Environmental Science Processes & Impacts

On the bio-accessibility of 14 elements in welding fumes

Journal:	*Environmental Science: Processes & Impacts*
Manuscript ID	EM-ART-09-2018-000425.R2
Article Type:	Paper
Date Submitted by the Author:	29-Jan-2019
Complete List of Authors:	Berlinger, Balazs; National Institute of Occupational Health, Department of Chemical and Biological Working Environment Weinbruch, Stephan; Technical University Darmstadt, Institute of Applied Geosciences Ellingsen, Dag; National Institute of Occupational Health, Zibarev, Evgeny; Northwest Public Health Research Centre Chashchin, Valery; Northwest Public Health Research Centre Chashchin, Maxim; Northwest Public Health Research Centre Thomassen, Y; National Institute of Occupational Health

Environmental significance

In epidemiological studies, welding fume exposure was found to be associated with a number of adverse health effects including cardiovascular, neurological and respiratory effects. Several in vivo and in vitro toxicological studies suggested that soluble metal compounds in WFs may play an important role in the observed adverse health effects. Despite the importance of soluble metal compounds in developing adverse health effects, relatively little work on the solubility of metals in WFs has been carried out, and these studies have focussed mainly on chromium, manganese and nickel. The aim of the present work is to apply a previously developed leaching procedure in an exposure characterization study to obtain a broader overview of the bio-accessible fractions of 14 metals in welding fume samples collected among shipyard welders and welders in a factory producing heavy machinery.

On the bio-accessibility of 14 elements in welding fumes

Balázs Berlinger[1], Stephan Weinbruch[1, 2], Dag G. Ellingsen[1], Evgeny Zibarev[3], Valery Chashchin[3], Maxim Chashchin[3] and Yngvar Thomassen[1]

[1]National Institute of Occupational Health, PO Box 5330 Majorstuen, N-0304 Oslo, Norway

[2]Institute of Applied Geosciences, Technical University Darmstadt, Schnittspahnstr. 9, D-64287 Darmstadt, Germany

[3]Northwest Public Health Research Centre, 2-Sovetskaya 4, St. Petersburg 191036, Russia

Abstract

The bio-accessibility of 14 elements in welding fume particulate matter was investigated in 325 personal air samples collected during welding in two shipyards and one factory producing heavy machinery. The apparent solubility in a synthetic lung lining fluid (Hatch's solution) was used as proxy for the bio-accessibility. The Hatch solubility of the different elements was highly variable with a median < 1% for Al, Fe, Pb, Ti, between 4 and 6% for Co, Cr, Ni, V, W, between 13 and 27% for Cd, Cu, Mn, Zn, and 41% for Mo. For many elements, the solubility was varying over a wide range of several tens of percent. The welding techniques used influenced the solubility of Co, Cr, Cu, Mn and V significantly. The plants investigated (i.e., the welded materials and used electrodes) had a significant influence on the solubility of Co, Cr, Cu, Mn, Mo, V and W. According to principal component analysis (PCA), the variation in solubility can be described by four components, which explain 69% of the variance. The first principal component mostly comprises elements, which can predominantly occur as divalent cations, the second principal component elements often forming oxyanions. The principal components are independent of the absolute value of the Hatch solubility. The

results of PCA indicate that the co-variation of Hatch solubility is mainly controlled by the most soluble compounds in contrast to the absolute value of apparent solubility, which is strongly influenced by the distribution of the elements between compounds with different equilibrium solubility. The observed large variability and the significant differences between welding techniques and plants clearly show that the bio-accessibility cannot be obtained from the literature but has to be studied experimentally at each location of interest.

1. Introduction

Air contaminants emitted from arc welding processes are a complex mixture of gases and solid particles. The polydispersive particulate matter (PM) is formed mainly by evaporation of the consumable electrode, and to a lesser degree from the base metal, followed by rapid condensation and particle growth under supersaturation conditions.[1] Typically, the major mass of welding fume (WF) PM is found in particles with aerodynamic diameters ranging from 0.1 to 1 μm.[1]

The chemical composition of WF PM strongly depends on the welding technique, welding parameters, welding electrode including the flux and base metal composition. X-ray diffraction studies[2-3] revealed a complex phase composition of WF PM with the presence of variable amounts of different spinel group oxides (e.g., magnetite, Fe_3O_4; jacobsite, $MnFe_2O_4$; iron(II) di-manganese(III) oxide, $FeMn_2O_4$), metallic iron (ferrite, α-Fe), potassium chromate (K_2CrO_4) and different fluorides (e.g., sodium fluoride, NaF; calcium fluoride, CaF_2; potassium calcium trifluoride, $KCaF_3$). Studies applying scanning electron and transmission electron microscopy, X-ray photoelectron spectroscopy and secondary ion mass spectrometry revealed core-shell structures of larger (> 100 nm) WF particles. The surfaces of such particles are usually enriched in more volatile elements, like fluorine (F), sodium (Na), potassium (K) and calcium (Ca), while the core mostly consists of metals and metal oxides.[1,5-7]

In epidemiological studies, WF exposure was found to be associated with a number of adverse health effects including cardiovascular,[8,9] neurological,[10,11] and respiratory effects.[12-17]

Several in vivo and in vitro toxicological studies suggested that soluble metal compounds in WFs may play an important role in the observed adverse health effects.[18-24] A recent study showed that circulating leukocytes became impaired following MMA stainless steel (SS) WF exposure.[18] A probable factor in the leukocyte dysfunction could be oxidative stress, which might partly be explained by soluble chromium (Cr) in MMA SS WF. Studies in both rats and mice showed that the soluble fraction of MMA SS WF contributed to pulmonary toxicity.[22,23] However, in the rat study both the soluble and insoluble fractions of the MMA SS WF were required to develop most pulmonary effects, indicating that the responses are not dependent on soluble metal compounds alone. Another study showed that more soluble MMA SS WF had higher cytotoxicity to lung macrophages in rats and had larger effect on their function when compared to less soluble GMA mild steel (MS) and GMA SS WFs.[19] Translocation of manganese (Mn) and Cr from the respiratory tract of rats treated by intratracheal instillation with manual metal arc-hardsurfacing (MMA-HS) WF leading to deposition in other organs was reported by a study in 2010.[21] Increased deposition of Mn was observed in e.g. discrete brain regions, including dopamine-rich areas (striatum and midbrain). MMA-HS WF was observed to be “highly water-soluble” in this study. Mn translocated from lungs of rats to kidney and specific brain regions (olfactory bulb, cortex and cerebellum) after GMA-MS WF inhalation.[20] A previous study showed that Mn deposition in striatum of rats was significantly higher after manganese dichloride ($MnCl_2$) intratracheal instillation compared to less soluble manganese dioxide (MnO_2) treatment via the same route.[24] Other administration routes, however, resulted in approximately similar amounts of

Mn deposited in different organs in case of both $MnCl_2$ and MnO_2. The Mn concentrations in the investigated organs and whole blood were significantly higher in case of exposed rats compared to controls. These results clearly indicate that workplace exposure to soluble Mn compounds poses a higher risk of neurological effects compared to insoluble Mn compounds.

