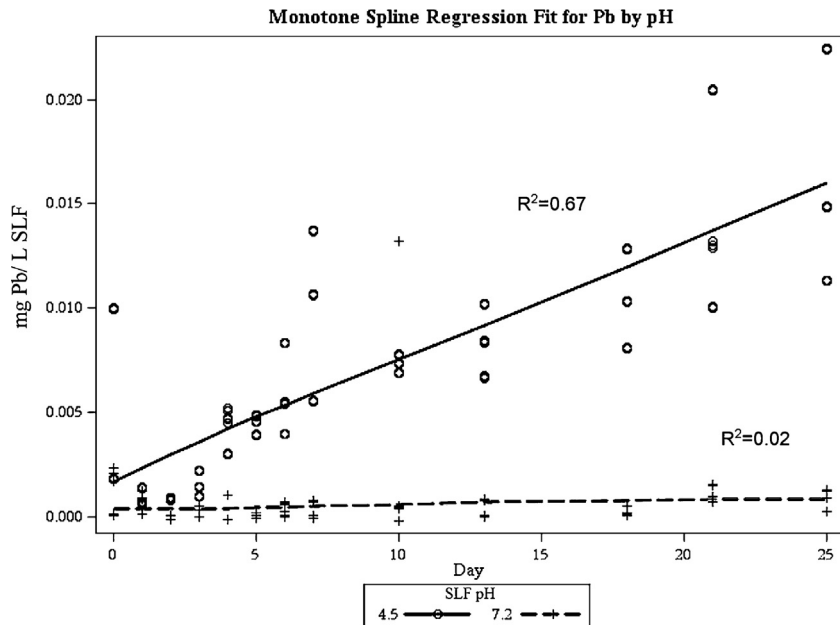


Figure 5. Synthetic lung fluid dissolution results for lead at pH 4.5 and 7.2.

Table 7. Element dissolution rates for two SLF pHs and time periods.

Element/ SLF pH	Dissolution rate for days 0–7 (mg/L)/day	Dissolution rate for days 7–25 (mg/L)/day
Ni/4.5	$4.32 \times 10^{-3}$	$2.71 \times 10^{-5}$
Ni/7.2	$1.17 \times 10^{-3}$	$1.79 \times 10^{-5}$
Cu/4.5	$4.83 \times 10^{-3}$	$4.23 \times 10^{-4}$
Cu/7.2	$2.08 \times 10^{-3}$	$7.80 \times 10^{-4}$
As/4.5	$4.85 \times 10^{-1}$	$5.27 \times 10^{-3}$
As/7.2	$2.03 \times 10^{-2}$	$1.47 \times 10^{-2}$
Cd/4.5	$4.94 \times 10^{-5}$	$6.17 \times 10^{-6}$
Cd/7.2	$9.58 \times 10^{-7}$	$-2.93 \times 10^{-7}$
Pb/4.5	$5.82 \times 10^{-4}$	$3.46 \times 10^{-4}$
Pb/7.2	$-7.46 \times 10^{-5}$	$3.19 \times 10^{-5}$

## CONCLUSION

The dissolved concentration of all inorganic elements, except lead in 7.2 pH SLF, increased over the sampling period, but varied between each element and each of the two pH levels used in this study. However, the concentration of all inorganic elements in SLF significantly differed in the two different pH solutions of SLF. The average rate of element dissolution was higher for days 0 to 7. After day 7 the dissolution rates of nickel, arsenic and cadmium slowed significantly as element concentrations approached equilibrium concentrations. Lead and copper concentrations continued to increase.

Some contamination with certain chemicals of interest to this study was found in the SLF before any ore had been added. Any future studies should use chemicals with even higher purity than reagent or enzyme grade to minimize contamination by inorganic chemicals that could reduce the accuracy of study results.

## ACKNOWLEDGEMENTS

Research reported in this publication was supported by the National Institute of Occupational Safety and Health under award number T42OH008414-08 and training grant number T42/OH008414. Mine ore for this study was provided by a

gold mine company located in the western USA.

## REFERENCES

- Ross, M. H.; Murray, J. Occupational respiratory disease in mining. *Occup Med (Lond)*, **2004**, *54*(5), 304–310.
- Marques,; Margreth, R. C.; Loebenberg, R.; Almkainzi, M. Simulated biological fluids with possible application in dissolution testing. *Dissolution Technologies*, **2011**, *August*, 15–27.
- Larson, R. R.; Story, S. G.; Hegmann, K. T. Assessing the solubility of silicon dioxide particles using simulated lung fluid. *Open Toxicol J*, **2010**, *4*, 51–55.
- Deubner, D. C.; Sabey, P.; Huang, W.; Fernandez, D.; Rudd, A.; Johnson, W. P.; Storrs, J.; Larson, R. Solubility and chemistry of materials encountered by beryllium mine and ore extraction workers: relation to risk. *J Occup Environ Med*, **2011**, *53*(10), 1187–1193.
- Duling, M. G.; Stefaniak, A. B.; Lawrence, R. B.; Chipera, S. J.; Virji, M. A. Release of beryllium from mineral ores in artificial lung and skin surface fluids. *Environ Geochem Health*, **2012**, *34*(3), 313–322.
- Stefaniak, A. B.; Virji, M. A.; Day, G. A. Dissolution of beryllium in artificial lung alveolar macrophage phagolysosomal fluid. *Chemosphere*, **2011**, *83*(8), 1181–1187.
- Huang, W.; Fernandez, D.; Rudd, A.; Johnson, W. P.; Deubner, D.; Sabey, P.; Storrs, J.; Larsen, R. Dissolution and nanoparticle generation behavior of Be-associated materials in synthetic lung fluid using inductively coupled plasma mass spectroscopy and flow field-flow fractionation. *J Chromatogr A*, **2012**, *1218*(27), 4149–4159.
- International Agency for Research on Cancer (IARC). *Cadmium and cadmium compounds*; Beryllium, cadmium mercury and exposure in the glass manufacturing industry. *IARC monographs on the evaluation of carcinogenic risks to humans*; IARC: Lyon, 1993, pp. 119–237.
- Järup, L.; Berglund, M.; Elinder, C. G.; Nordberg, G.; Vahter, M. Health effects of cadmium exposure – a review of the literature and a risk estimate. *Scand J Work Environ Health*, **1998**, *24*(1), 1–51.
- ACGIH. *Threshold limit value documentation*; Arsenic and Its Inorganic Compounds. ACGIH: Cincinnati, OH, 2001.
- Griffin, T. B.; Coulston, F.; Goldberg, L.; et al. *Clinical studies on men*

- continuously exposed to airborne particulate lead, In Griffin, T. B.; Knelson, J. G. (Eds.), *Lead*, Georg Thieme Publishers: Stuttgart FRG, 1975, pp. 221–240.
12. ACGIH. *Threshold limit value documentation*; Lead and Its Inorganic Compounds. ACGIH: Cincinnati, OH, 2001.
  13. ACGIH. *Threshold limit value documentation*; Copper. ACGIH: Cincinnati, OH, 2001.
  14. ACGIH. *Threshold limit value documentation*; Nickel and Inorganic Compounds, including Nickel Subulfide. ACGIH: Cincinnati, OH, 2001.
  15. Croghan, C. W.; Egeghy, P. P. *Methods of Dealing with Values Below the Limit of Detection using SAS*; US-EPA: Research Triangle Park, NC, 2003.