BIOACCESSIBILITY OF FERRO-CHROMIUM AND FERRO-SILICON-CHROMIUM PARTICLES COMPARED TO PURE METALS AND STAINLESS STEEL – ASPECTS OF HUMAN EXPOSURE

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ABSTRACT

Product safety legislation requires that industry indentifies and demonstrates any human risks associated with the manufacture and use of products which are placed on the market throughout their entire life cycle. This process involves detailed assessment of potential hazards of the products/material related to health effect endpoints, and requires accurate generation and interpretation of data which can be used to determine essential characteristics of the material.

Temporary or permanent adverse health effects depend either on the shape or physical characteristics of the particles, and/or on chemical interactions with the particle surface upon human exposure. Since alloys represent the most significant and widespread use of many engineering metals, it is important to develop a detailed understanding of the characteristics and behaviour of this group of materials with a minimum dependence on in-vivo testing.

The aim of this presentation is to summarize generated bioaccessibility data for ferro-chromium and ferro-silicon-chromium alloys in particulate form when exposed to different synthetic biological media. The selection of test media aims to mimic relevant human exposures, as far as practical, with the focus on inhalation and subsequent ingestion of inhaled particles. The generation of bioaccessibility data combined with detailed particle and material characterization, also from a surface perspective, is essential for accurate risk assessment and understanding of potential adverse effects that may be caused by ferro-chromium and ferro-silicon-chromium alloys. For comparison, a similar approach has been conducted on particles of pure iron, pure chromium and stainless steel grade AISI 316L. Generated data is used within the framework of risk assessment on ferro-chromium and ferro-silicon-chromium alloys conducted by the Finnish Institute of Occupational Health, Helsinki, Finland.

1 INDUSTRY IS REQUIRED TO ASSESS THEIR PRODUCTS WITH RESPECT TO POTENTIAL ADVERSE HEALTH AND ENVIRONMENTAL EFFECTS.

The European product safety legislation, REACH, requires that companies that manufacture, import or use chemicals (including metals and alloys) demonstrate safe use and high level of protection of their products placed on the market. Any human or environmental risks associated with the manufacture and uses of products should be identified and adequately controlled throughout their life cycle. This process involves a detailed assessment of potential hazards potentially induced by the substance/material in question against a series of health and environmental effect endpoints and the generation and interpretation of data used to determine essential characteristics of the substance/material.

Alloys represent the most significant and widespread use of many engineering metals in all kind of applications in the society, and therefore it is important to develop a detailed understanding of the characteristics and behavior of this group of materials. Many alloys have existed for a very long time and the benefits of their intrinsic properties such as mechanical strength, hardness, ductility and corrosion resistance are generally well known, and documented. However, potential adverse effects induced on human health and the environment, caused upon manufacture and use of alloys are very seldom assessed.

In the United Nations Globally Harmonized System of Classification and Labeling of Chemicals [1] alloys are explicitly addressed as simple mixtures of metals, with hazard identification and classification based on the intrinsic properties of their individual alloy constituents. This simplified view is in the case of an alloy such as stainless steel, highly erroneous. From a metal release perspective, this is for instance evident when comparing amounts of chromium, iron and nickel released from stainless steel grade AISI 316L with those from its pure metal constituents in different kind of media [2,3]. These studies indicate that stainless steel grade 316L, containing 17.2wt% chromium and 10.7wt% nickel actually behaves from a metal release perspective as a chromium-based material containing 0.02wt% iron and 0.005wt% nickel, both well below the lowest threshold concentration for hazard classification [4].

A statement saying that "*Alloys are preparations under REACH albeit special ones where the properties of the preparation do not always simply match the properties of the components*" ensures that the misleading view on alloys as simple mixtures of metals can be avoided for assessment of this group of materials under REACH [5]. For alloys it is highly likely that it is the chemistry of the alloy system that is the most important factor governing their bioaccessibility in biological systems.

Large gaps of knowledge related to bioaccessibility aspects of metals and alloys need to be filled to meet the demands of REACH, and to accomplish the generation of accurate risk assessment dossiers.

2 GENERATED BIOACCESSIBILITY DATA HAS TO BE BASED ON SCIENTIFICALLY SOUND AND RELEVANT RESEARCH APPROACH WITH A MINIMUM USE OF ANIMAL TESTING.

