

Nickel release from nickel particles in artificial sweat

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Nickel is widely used in a broad range of products, primarily made of alloys, used by humans on a daily basis. Previous assessments have shown that skin contact with some such products may cause nickel allergic contact dermatitis, induced by the release of nickel. However, data on nickel release from small nickel particles in artificial sweat for assessment of potential risks of workers in nickel-producing and nickel-using facilities are not available. The objective of this study was to fill this knowledge gap by determining nickel release from fine nickel powder ($\sim 4 \mu\text{m}$ diameter) of different loadings varying from 0.1 to 5 mg/cm², when immersed in artificial sweat. The amount of nickel released increased with increasing particle loading, whereas the highest release rate per surface area of particles was observed for the medium particle loading, 1 mg/cm², at current experimental conditions. All particle loadings showed time-dependent release rates, reaching a relative steady-state level of less than 0.1 $\mu\text{g}/\text{cm}^2/\text{hr}$ after 12 hr of immersion, whereby less than 0.5% of the nickel particle loading was released. Nickel release from particles was influenced by the surface composition, the active surface area for corrosion, particle size, and loading.

Key words: artificial sweat; nickel release; nickel powder particles; particle loadings; release kinetics; surface area. © Blackwell Munksgaard, 2007.

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Nickel is a metallic element naturally present in the earth's crust. Due to its unique physical and chemical properties, metallic nickel and its alloys are widely used in a broad range of products. However, the frequent usage of products containing nickel may cause adverse environmental and health effects as a result of nickel released in sufficiently high amounts during production, use, recycling, or disposal.

Human exposure to nickel can occur via inhalation, ingestion, and skin contact due to occupational or consumer exposure, and diet. Significant amounts of released nickel may interact with the human body to cause adverse health effects (1–4). Although nickel is essential for some plants and animals, the essentiality of nickel for humans is in question (4, 5–7).

Nickel-induced contact dermatitis is known to be the most frequent contact allergy to man-made products, affecting 10–15% of women and 1–2% of men in the industrialized parts of the Europe (8, 9). The EU Nickel Directive aims at preventing nickel allergy and limiting the released nickel for products intended for direct and prolonged contact with the skin e.g. jewellery, watches, and buttons. The Directive was adopted by the European

Parliament and Council (Directive 94/27/EC and amended in 2004/96/EC) with release limits of 0.2 $\mu\text{g Ni}/\text{cm}^2/\text{week}$ for items worn in pierced body parts or 0.5 $\mu\text{g Ni}/\text{cm}^2/\text{week}$ for all other items (10, 11). These limits are based on nickel release measured using the EN1811 standard developed for this Directive, i.e. immersion in artificial sweat for 1 week.

The nickel release from consumer products has been assessed in numerous studies (9, 12–15). Several laboratory investigations of different materials containing nickel have been conducted and nickel release rates have been assessed from massive sheet surfaces (16–18). However, at present, there are no published data available on nickel release from small nickel particles in artificial sweat. Such studies are more relevant for some occupational scenarios of human occupational exposure of the skin to nickel, for example, within nickel metal powder production and powder metallurgical production facilities.

The aim of this paper was to assess the amount of nickel released from nickel powder particles immersed in artificial sweat in order to simulate an occupational exposure scenario with nickel particles in contact with human skin as far as

practicable. A worst-case scenario was created by measuring nickel release from a relatively small particle-sized (high surface area) nickel powder in a relatively large volume of artificial sweat, during time periods relevant for an occupational scenario. The effect of particle loading and the time-dependent release process were studied and analysed, in particular, with respect to specific surface area.

Materials and Methods

Nickel powder

The nickel powder used for metal release experiments was a commercially available Inco 123 powder provided by Nickel Producers Environmental Research Association (NiPERA), sized 3–7 μm according to the Inco material safety data sheet. The specific surface area of the nickel powder was measured to 0.43 m^2/g by Canada Centre for Mineral and Energy Technology (CANMET) using BET (Brunauer Emmett Teller) analysis (19). This area was confirmed with BET measurements in this study.

Artificial sweat

The artificial sweat solution used for metal release immersion tests was prepared similar to EN1811, using 0.5 wt% sodium chloride, 0.1 wt% lactic acid, 0.1 wt% urea and normal ultrapure water (not aerated as described in the standard) (20, 21). The pH of the solution was adjusted to pH 6.5 using 1 wt% ammonia solution. The artificial sweat solution was stored in darkness and used within 3 hr of preparation. The pH was measured before and after immersion.

Metal release

Sample preparation. 5 different powder loadings were prepared according to Table 1 and placed into 60 ml TPX Nalgene[®] test vessels. The bal-

ance used was a Mettler AT20 with a readability of 2 μg . The vessels used for the immersion tests had a flat bottom area of 14.93 cm^2 (inner diameter: 4.36 cm). All powder samples were immersed in 0.5 ml artificial sweat per cm^2 bottom area of the test vessel, i.e. equal to 7.5 ml in total volume. This volume corresponds to an approximate thickness of 0.5 cm of artificial sweat layer in the vessel (Fig. 1). A thinner layer, e.g. 0.1 cm, would be more realistic for human exposure, however not practically applicable to ensure proper mixing and to avoid agglomeration of particles during gentle shaking.