Despite the importance of soluble metal compounds in developing adverse health effects, relatively little work on the solubility of elements in WFs has been carried out, and these studies have focused mainly on Cr, Mn and nickel (Ni). A variety of different solvents were used in previous studies including deionized (DI) water,[21,25-27] ammonium acetate,[3,28] phosphate buffered saline[19,29,30] and lung lining fluid simulants (Gamble's and Hatch's solution)[31]. Hatch's solution as leaching solution and a dissolution time of 24 hours was suggested to be a reasonable choice when investigating bio-accessibility of elements in WFs.[31] The leaching method applied in this study is a static one, using the same volume to each sample regardless of the particulate mass and without agitation of the samples during the incubation period. It might be mentioned that dynamic extraction systems have also been previously applied e.g., to investigate soluble metal components in airborne PM.[32-34] There is no clear evidence, however, that using a dynamic flow through system, normalizing the volume of the leaching fluid or agitation of the tubes during the incubation period give results, which are more realistic, than results gained with the current model system in comparison with the processes in the human body. One clear strength of the model used in this study is the fact that the composition of Hatch´s solution is the most similar to the composition of the lung lining fluid.

The aim of the present work was to apply the previously developed procedure[31] in an exposure characterization study to obtain a broader overview of the bio-accessible element fractions in WF samples collected among shipyard welders and welders in a factory producing heavy machinery. Special emphasis was placed on the variability between different welding techniques and plants.

2. Materials and methods

2.1 Sampling

Welding fume samples were collected in three facilities in St. Petersburg (Russia), two shipyards (plant 1 and 2) and a factory producing heavy machinery (plant 3) among 137 male welders performing manual metal arc (MMA) as well as automatic and semi-automatic metal inert gas (MIG) welding. The base metal was unalloyed structural steel in most of the cases and in some instences corrosion resistant steel was also welded. Eleven different types of welding electrodes were used with varying frequencies and compositions. Most of them had low amount of alloying elements. For example, the Mn content was between 0.6 and 2.2% in the different welding electrodes. Some electrodes contained Cr and Ni up to 19 and 9.8%, respectively. The electrode types and their composition were registered when performing the sampling. These data were, however, not used later because they would make the statistical analysis of the results very complicated. The welding mode, such as current and voltage, the shielding gases and their flows were neither registered or used because of the same considerations.

Personal full-shift sampling was performed in the welders´ breathing zone on two consecutive days. In many cases not only one, but two, in a few cases three or four samples were needed to assess full-shift exposure of one welder. In such cases, sampling cassettes had to be changed in many cases during a full-shift period due to high particle filter load which resulted in reduced flow rates.

Altogether, 325 air samples were collected with Millipore (25 mm) “total” aerosol plastic cassettes (Merck KGaA, Darmstadt, Germany) equipped with 5.0 μm pore-size polyvinyl chloride membrane filters (SKC Ltd., Dorset, UK) mounted underneath the welding helmet in the welders´ breathing zone, as previously described.[35] SKC Sidekick pumps (SKC

Ltd., Dorset, UK) operated at an initial air flow rate of 2.0 L min^{-1} were used. The flow rate drop (typically between 0 and 40%) was considered in the calculation of individual air volumes. The uncertainty of air flow volumes is less than 20%, and influences only air concentration data but not the solubility obtained from leaching experiments. The samples were stored typically several months after collection until they were analysed. According to our previous experiments (data not published), the storage time (from one hour after collection) and conditions (such as temperature) were not affecting the solubility of metal compounds in welding fume samples taken by MMA and MIG welding.

2.2 Gravimetry

For 229 out of 325 filter samples, the collected aerosol particulate mass was determined gravimetrically with a Sartorius Micro model MC5 balance (Sartorius AG, Göttingen, Germany) in a weighing room dedicated to low filter mass measurements, under controlled relative humidity (40 ± 2%) and temperature (20 ± 1 °C) conditions. The balance was calibrated daily. Accuracy and precision of gravimetry were assessed by weighing certified reference masses (19.989 ± 0.030 and 49.953 ± 0.040 mg). The mass detection limits (DLs) calculated as 3 times standard deviation of all field blanks were below 0.01 mg for the filters used in our study.

2.3 Analytical procedures

Sample preparation and leaching experiments were performed with slight modifications as outlined in earlier publications.[31,36] Details are given in the electronic supplementary information.

Element contents of the Hatch soluble (bio-accessible) and Hatch insoluble fractions were determined by an Element2 (Thermo Fisher Scientific Inc., Bremen, Germany) inductively coupled plasma sector field mass spectrometer (ICP-SF-MS) and a Perkin Elmer Optima 7300 (Perkin Elmer Inc., Waltham, MA, USA) inductively coupled plasma optical emission spectrometer (ICP-OES), respectively. The ICP-SF-MS was required for the measurements of the element concentrations in diluted leachates. Both instruments were calibrated with matrix-matched solutions (Hatch´s solution and/or acids). Accuracy was assessed by comparing compositions of realistically exposed welding aerosol filters – obtained by a previously validated method[37] – to the total amounts of elements (Hatch soluble + Hatch insoluble) determined by ICP-SF-MS and ICP-OES. DLs as well as recoveries are listed in the electronic supplement (Table S1).

2.4 Statistical analysis

As a significant fraction of the samples investigated contained values below DL (Table 1), the statistical analysis of solubility consistently followed the recommendations given by Helsel for censored data.[38]

The main focus of our contribution is the Hatch solubility (HS) of WF components which was calculated as the ratio of the mass of the soluble fraction of an element in the WF sample (m_{sol}) and the sum of the mass of the soluble and Hatch insoluble fractions (m_{insol}):

$$HS = \frac{m_{sol}}{m_{sol} + m_{insol}}\,.$$

If both fractions are below DL, no information on the HS is obtained, as HS can vary between 0 and 1. If only one of the two fractions is below DL, the HS is interval censored. For $m_{sol} \geq$ DL and $m_{insol} <$ DL, the following interval is obtained for HS:

$$\frac{m_{sol}}{m_{sol} + DL_{insol}} < HS \leq 1,$$

with DL_{insol} the DL of the Hatch insoluble fraction.