Metals and alloys are used in a large variety of engineering applications in the society improving the quality of our daily life. Humans are hence regularly in contact with different items made of metals and alloys such as cutlery, watches, jewelry, door handles, water taps etc. However, most such human interactions do not pose any adverse health problems, although direct contact with nickel containing metal surfaces in for instance coins or in piercing jewelry, can at specific conditions cause contact dermatitis. Bioaccessibility of metals released from implant materials has lately increased the concern related to diffuse emissions of metals.

Human exposure to particulate matter in our daily environment has become an issue of general concern in the society. Particles with metal components can be generated at certain exposure scenarios related to occupational activities such as metal and metal alloy manufacture and processing, combustion, or generated in the traffic environment, or by natural processes through erosion of minerals and volcanic eruptions. Different kind of particles exists with varying composition ranging from pure metals, metallic components, metal alloys with oxidized surfaces to particles consisting of metal oxides or compounds. Potential adverse effects on human health caused by the exposure of such metal particles or metal compounds through the main routes, oral – ingestion, dermal – skin contact and/or inhalation, and their subsequent potential for particle dissolution and metal release in contact with the human body, show significant gaps of knowledge.

To assess whether any systemic or organ toxicity in humans will occur upon exposure of such particles via skin contact, via inhalation, or via the gastrointestinal tract to the stomach, the generation of reliable quantitative bioaccessibility data in different synthetic biological media and its relation to surface properties and particle interactions is essential. Bioaccessibility data is in this context defined as the pool of metals released from a metal or alloy that potentially can be available for absorption by an organism. The metal release process is governed by a combination of corrosion (electrochemical),

dissolution (primarily chemical) and wear processes, and its extent depends on a large number of interacting parameters including barrier properties and composition of surface oxides, and prevailing environmental and exposure conditions.

In addition to information on bioaccessibility, the chemical form of released metals and the complexing capacity of the surrounding medium are crucial parameters to assess, since they govern the bioavailability of released metals, i.e. their possibility to be absorbed to humans through different routes.

In order to fulfill the demands of REACH, a large amount of new and unique data is hence required to be generated and assessed. It is therefore crucial that this generation of data is based on a scientifically sound approach that ensures accurate and quantitative research efforts of relevance covering all, or at least most, aspects of potential adverse effects on human health and the environment with a minimum dependence on in-vivo testing. The generation of a comprehensive picture combining bioaccessibility data with surface and particle characteristics of an alloy provides an applicable fingerprint of a given material and can be used to: *i)* justify the use of read across from human adverse effect data for similar materials, *ii)* group similar materials with respect to health and environmental effects, *iii)* demonstrate differences in bioaccessibility between pure metals and alloys, *iv)* make scientifically sound proposals for hazard classification, and v) select candidate alloys for in-vivo testing.

A reliable in-vitro test methodology (bio-elusion test) simulating human exposure to particles has been developed and elaborated at the Division of Surface and Corrosion Science, Royal Institute of Technology (KTH) during the past decade. The output from the test methodology, which can be applied on any material, is bioaccessibility data on released metals during exposure of particles to different synthetic biological media mimicking different human exposure scenarios, for instance *Artificial gastric fluid* (GST, pH 1.5), *Artificial lysosomal fluid* (ALF, pH 4.5), *Gamble's solution* (GMB, pH 7.4), *Artificial sweat* (ASW, pH 6.5) and *Phosphate buffered saline* (PBS, pH 7.4). This methodology has in this study been applied to generate bioaccessibility data for particles of ferro-chromium and ferro-silicon-chromium alloys in different synthetic test media and time periods simulating an actual human exposure scenario mimicking inhalation and digestion. Short (from 2 hours) and longer exposure periods up to 24 days were investigated to obtain kinetic information on the metal release process and to simulate long term exposure scenarios. Particles of commercially available ferro-chromium and ferro-silicon-chromium alloys were prepared in size fractions relevant for an inhalation scenario, i.e. < 100 µm, or as small as possible but still relevant for the real products. More detailed information related to the test procedures, synthetic solutions and materials are given in different publications by the authors (on-going publications).

3 PRODUCTS AND TEST ITEMS HAVE TO BE THOROUGHLY CHARACTERIZED FROM A BULK AND SURFACE PERSPECTIVE.

Except for the prevailing exposure conditions, the metal release process including both corrosion-induced metal release as well as chemical dissolution, depends on a large number of interacting parameters such as barrier properties and composition of surface oxides, morphology, size and surface area of particles. Information on these and other parameters is essential to facilitate the interpretation of bioaccessibility data.

The specific surface area of alloy particles of ferro-chromium (Charge-chrome: 54wt% Cr, 32 wt% Fe) and ferro-silicon-chromium (36wt% Cr, 43 wt% Si) was measured by means of BET (Brunauer Emmet Teller) analysis via adsorption of nitrogen at cryogenic condition. Morphology investigations using Scanning Electron Microscopy (SEM) provided a general picture of particle morphology including shape, surface structure and size, and X-ray photoelectron spectroscopy (XPS) was applied to provide compositional and chemical state information of metals in surface oxides. The full particle size distribution of the ferro-chromium and ferro-silicon-chromium test materials when dispersed in PBS was determined using a laser diffraction technique (LD). The extent of metals released upon exposure in the synthetic biological media was determined by means of atomic absorption spectroscopy with a graphite furnace accessory (GF-AAS) and inductively coupled plasma optical emission spectroscopy (ICP-OES). A schematic overview of the research approach is given in Fig.1.

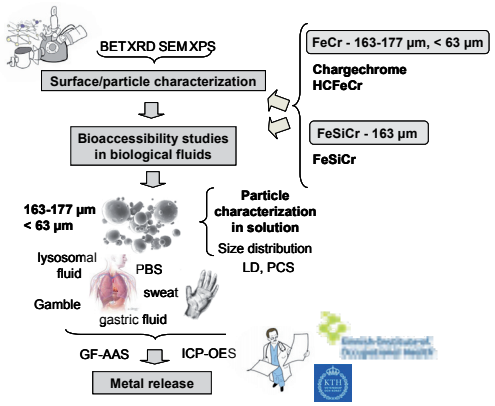

Figure 1: Schematic overview of research approach

By combining information gained from this multi-analytical approach, an indirect assessment of the extent of eventual agglomeration of particles during exposure to synthetic biological media was made. General information on specific surface areas, particle morphologies and size distributions for alloy particles of ferro-chromium (top) and ferro-silicon-chromium (bottom) is given in Fig. 2.