For m_{sol} < DL and $m_{insol} \geq$ DL, HS lies in the following interval:

$$0 \leq HS < \frac{DL_{sol}}{DL_{sol} + m_{insol}},$$

with DL_{sol} the DL of the soluble fraction.

Summary statistics for the whole data set as well as for subgroups (plants and welding techniques separately) was computed using nonparametric survival analysis methods. As the data set consists of interval censored data, the nonparametric maximum likelihood estimate of Turnbull was used to calculate a survival function and to determine quantiles.[39]

Possible influence of plant and welding technique on Hatch solubility (later often referred to as solubility) was investigated with two different approaches: (a) logrank test for interval censored data,[40] and (b) two-way analysis of variance (ANOVA) using ranks.[41,42] In both cases, the data set originally consisting of 325 samples was reduced by eliminating samples with unknown plant (12 samples), and with mixed or unknown welding technique (50 samples). The remaining 263 samples were from three different plants and included three different welding techniques (manual MMA, automatic MIG, semi-automatic MIG). Group comparisons using the logrank test were conducted separately for welding technique and plant. The scores used for group comparison were calculated after Sun and gave a constant weight to all measurements in contrast to the often used Wilcoxon-type tests which emphasize early differences (i.e., differences at low solubility).[43] Pairwise comparisons were then conducted (also with the log rank test) for all elements with a significant difference in the overall group comparison. Bonferroni correction was applied to assess the significance of these pairwise comparisons. In addition to the logrank test, potential influence of plant and welding technique was assessed with two-way ANOVA using ranks.[41,42] With this approach it is possible to investigate main and interaction effects whereas in the survival analysis approach (logrank test) only main effects can be studied.

Principal component analysis (PCA) was used for dimension reduction and for extraction of chemically interpretable factors. PCA was performed with ranks (for the complete data set as well as for each plant and welding technique separately) as recommended by Helsel for interval censored data.[38] The ranks used in two-way ANOVA and in PCA were calculated from generalized Wilcoxon-Mann-Whitney scores.[40]

All statistical calculations were performed with R version 3.0.3,[44] and using the packages interval[40] and psych.[45]

3. Results

An overview of particle mass and element concentrations according to Hatch solubility encountered in the workplace air is given in Table 1. The Hatch soluble ratios of different elements obtained from all 325 samples are summarized in Table 2. The solubility of elements is quite variable. Very low values with a median below 1% were observed for aluminium (Al), iron (Fe), lead (Pb) and titanium (Ti). Higher solubility was found for cobalt (Co), Cr, Ni, vanadium (V), and tungsten (W) with a median between 4 and 6%, as well as for cadmium (Cd), copper (Cu), zinc (Zn) and Mn with a median between 13 and 27%. The highest solubility (median of 41%) was obtained for molybdenum (Mo). For many elements the solubility varies over a remarkably wide range (Table 1). For example, values between approximately 1 and 56% (0.05 and 0.95 quantile) were observed for Cr, between 3 and 59% for Cu, and between 16 and 81% for Mo.

The influence of welding technique and plant on solubility was studied with two different approaches (see chapter 2.3). If the p-values (Tables S2 and S3) are classified into three categories ($p \geq 0.05$ not significant; $0.01 \leq p < 0.05$ significant; $p < 0.01$ highly significant), it becomes obvious that both approaches (survival analysis techniques and two-way ANOVA on ranks) yield for most elements the same result when the influence of the plant on solubility is considered. Merely for Al and W, a slight difference (significant vs. highly significant) was obtained. With respect to welding technique, there is less agreement between the two statistical approaches. Still, for 10 of the 14 elements identical findings were obtained. However, for Cd, Co, Fe and Mo the two analysis procedures yield conflictive results. Summary statistics of the solubility is given in Table 3, separately for the three different welding techniques and the three different plants. The elements: Al, Fe, Pb, and Ti with very low solubility (median always < 1%) often show statistically highly significant differences between the three plants as well as between the three welding techniques. However, due to their very low solubility these differences are regarded as of no practical relevance and are not considered further. The elements Cd, Mo, Ni, W, and Zn have approximately similar solubility independent on welding technique. All other elements show significant differences in solubility if the different techniques are compared. For the different plants, approximately similar solubility is only observed for Cd, Ni, and Zn. The solubility of all other elements differs significantly in the three plants investigated.

Principal component analysis (PCA) was first performed with all 325 samples for the assessment of the solubility of the different elements. The number of extracted components was derived from the Kaiser-Guttman criterion, i.e., only principal components with an eigenvalue > 1 were taken into account. After applying varimax rotation, a clear pattern was obtained (Table 4). The first rotated component explaining 24% of the variance has high loadings (> 0.8) on Fe, Mn, Ni and Zn. The correlation between Fe and Mn is illustrated in Figure 1. The second rotated component explaining 22% of the variance has high loadings (≥

0.5) on Al, Cr, Ti, V and W. The third rotated component (12% explained variance) has high loadings (> 0.7) on Cd and Cu, the fourth rotated component (11% explained variance) on Mo (> 0.7). In a second step, PCA was performed separately for the different welding techniques and plants. Despite some differences in the factor loadings, the first two components obtained from all samples remained stable (albeit changing their order in some cases). It is important to note here that elements, which load high on the same principal component, may have very different solubility. For the first component, the median solubility varies about a factor of 28, for the second component about a factor of 58.

We did not find a correlation between the solubility and the total air concentration of an element. In addition, none of the elements` solubility correlated with the respective amount of the element in the particulate mass.

4. Discussion

The median value of the solubility of the different elements was found to vary considerably between < 1% (Al, Fe, Pb, Ti) and 41% (Mo). It must be emphasized here, that we have measured an apparent solubility which is the solubility obtained in the current leaching experiments without necessarily having reached equilibrium. Thus, the large variation observed does not reflect differences in equilibrium solubility of the different compounds present. Rather, the large variation of solubility between the investigated elements may be to a large extent caused by differences in the distribution of an element among compounds with higher and lower equilibrium solubility. For example, Fe is predominantly contained in oxides or occurs as metallic phase with low equilibrium solubility, which should also lead to a low solubility of this element. The same is generally true for Mn, but some fraction of Mn may be also present in more soluble compounds (e.g., Mn_2O_7). Thus, the higher solubility of Mn (compared to Fe) may simply reflect the presence of a larger fraction of more soluble Mn compounds.

In addition to chemical and phase composition, the solubility of elements in WF particles is also influenced by further parameters, such as size and morphology of the particles, composition of the solvent as well as characteristics of the leaching process including volume and pH of the solvent, leaching time and temperature. Due to the complex solubility behaviour, it is difficult to make general statements on element solubility/bio-accessibility in WFs. In addition, interpretation of the measured solubility is hampered by the fact that the compounds present and the distribution of the elements investigated among these compounds are not known.

The phase composition of WF PM was studied previously by X-ray diffraction (XRD) spectrometry, and various oxides as well as other compounds were found.[2-4] Magnetite (Fe_3O_4) is the most often identified phase in gas metal arc (GMA) and MMA WF. Di- and trivalent ions like $Mn^{2,3+}$, Ni^{2+}, Cr^{3+} can substitute for Fe in the magnetite crystal lattice. Beside magnetite, other spinel group oxides, like jacobsite ($MnFe_2O_4$), and iron(II) di-manganese(III) oxide ($FeMn_2O_4$) as well as metallic Fe (ferrite, α-Fe) were observed by XRD. Potassium chromate (K_2CrO_4) was also found.[2-4] The relatively low (median ≤ 4%) solubility of Fe, Cr, Ni, and Ti can be explained by the predominant occurrence of these elements as spinel group oxides or metallic particles. Mn does also occur as spinel group oxides (see above). However, the much higher solubility (median 12.6%) most likely indicates the presence of some more soluble Mn containing compounds.

The low percentages of Hatch soluble Al and Fe might be partly explained by the slightly basic (pH 7.4) conditions of the solution, as dissolved Al^{3+} and $Fe^{2,3+}$ can precipitate as hydroxides.[46] The high solubility of Mo might be caused by the presence of hexavalent Mo as molybdate (MoO_4^{2-}) anion at the slightly alkaline pH of the Hatch´s solution.[47] Based on this finding, it is suggested that a higher fraction of Mo is present in form of soluble hexavalent compounds in different WFs compared to Cr, which is typically present in form of soluble chromates only in certain type of WFs like MMA WF.[48,49] Molybdenum trioxide

(MoO_3) is slightly soluble (0.4 – 2 g/L) in water and is mainly present as molybdate anion.[50] Based on these findings MoO_3 might be the main Mo compound in most of the welding fumes in which Mo is present. The generally relatively high solubility of Cd, Cu and Zn in Hatch´s solution is in principle in good accordance with the higher equilibrium solubility of the different Cd, Cu and Zn compounds compared to the other metal compounds, which can be present in WFs.[51] However, without knowledge of the distribution of these elements among the different compounds no definite conclusion can be drawn. Cr, V and W can be present both as cations and anions in WF leachates with chromate (CrO_4^{2-}), vanadate (VO_4^{3-}) and tungstate (WO_4^{2-}) as the dominant anions at higher pHs.[47] Although the median solubility of these elements was quite low (3 – 6%), it was changing over a wide range, suggesting the presence of variable amount of these oxyanions. Ni and Co solubility was lower than 5% in more than half of the samples. For both elements, the most common oxidation state is +2. As Co(II) and Ni(II) salts are usually highly soluble, it is concluded that these elements are present in WFs mostly as or contained in less soluble or insoluble oxides.

The composition of the solvent also has a strong influence on solubility of WF. Mo, Pb, and Ti solubility was very different in water and in Hatch´s solution in case of MIG and MMA WFs.[31] The Pb compounds which can be formed from Pb^{2+} cations and the anions present in higher concentrations in Hatch´s solution (carbonate, chloride, phosphate, sulphate) have generally low solubility, which might explain the low solubility of Pb in Hatch´s solution.[51] Ti^{4+} forms insoluble precipitates with sulphate ions, which may also contribute to the low solubility of Ti in Hatch´s solution.[51]

As the applied welding technique had little or no influence on the Hatch solubility of Al, Cd, Fe, Mo, Ni, Pb, Ti, W and Zn, it is suggested that the lung bio-accessibility of these elements present in the deposited WF particles is also independent on the welding technique. In contrast, solubility of Co, Cr, Cu, Mn and V was more dependent on the welding technique used, indicating that these elements can be present in a larger variety of different compounds compared to other elements investigated. For example, Cr in MIG WF is more likely to be present as Cr(III), while in MMA WF as Cr(VI) compounds.[49] Based on our results the situation could be similar for V, which might be present in lower oxidation states in MIG and in higher oxidation states in MMA WFs. The large amount of Cr(VI) present in stainless steel MMA WF has been shown to be associated with Na and K compounds in MMA welding fluxes.[52] Na and K chromates are more stable at higher temperatures than most other chromates and this could explain the presence of Cr(VI) in larger amounts in MMA WF compared to MIG WF.[53] In an earlier study conducted in the same facilities as the present study, much higher concentrations of K and Na were found in personal air samples collected by manual welding compared to automatic and semi-automatic welding.[35] The higher solubility of Cr in air samples collected by manual welding might be explained by the presence of soluble Na and K chromates in larger extent compared to the other two techniques. If the Mn solubility is evaluated with respect to the potential health risks of soluble Mn compounds,[20,24] it might be suggested that WF generated by semi-automatic MIG represents a higher risk due to the higher solubility compared to the two other techniques. As some previous studies indicated,[29,30] welding operating parameters might have an effects on the welding fume composition and thus on the solubility of compounds. To investigate this very complex issue is, however, beyond the possibilities of any field studies performed in huge welding plants.

The differences in solubility of elements between the different plants may be caused by different materials welded and by use of different electrode materials. Plant 1 and 2 are both shipyards with similar production processes, thus similar solubility of elements is expected for both plants. However, the pronounced differences between these two plants observed for Mo, V, and W draw the attention to the importance of local assessment.

An important result of PCA is that the leaching behaviour of the different elements is independent of the absolute solubility. For example, the first principal component has high loadings on Fe, Mn, Ni and Zn, elements, which occur predominantly as divalent cations, except Fe, which also often exist as Fe^{3+}. Their median solubility varies between 0.7 and 19.8%. The second principal component has high loadings on Al, Ti, Cr, V and W. The latter three elements often form oxyanions. Again, the solubility of the elements strongly contributing to this factor varies considerably between 0.1 and 5.8%. It should be mentioned here that if the elements with very low (< 1%) solubility (Fe in the first, and Al and Ti in the second principal component) are omitted, the chemical interpretation of these two components becomes more obvious: the first principal component consists of elements forming predominantly divalent cations, the second principal component of elements forming oxyanions.