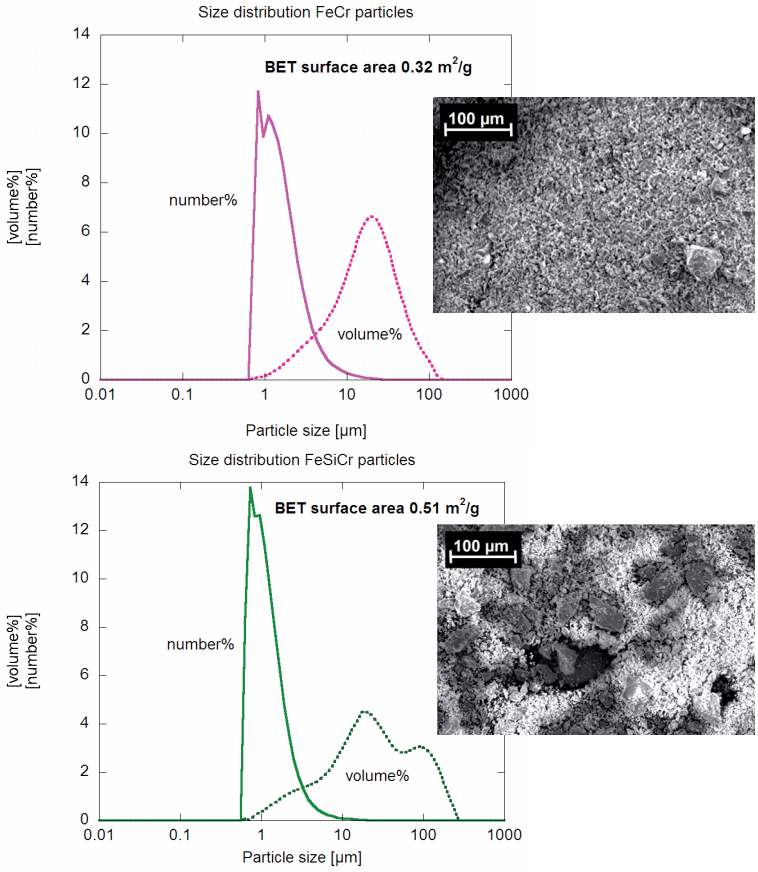

Figure 2: Information related to specific surface area, morphology and size distributions in solution for alloy particles of ferro-chromium-FeCr (top) and ferro-silicon-chromium-FeSiCr (bottom)

The nature and stability of surface oxides on particles are essential properties that govern the metal release process since their presence hinders direct contact between the bare non-oxidized metal alloy

surface and the surrounding medium. The barrier properties of these oxides regulate the extent of metal release from the alloy. For corrosion resistant alloys, there is usually a critical concentration for the alloying corrosion inhibiting element below which the corrosion resistance and in addition, the metal release resistance deteriorates significantly. For example if the amount of chromium in chromium-containing ferroalloys such as stainless steels is less than 10.5-13 wt%, their high corrosion resistance properties diminish and disappear [6].

All metal alloy surfaces are naturally oxidized at ambient conditions. This means that metal oxides of varying composition, thickness and barrier properties (passive properties) spontaneously form on the surface of the ferro-chromium and ferro-silicon-chromium alloy particles investigated. Multi-area compositional analysis by means of XPS of surface oxides clearly revealed for both alloys that their relative surface content of chromium, iron and silicon (as oxides) was different from their bulk alloy relation, Fig. 3.

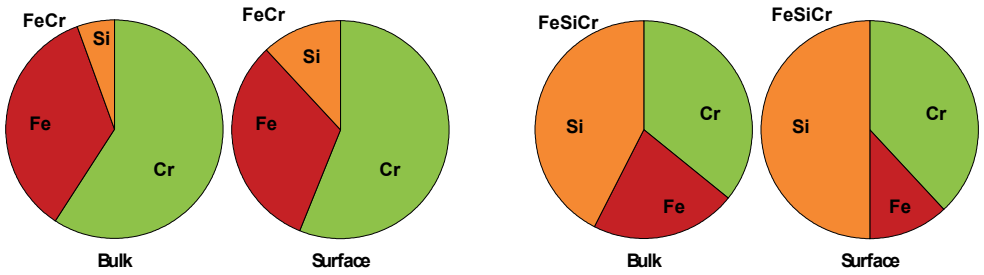

Figure 3: Relative surface content (wt%) of chromium, iron and silicon for alloy particles of ferro-chromium (FeCr) and ferro-silicon-chromium (FeSiCr)

Surface compositional measurements by means of XPS after exposure to the different synthetic media revealed increasing oxide thickness with time and changes in the relative proportion of chromium, iron and silicon in surface oxides of both alloys. These changes were interpreted as a result of the preferential release of iron into solution, and as a consequence, the enrichment of silica and chromium(III)oxides on the surface of particles. These effects are presented in Fig. 4 for particles of ferro-chromium (left) and ferro-silicon-chromium (right) alloys.

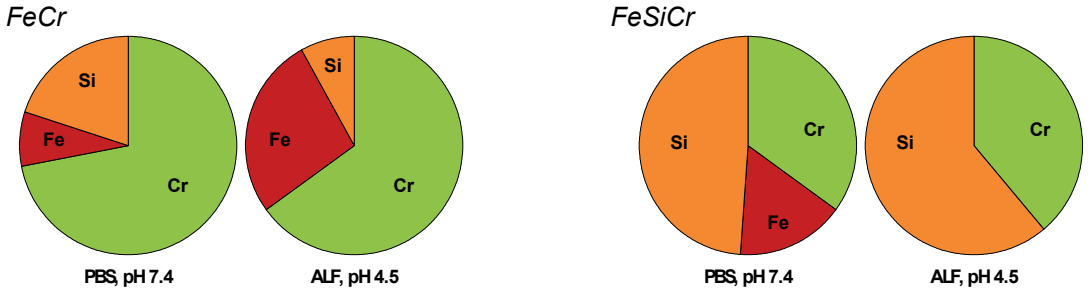

Figure 4: Changes in relative surface content (wt%) of chromium, iron and silicon for alloy particles of ferro-chromium (FeCr) – left, and ferro-silicon-chromium (FeSiCr) – right, exposed for one week in PBS (pH 7.4) and artificial lysosomal fluid, ALF (pH 4.5)

Neither the relative bulk alloy composition nor the surface composition can be used to predict or assess the extent of metals released in different synthetic biological media. It is evident that ferro-chromium and ferro-silicon-chromium alloys cannot be assessed from the behavior of their pure metal constituents.

4 BIOACCESSIBILITY DATA ON MAIN AND MINOR ALLOY CONSTITUENTS SHOULD BE GENERATED.

Any supplier or manufacturer of an article (in this case the ferro-chromium and ferro-silicon-chromium alloys) which contains a hazardous substance (in this case a metal component) at, or above its classification threshold value must according to Article 33 in the REACH regulation [7,8] provide sufficient information to allow safe use of the article. A screening investigation by means of ICP-OES of in total 32 different elements was therefore conducted to assess if other elements than the main constituents iron and chromium were released from alloy particles of ferro-chromium and ferro-silicon-chromium into the synthetic biological media investigated. Bulk metal components of the alloys exceeding 0.1 wt% are except for iron and chromium, silicon, nickel and vanadium for the ferro-silicon-chromium alloy, and silicon for the ferro-silicon-chromium alloy. Low concentrations of silicon and no measureable amounts of either nickel or vanadium were released from any of the alloys. Nickel compounds are placed on the candidate list of substances of very high concern by the International Chemical Secretariat [9]. Released concentrations of nickel were below the limit of detection and if recalculated into release rates considerably lower compared to the available threshold value of 0.5 µg Ni/cm^2/week in artificial sweat [10]. However, this threshold rate is relevant for skin sensitization and not for inhalation or ingestion. Except for iron and chromium, low concentrations of trace constituents of manganese, aluminium, and titanium were released, Fig. 5. Their origin could also be from additives during alloy processing. Measured concentrations of magnesium were believed to be related to matrix effects and not to originate from the alloy itself.

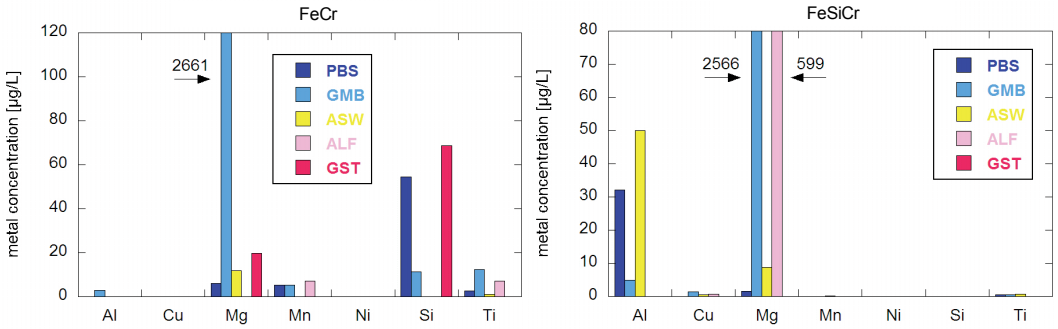

Figure 5: Released trace elements (iron and chromium not included) from ferro-chromium-FeCr (left) and ferro-silicon-chromium-FeSiCr (right) particles exposed for 24 hours in the different test media investigated

Detailed kinetic information was generated on the released amount of iron and chromium from ferro-chromium and ferro-silicon-chromium alloy particles exposed in the different synthetic biological media investigated. Kinetic results, presented as total average metal release rates per unit surface area for ferro-chromium alloy particles exposed in different test media are displayed in Fig 6. Release rates of both iron and chromium were generally very low. Iron was the preferentially released element in all test media for all time periods investigated. Release rates of iron and chromium from both ferro-chromium and ferro-silicon-chromium alloy particles decreased with time and were after one week of exposure less than 0.004 and 0.01 µg/cm^2/h for chromium and iron, respectively, released from the ferro-chromium alloy. For the ferro-silicon-chromium alloy, slightly more chromium was released compared to iron although at very low rates being less than 0.003 µg/cm^2/h for both elements after one week of exposure.