As already mentioned, the absolute value of solubility of an element is strongly influenced by the distribution of this element between compounds with different equilibrium solubility. In contrast, the co-variation of the solubility of the different elements is mainly depending on the most soluble compound(s), which often contribute only a small fraction to the total abundance of an element. Therefore, it is reasonable that the principal components are not depending on the absolute value of solubility.

Mo the highest solubility and does not covariate with any other elements. This observation most likely indicates that a large fraction of Mo is present in solution as molybdate. In contrast, only a much smaller fraction of Cr, V and W, which also form soluble oxyanions, seem to occur as such soluble compounds. The major fraction of the latter elements may be present as less soluble oxides or metal phases. However, the small fraction of more soluble compounds controls the co-variation of the solubility leading to a distinct principal component.

5. Conclusions

(1) The bio-accessibility of elements in welding fumes cannot be obtained from literature data. Due to the large variations observed in solubility, it is recommended to experimentally determine the bio-accessibility separately for each welding technique and plant under consideration.

(2) It is further advocated to always determine the phase composition (e.g., by X-ray diffraction analysis) in future leaching experiments to better understand the observed solubility data.

(3) If the variation of the solubility of elements in different samples (e.g., from different plants) is the main focus of a research project (i.e., not the absolute solubility value), it may be assumed that elements forming divalent cations as well as elements forming oxyanions behave similarly.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

The study was supported by Grant Number W81XWH-05-1-0239 from the National Institutes of Health, the United States Department of Defense, and the United States Army Medical Research and Materiel Command through Vanderbilt University. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health, the United States Department of Defense, the United States Army Medical Research and Materiel Command or Vanderbilt University.

Michael P. Fay (National Institute of Allergy and Infectious Diseases) and Tina Felber (Technical University Darmstadt, Department of Mathematics) are acknowledged for their helpful discussions on analysis of interval censored data, and William Revelle (Northwestern

University, Department of Psychology) for helpful discussions on principal component analysis with the R package psych.

References

1. B. Berlinger, N. Benker, S. Weinbruch, B. L'Vov, M. Ebert, W. Koch, D. G. Ellingsen and Y. Thomassen, Physicochemical characterisation of different welding aerosols, *Anal. Bioanal. Chem.*, 2011, **399**, 1773-1780.

2. M. J. Gonser, J. C. Lippold, D. W. Dickinson, J. W. Sowards and A. J. Ramirez, Characterization of Welding Fume Generated by High-Mn Consumables, *Weld. J.*, 2010, **89**, S25-S33.

3. B. Berlinger, M. Naray, I. Sajo and G. Zaray, Critical Evaluation of Sequential Leaching Procedures for the Determination of Ni and Mn Species in Welding Fumes, *Ann. Occup. Hyg.*, 2009, **53**, 333-340.

4. J. W. Sowards, J. C. Lippold, D. W. Dickinson and A. J. Ramirez, Characterization of Welding Fume from SMAW Electrodes — Part I, *Weld. J.*, 2008, **87**, 106S-112S.

5. J. W. Sowards, A. J. Ramirez, D. W. Dickinson and J. C. Lippold, Characterization of Welding Fume from SMAW Electrodes — Part II, *Weld. J.*, 2010, **89**, 82S-90S.

6. P. Konarski, I. Iwanejko and M. Cwil, Core–shell morphology of welding fume micro- and nanoparticles, *Vacuum*, 2003, **70**, 385-389.

7. E. Minni, T. E. Gustafsson, M. Koponen and P. L. Kalliomaki, A study of the chemical-structure of particles in the welding fumes of mild and stainless-steel, *J. Aerosol Sci.*, 1984, 15, 57-68.

8. E. Ibfelt, J. P. Bonde and J. Hansen, Exposure to metal welding fume particles and risk for cardiovascular disease in Denmark: a prospective cohort study, *Occup. Environ. Med.*, 2010, **67**, 772-777.

9. B. Sjogren, F. Gyntelberg and B. Hilt, Ischemic heart disease and welding in Scandinavian studies, *Scand. J. Work Environ. Health*, 2006, **Suppl. 2**, 50-53.

10. J. M. Antonini, A. B. Santaimaria, N. T. Jenkins, E. Albini and R. Lucchini, Fate of manganese associated with the inhalation of welding fumes: Potential neurological effects, *Neurotoxicology*, 2006, **27**, 304-310.

11. C. M. Fored, J. P. Fryzek, L. Brandt, G. Nise, B. Sjogren, J. K. McLaughlin, W. J. Blot and A. Ekbom, Parkinson's disease and other basal ganglia or movement disorders in a large nationwide cohort of Swedish welders, *Occup. Environ. Med.*, 2006, 63, 135-140.

12. L. Lillienberg, J. P. Zock, H. Kromhout, E. Plana, D. Jarvis, K. Toren and M. Kogevinas, A Population-Based Study on Welding Exposures at Work and Respiratory Symptoms, *Ann. Occup. Hyg.*, 2008, **52**, 107-115.

13. K. T. Palmer, R. McNeill-Love, J. R. Poole, D. Coggon, A. J. Frew, C. H. Linaker and J. K. Shute, Inflammatory responses to the occupational inhalation of metal fume, *Eur. Respir. J.*, 2006, **27**, 366-373.

14. J. C. J. Luo, K. H. Hsu and W. S. Shen, Pulmonary Function Abnormalities and Airway Irritation Symptoms of Metal Fumes Exposure on Automobile Spot Welders, *Am. J. Ind. Med.*, 2006, **49**, 407-416.

15. T. Hannu, R. Piipari, H. Kasurinen, H. Keskinen, M. Tuppurainen and T. Tuomi, Occupational asthma due to manual metal-arc welding of special stainless steels, *Eur. Respir. J.*, 2005, **26**, 736-739.

16. M. El-Zein, J. L. Malo, C. Infante-Rivard and D. Gautrin, Prevalence and association of welding related systemic and respiratory symptoms in welders, *Occup. Environ. Med.*, 2003, **60**, 655-661.

17. J. M. Antonini, Health Effects of Welding, *Crit. Rev. Toxicol.*, 2003, **33**, 61-103.

18. A. Erdely, J. M. Antonini, S.-H. Young, M. L. Kashon, J. K. Gu, T. Hulderman, R. Salmen, T. Meighan, J. R. Roberts and P. C. Zeidler-Erdely, Oxidative stress and reduced responsiveness of challenged circulating leukocytes following pulmonary instillation of metal-rich particulate matter in rats, *Part. Fibre Toxicol.*, 2014, **11**, 34.

19. J. M. Antonini, N. J. Lawryk, G. G. K. Murthy and J. D. Brain, Effect of welding fume solubility on lung macrophage viability and function in vitro, *J. Toxicol. Environ. Health-Part A*, 1999, **58**, 343-363.

20. J. M. Antonini, K. Sriram, S. A. Benkovic, J. R. Roberts, S. Stone, B. T. Chen, D. Schwegler-Berry, A. M. Jefferson, B. K. Billig, C. M. Felton, M. A. Hammer, F. Ma, D. G. Frazer, J. P. O'Callaghan and D. B. Miller, Mild steel welding fume causes manganese accumulation and subtle neuroinflammatory changes but not overt neuronal damage in discrete brain regions of rats after short-term inhalation exposure, *Neurotoxicology*, 2009, **30**, 915-925.

21. J. M. Antonini, J. R. Roberts, R. S. Chapman, J. M. Soukup, A. J. Ghio and K. Sriram, Pulmonary toxicity and extrapulmonary tissue distribution of metals after repeated exposure to different welding fumes, *Inhal. Toxicol.*, 2010, **22**, 805-816.

22. P. C. Zeidler-Erdely, M. L. Kashon, L. A. Battelli, S.-H. Young, A. Erdely, J. R. Roberts, S. H. Reynolds and J. M. Antonini, Pulmonary inflammation and tumor induction in lung tumor susceptible A/J and resistant C57BL/6J mice exposed to welding fume, *Part. Fibre Toxicol.*, 2008, **5**, 12.

23. M. D. Taylor, J. R. Roberts, S. S. Leonard, X. L. Shi and J. M. Antonini, Effects of Welding Fumes of Differing Composition and Solubility on Free Radical Production and Acute Lung Injury and Inflammation in Rats, *Toxicol. Sci.*, 2003, **75**, 181-191.

24. H. Roels, G. Meiers, M. Delos, I. Ortega, R. Lauwerys, J. P. Buchet and D. Lison, Influence of the route of administration and the chemical form ($MnCl_2$, MnO_2) on the absorption and cerebral distribution of manganese in rats, *Arch. Toxicol.*, 1997, **71**, 223-230.

25. B. Berlinger and M. Harper, Interlaboratory comparison for the determination of the soluble fraction of metals in welding fume samples, *J. Occup. Environ. Hyg.*, 2018, **15**, 152-156

26. C. S. Yoon, N. W. Paik, J. H. Kim and H. B. Chae, Total and Soluble Metal Contents in Flux-Cored Arc Welding Fumes, *Aerosol Sci. Technol.*, 2009, **43**, 511-521.

27. W. Matczak and J. Chmielnicka, Relation between Various Chromium Compounds and Some Other Elements in Fumes from Manual Metal Arc Stainless Steel Welding, *Brit. J. Ind. Med.*, 1993, **50**, 244-251.

28. B. Berlinger, M. Naray and G. Zaray, Distribution of metals between inhalable and respirable fractions of welding fumes generated in gas metal arc welding, *Sci. Technol. Weld. Joi.*, 2008, **13**, 721-725.

29. M. Keane, S. Stone and B. Chen, Welding fumes from stainless steel gas metal arc processes contain multiple manganese chemical species, *J. Environ. Monit.*, 2010, **12**, 1133-1140.

30. M. Keane, S. Stone, B. Chen, J. Slaven, D. Schwegler-Berry and J. Antonini, Hexavalent chromium content in stainless steel welding fumes is dependent on the welding process and shield gas type, *J. Environ. Monit.*, 2009, **11**, 418-424.

31. B. Berlinger, D. G. Ellingsen, M. Naray, G. Zaray and Y. Thomassen, A study of the bio-accessibility of welding fumes, *J. Environ. Monit.*, 2008, **10**, 1448-1453.

32. V. Mohr, M. Miro and A. Limbeck, On-line dynamic extraction system hyphenated to inductively coupled plasma optical emission spectrometry for automatic determination of oral bioaccessible trace metal fractions in airborne particulate matter, *Anal. Bioanal. Chem.*, 2017, **409**, 2747-2756.

33. M. Rosende and M. Miro, Recent trends in automatic dynamic leaching tests for assessing bioaccessible forms of trace elements in solid substrates, *Trends Anal. Chem.*, 2013, **45**, 67-78.

34. A. Limbeck, C. Wagner, B. Lendl and A. Mukhtar, Determination of water soluble trace metals in airborne particulate matter using a dynamic extraction procedure with on-line inductively coupled plasma optical emission spectrometric detection, *Anal. Chim. Acta*, 2012, **750**, 111-119.

35. D.G. Ellingsen, L. Dubeikovskaya, K. Dahl, M. Chaschin, V. Chaschin, E. Zibarev and Y. Thomassen, Air exposure assessment and biological monitoring of manganese and other major welding fume components in welders, *J. Environ. Monit.*, 2006, **8**, 1078-1086

36. D. G. Ellingsen, E. Zibarev, Z. Kusraeva, B. Berlinger, M. Chashchin, R. Bast-Pettersen, V. Chashchin and Y. Thomassen, The bioavailability of manganese in welders in relation to its solubility in welding fumes, *Environ. Sci. Process Impacts*, 2013, **15**, 357-365.

37. Y. Thomassen, E. Nieboer, D. Ellingsen, S. Hetland, T. Norseth, J. O. Odland, N. Romanova, S. Chernova and V. P. Tchachtchine, Characterisation of workers' exposure in a Russian nickel refinery, *J. Environ. Monit.*, 1999, **1**, 15-22.

38. D. R. Helsel, *Statistics for censored environmental data using Minitab and R*, 2nd ed., Wiley, 2012, pp. 324.

39. B. Turnbull, Multiple decision rules for comparing several populations with a fixed known standard, *J. Royal Statistical Soc. B*, 1976, **38**, 290-295.

40. M. P. Fay and P. A. Shaw, 2010, *J. Statistical Software*, 2010, 36, 1-34. http://www.jstatsoft.org/v36/i02/.

41. W. J. Conover and R. L. Iman, Some alternative procedures using ranks for analysis of experimental-designs, *Commun. Stat. Theory Methods*, 1976, **5**, 1349-1368.

42. W. J. Conover and R. L. Iman, Rank transformations as a bridge between parametric and nonparametric statistics, *Am. Statist.*, 1981, **35**, 124-129.

43. J. Sun, A non-parametric test for interval-censored failure time data with application to AIDS studies, *Stat. Med.*, 1996, **15**, 1387-1395.

44. R Core Team, R*: A language and environment for statistical computing, R Foundation for Statistical Computing*, Vienna, Austria, 2014, http://www.R-project.org/.