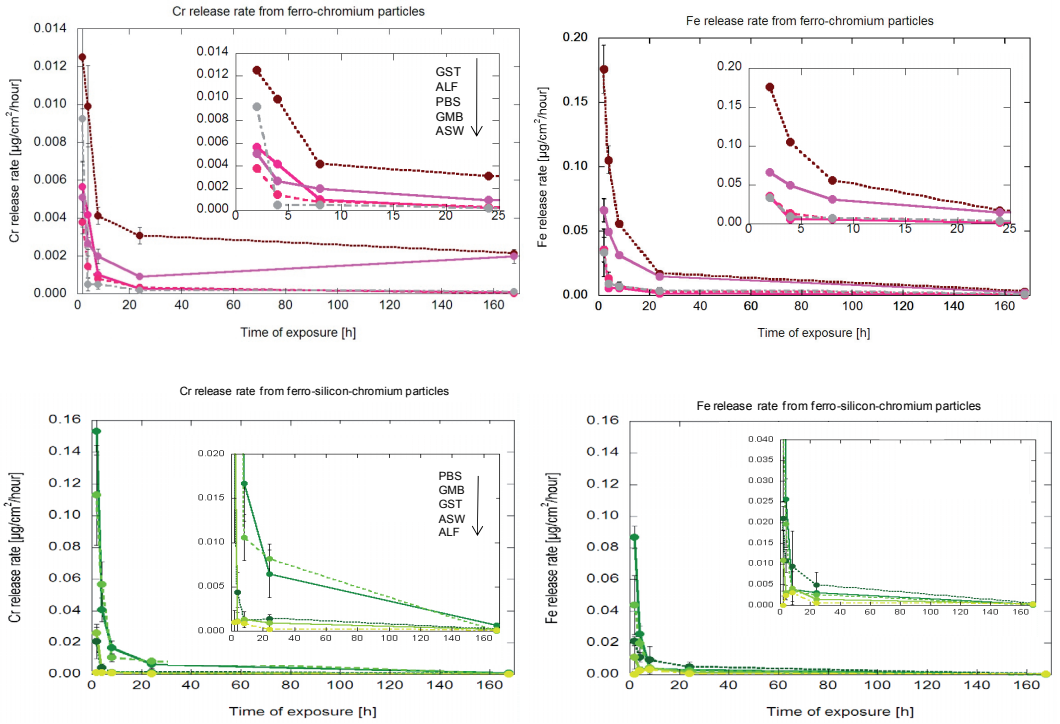

Figure 6: Release rates of chromium and iron from particles of ferro-chromium (top) and ferro-silicon-chromium (bottom) exposed for 168 hours in the different test media investigated

Bioaccessibility data expressed as the amount of metals released per amount of particles loaded for alloy particles of ferro-chromium and ferro-silicon-chromium are presented in Fig. 7 together with corresponding amounts of released metals from particles of pure iron and chromium as well as stainless steel grade AISI 316L (18.5 wt% Cr, 65.5 wt% Fe) after one week of exposure in ALF (pH 4.5). As expected, alloy particles of ferro-chromium, ferro-silicon-chromium and stainless steel 316L released significantly less iron compared to pure iron as a result of their presence of passive surface oxides of superior barrier properties. However, slightly more iron was released from particles of both ferro-chromium, ferro-silicon-chromium alloys compared to stainless steel, although still at very low levels, which reflects the passivating properties of the surface oxides. The released amount of iron from particles of the ferro-chromium alloy was approximately three times higher compared to the ferro-silicon-chromium alloy, partially due to a larger surface area for particles of the ferro-silicon-chromium alloy. The release of chromium was very low for all materials investigated although slightly higher for the ferro-chromium alloys compared with stainless steel and pure chromium. Less than 0.15% of the amount of particles loaded was released as chromium and less than 0.13 % was released as iron from the different alloys investigated.