45. W. Revelle, psych: Procedures for personality and psychological research, Northwestern University, Evanston, Illinois, USA, 2014, https://cran.r-project.org/src/contrib/psych_1.4.8.tar.gz.

46. U. Schwertmann, Oxide und Hydroxide, in: Jasmund K. and Lagaly G., Tonminerale und Tone, 1993, chapter 2.6, 68-78.

47. J. Scancar, B. Berlinger, Y. Thomassen and R. Milacic, Simultaneous speciation analysis of chromate, molybdate, tungstate and vanadate in welding fume alkaline extracts by HPLC–ICP-MS, *Talanta*, 2015, **142**, 164-169.

48. D. Naranjit, Y. Thomassen and J. C. Vanloon, Development of a procedure for studies of the chromium(III) and chromium(VI) contents of welding fumes, *Anal. Chim. Acta*, 1979, **110**, 307-312.

49. U. Ulfvarson and D. Tech, Survey of air contaminants from welding, *Scand. J. Work Environ. Health*, 1981, **7**, 1-28.

50. P. C. H. Mitchell, *Report for the International Molybdenum Association*, REACH Molybdenum Consortium, 2009, http://www.imoa.info/download_files/HSE/Uv_analysis_Mo_compounds.pdf

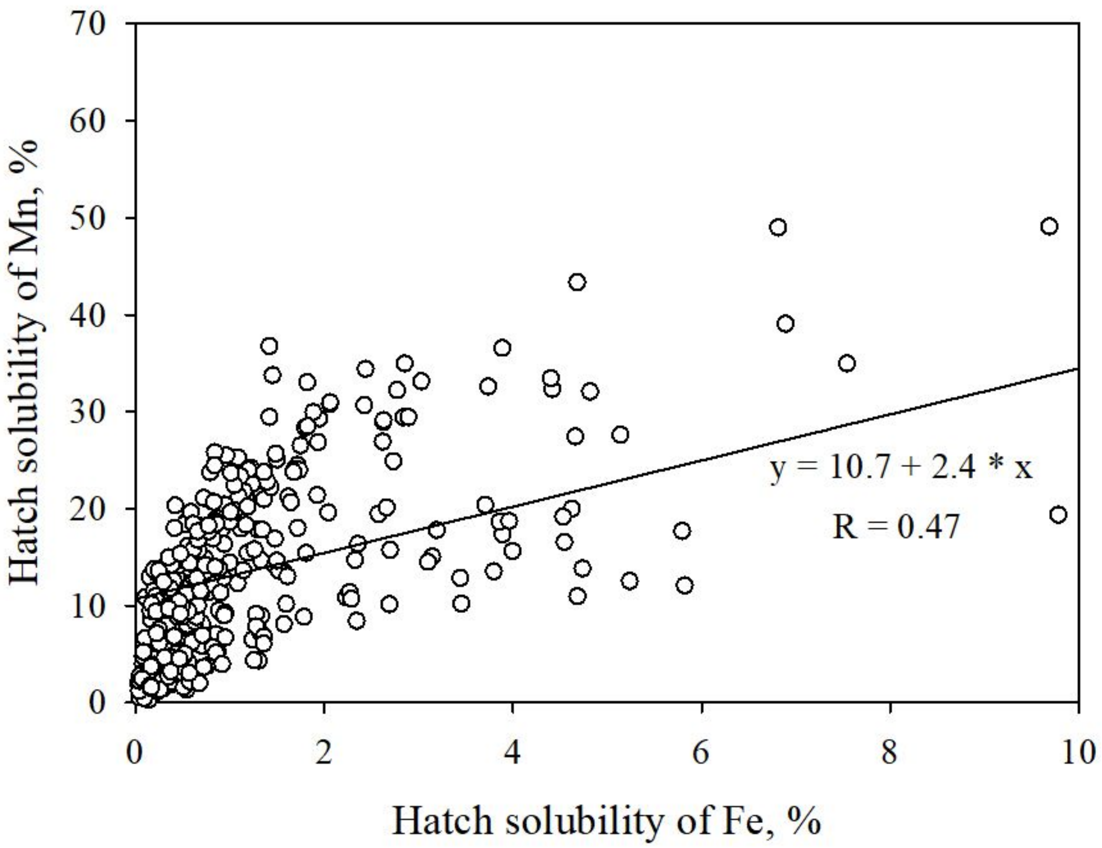
51. CRC Handbook of Chemistry and Physics, ed. R. C. Weast, CRC Press Inc., Boca Raton, FL, 1984, table B-68–161.

52. S. Kimura, M. Kobayasi, T. Godai and S. Minato, Investigations on chromium in stainless-steel welding fumes, *Weld. J.*, 1979, **58**, S195-S204.

53. C. N. Gray, A. Goldstone, P. R. M. Dare and P. J. Hewitt, The evolution of hexavalent chromium in metallic aerosols, *Am. Ind. Hyg. Assoc. J.*, 1983, **44**, 384-388.

Figures

Figure 1: Correlation between the Hatch solubility of manganese and iron assessed in welding fume samples.



Tables

Table 1: Overview of particle mass (mg m^{-3}; n = 229) and element (µg m^{-3}; n = 325) concentrations in workplace air.

	Below dl[1]		**Minimum**		**Median**		**0.90 quantile**		**Maximum**	
Particle mass	0		0.06		9.0		24.9		90.5	
Element	H_{sol}[2]	H_{insol}[3]	H_{sol}[2]	H_{insol}[3]	H_{sol}[2]	H_{insol}[3]	H_{sol}[2]	H_{insol}[3]	H_{sol}[2]	H_{insol}[3]
Al	219	2	< 0.16	< 0.77	< 0.16	35.2	1.14	122	7.64	2040
Cd	9	147	< 0.0006	< 0.015	0.020	0.092	0.097	0.22	8.34	11.5
Co	150	35	< 0.011	< 0.017	0.027	0.31	0.062	1.27	0.72	11.3
Cr	8	10	< 0.027	< 0.24	0.20	6.20	2.03	18.6	4270	1300
Cu	26	37	< 0.13	< 0.76	3.19	16.5	19.6	75.9	85.9	164
Fe	6	0	< 0.25	1.5	16.6	2060	58.4	7780	152	13700
Mn	2	2	< 0.040	< 0.16	33.3	249	260	1630	796	6090
Mo	17	162	< 0.013	< 0.16	0.14	0.41	1.19	1.66	36.2	31.4
Ni	4	5	< 0.017	< 0.22	0.21	4.84	0.98	24.2	96.3	490
Pb	230	12	< 0.0014	< 0.085	<-0.0014	4.11	0.063	14.3	3.39	968
Ti	201	2	< 0.010	< 0.16	< 0.010	13.0	0.24	103	8.27	4300
V	60	71	< 0.0050	< 0.10	0.021	0.47	0.18	2.65	10.3	33.6
W	30	40	< 0.0027	< 0.097	0.027	1.04	0.21	4.93	54.1	65.9
Zn	9	36	< 0.069	< 1.1	13.1	48.5	68.2	271	527	3650

[1]number of samples below detection limit, [2]soluble in Hatch´s solution, [3]insoluble in Hatch´s solution

Table 2: Summary statistics of Hatch solubility (ratios) of all 325 samples.