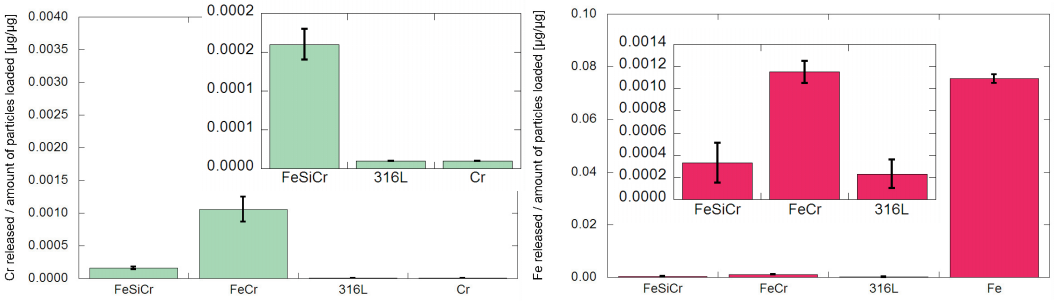

Figure 7: Released amount of chromium (left) and iron (right) per amount of particles loaded of ferro-chromium (FeCr), ferro-silicon-chromium (FeSiCr), stainless steel (316L) and pure chromium (Cr) and pure iron (Fe) after 168 hours of exposure in the different test media investigated.

5 THE BIOAVAILABLE FRACTION OF THE BIOACCESSIBLE POOL OF METALS SHOULD BE ASSESSED

Bioaccessibility data provide information about total amounts of metals released from an alloy or a pure metal that may potentially be accessible for humans (or other organisms). Any adverse health effects induced by released metals cannot accurately be assessed without having information on their bioavailability, which is determined by the chemical form of released metals (metal speciation), and whether any of these metal species can be absorbed by humans through the gastrointestinal system, the pulmonary system or the skin. The chemical speciation of released metals is strongly correlated to the chemical composition and acidity of the surrounding environment (the test medium).

Information of the chemical speciation of released metals is seldom available due to its complexity to be analysed and to low concentrations of released metals.

Speciation measurements of chromium released from alloy particles of the ferro-chromium alloy, stainless steel AISI 316L and pure chromium were conducted to assess its oxidation state in solution and its potential complexation to inorganic or organic compounds of the synthetic test media investigated within the study. Concentrations of active (free) chromium(VI), if any and total chromium (the difference interpreted as active and inactive chromium(III)) were determined by means of voltammetry (DPAdCSV) after 24 hours of immersion in GMB, PBS, ALF, and GST, respectively. For media of high salt content, this technique is advantageous at low chromium concentrations (< 1 µg/L) compared to GF-AAS in terms of accuracy, detection limit and the possibility to determine speciation.

Chromium was released from particles of the ferro-chromium alloy, pure chromium and stainless steel 316L as chromium(III) species without any presence of active chromium(VI) species for all media investigated. No measurements were performed on the ferro-silicon-chromium alloy. However, it is anticipated that similar results are expected.

Measurements of released concentrations of total chromium by means of DPAdCSV were consistent and reproducible results obtained compared to total chromium concentrations (bioaccessible chromium) measured by means of GF-AAS. All synthetic biological media except ALF showed a low capacity to form complexes with released chromium as a result of their predominance of inorganic salts. ALF, which in addition contains large quantities of organic compounds showed a high capacity to form strong chromium complexes. The complexing capacity could not be defined precisely due to an interfering peak, probably deriving from the reduction of pyruvic acid to lactic acid. However, it was clearly concluded that active (free) chromium was complexed to a high extent (almost to 100%) at low (< 2µg/L) concentrations.

6 CONCLUSIONS

The following main conclusions were drawn:

- Accurate risk assessment of alloys requires scientifically based information and relation between reliable bioaccessibility data of individual alloying constituents, and detailed material characterisation both from a bulk and a surface perspective.
- From a bioaccessibility perspective, alloys cannot be assessed from their pure metal constituents.
- Very low amounts of chromium and iron (<0.15%) released from particles of ferro-chromium and ferro-silicon-chromium alloys in synthetic biological media of varying pH and composition.
- No release of nickel and vanadium from particles of ferro-chromium and ferro-silicon-chromium alloys was detected.
- Chromium was released as chromium(III) from both alloys in all media investigated. Organic species in the ALF media (pH 4.5) formed strong complexes with active chromium, hence reducing its bioavailability.

7 ACKNOWLEDGEMENT

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