Element	Minimum	0.05 quantile	0.25 quantile	Median	0.75 quantile	0.95 quantile	Maximum
Al	< 0.001	< 0.001	< 0.001	0.003	0.009	0.032	0.239
Cd	< 0.012	0.098	0.172	0.272	0.379	0.666	0.669 – 1
Co	< 0.006	0.010	0.030	0.049	0.094	0.343	0.623
Cr	< 0.002	0.007	0.017	0.036	0.119	0.561	0.802
Cu	< 0.012	0.028	0.120	0.234	0.327	0.594	0.827 – 1
Fe	< 0.001	0.001	0.004	0.007	0.015	0.045	0.209
Mn	< 0.003	0.019	0.062	0.126	0.192	0.321	0.491
Mo	< 0.036	0.157	0.285	0.407	0.528	0.807	0.906
Ni	< 0.009	0.018	0.029	0.040	0.054	0.093	0.175
Pb	< 0.001	< 0.001	0.001	0.001	0.004	0.033	0.614 – 1
Ti	< 0.001	< 0.001	0.001	0.001	0.003	0.014	0.075
V	< 0.001	0.004	0.032	0.058	0.099	0.249	0.368
W	< 0.002	0.003	0.011	0.038	0.070	0.284	0.691
Zn	< 0.019	0.047	0.134	0.198	0.304	0.506	0.835 – 1

Table 3: Summary statistics of Hatch solubility (ratios) separately for different plants and welding techniques (263 samples).

Element	Quantile	Plant 1	Plant 2	Plant 3	Manual MMA	Semi-automatic MIG	Automatic MIG
Al	0.1	< 0.002	0.001	0.002	0.001	0.001	0.004
	0.5	0.003	0.003	0.002	0.004	0.001	0.013
	0.9	0.020	0.010	0.018	0.029	0.011	0.018
Cd	0.1	0.113	0.133	0.109	0.119	0.121	0.166
	0.5	0.231	0.255	0.253	0.302	0.223	0.280
	0.9	0.378	0.540	0.485 – 1	0.485 – 1	0.540	0.304 – 1
Co	0.1	< 0.012	0.012	0.023	< 0.013	0.012	0 – 0.069
	0.5	0.033	0.043	0.140	0.053	0.044	0.172
	0.9	0.069	0.105	0.328	0.327	0.126	0.477
Cr	0.1	0.011	0.008	0.024	0.021	0.009	0.048
	0.5	0.033	0.022	0.199	0.183	0.022	0.142
	0.9	0.065	0.096	0.728	0.728	0.059	0.384
Cu	0.1	0.024	0.050	0.035	0.099	0.035	0.168
	0.5	0.242	0.185	0.404	0.272	0.194	0.594
	0.9	0.320	0.371	0.639 – 1	0.639 – 1	0.364	0.594
Fe	0.1	0.002	0.002	0.002	0.001	0.002	0.004
	0.5	0.007	0.009	0.006	0.006	0.009	0.006
	0.9	0.039	0.028	0.018	0.024	0.028	0.027
Mn	0.1	0.046	0.059	0.016	0.019	0.064	0.022
	0.5	0.134	0.178	0.047	0.059	0.177	0.047
	0.9	0.269	0.299	0.141	0.149	0.306	0.136
Mo	0.1	0.166	0.262	0.199	0.165	0.214	0.138
	0.5	0.308	0.582	0.380	0.390	0.431	0.335
	0.9	0.499	0.745 – 1	0.632	0.644	0.680	0.508
Ni	0.1	0.017	0.029	0.016	0.015	0.024	0.020
	0.5	0.034	0.043	0.026	0.029	0.041	0.028
	0.9	0.084	0.075	0.051	0.073	0.068	0.060
Pb	0.1	0.000	0.001	0.000	0.000	0.001	0 – 0.001
	0.5	0.001	0.001	0.002	0.001	0.001	0.009
	0.9	0.002	0.012	0.025	0.012	0.007	0.060
Ti	0.1	0.001	0.001	0.001	0.001	0.001	0 – 0.001
	0.5	0.001	0.001	0.005	0.005	0.001	0.003
	0.9	0.005	0.005	0.014	0.014	0.002	0.016
V	0.1	0.033	0.005	0.017	0.032	0.005	0 – 0.027
	0.5	0.073	0.043	0.071	0.088	0.044	0.042
	0.9	0.145	0.138	0.237	0.258	0.133	0.201
W	0.1	0.006	0.003	0.025	0.021	0.003	0.029
	0.5	0.048	0.013	0.041	0.054	0.021	0.040
	0.9	0.088	0.116	0.099	0.160	0.104	0.070
Zn	0.1	0.086	0.100	0.038	0.047	0.086	0.066
	0.5	0.238	0.186	0.190	0.176	0.200	0.254
	0.9	0.530	0.342	0.394	0.464	0.375	0.381 – 1

Table 4: Principle component analysis (using ranks) of the solubility*

Element	Factor loadings			
	RC 1#	**RC 2#**	**RC 3#**	**RC 4#**
Al	0.25	0.69	0.12	0.13
Cd	0.32	0.10	0.75	0.04
Co	0.17	0.04	0.25	0.58
Cr	-0.03	0.86	0.16	0.08
Cu	-0.34	0.25	0.72	0.04
Fe	0.86	0.06	0.04	0.24
Mn	0.83	-0.37	-0.18	-0.08
Mo	0.07	0.05	0.32	-0.73
Ni	0.82	0.11	0.08	-0.09
Pb	0.47	0.20	0.34	0.51
Ti	-0.04	0.79	0.21	0.27
V	0.05	0.76	-0.19	-0.34
W	0.01	0.52	0.33	-0.21
Zn	0.81	0.26	0.09	0.19
Variance [%]	24	22	12	11

*based on correlation matrix and applying varimax rotation, all 325 samples
#rotated components, only components with an eigenvalue > 1 extracted