All test vessels were enclosed with lids and sealed with parafilm prior to immersion. Triplicate samples were prepared for each particle loading and time period. Control blanks without any nickel powder (triplicate blanks for each time period) were also included, using the same experimental procedures as test vessels with powders.

Immersion. All samples were immersed at dark conditions in a MERCK mini incubator, at 30 ± 2 degrees celcius for 5 different time durations: 0.5, 1, 4, 8, and 12 hr, respectively. Aiming at simulating a realistic exposure scenario, these time periods were considered as more relevant than the standardized 1-week immersion of articles in artificial sweat (21). The incubator was placed on a bilinear shaking table regulated at a maximum angle of 12° and an intensity of 25 cycles/min. This set-up of gentle shaking of the test vessels ensures a good mixing of particles to the test solution, and prevents eventual agglomeration of particles (22).

Separation. After immersion, the pH of the artificial sweat solution was measured. The test solution (including nickel powder particles) was poured into a 10 ml centrifuging tube and centrifuged at 4000 rpm (1252 g) for 10 min to separate

Table 1. Amount of particles loaded, expressed per surface area, solution volume and ratio of the test vessel, per solution volume or per total surface area of powder particle loading to solution volume ratio.

Particle loading	Ni particles loaded/Surface area of test vessel (mg/cm^2)	Ni particles loaded/Solution volume (g/l)	Particle loading/Solution volume ratio (cm^2/ml)
I	0.1	0.2	0.85
II	0.5	1	4.3
III	1	2	8.5
IV	3	6	26
V	5	10	43

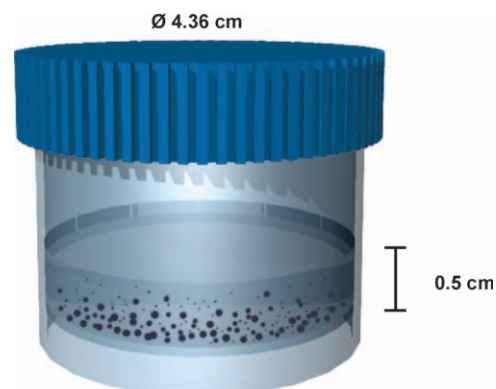


Fig. 1. Schematic illustration of the approximate thickness of the artificial sweat solution covering nickel particles in the test vessels.

the particles from the test solution. The majority of the nickel particles were centrifuged to a pellet, but occasionally (when handling the lower particle loadings), some small particles were still floating on the surface after centrifugation, probably due to the high surface tension of the artificial sweat solution. In these cases, pasteur pipettes were used to carefully remove the floating particles before decanting approximately half of the supernatant solution (≈ 3 ml) into a storage vessel. After the separation procedure, 3 μ l of 65% ultrapure HNO_3 was added to the artificial sweat solution sample to reduce the pH to <2 and to conserve the sample for solution analysis, a standard procedure for metal analysis.

Solution analysis. The total concentration of nickel in the separated solution was analysed by GF-AAS, graphite furnace atomic absorption spectroscopy (Instrumental Laboratory Model IL551, Instrumental Laboratory Inc., Wilmington, MA, USA). The detection limit was 10 $\mu\text{g/l}$. The solution samples were diluted when necessary, using ultrapure water. As nickel concentrations in blank reference samples were generally below the detection limit, background nickel contribution was not taken into account.

Surface analysis. The composition of the outermost surface layer was evaluated, for as-received and selected nickel powder samples after immersion, with X-ray photoelectron spectroscopy, XPS (AXIS HS; Kratos, Kratos Analytical, Manchester, UK). All measurements were performed with a monochromatic $\text{AlK}\alpha$ X-ray source (1486.6 eV) operated at 300 W (15 kV/20 mA). Due to the magnetic properties of the nickel powder, all measurements were performed with an

electrostatic lens, reducing peak intensities. Wide scans and detailed scans of Ni 2p, O 1s and C 1s (elements and associated electron orbitals) were acquired. The elemental peak positions on the binding energy scale provide chemical state information.

Results

Changes in released total nickel concentrations with time are presented for the two lower (I and II, continuous lines) and the three higher (III–V, continuous lines) particle loadings (Fig. 2, left and right, respectively). Measured nickel concentrations are directly related to the particle loading, i.e. an increasing released nickel concentration with increasing particle loading. After 8–12 hr of immersion, released nickel reached a relatively stable concentration, an almost steady-state level, for the lowest particle loadings (I–IV). However, no steady-state condition was reached for the highest particle loading (V). No linear correlation exists between the particle loading and the released amount of nickel. The highest particle loading, V (5 mg/cm^2), resulted in a released concentration of 0.025 mg/ml after 12 hr of immersion, whereas a lower amount of particles, e.g. 5 times lower, III (1 mg/cm^2), resulted in a concentration of 0.009 mg/ml , i.e. 64% lower compared to the highest loading.

The results, expressed as the released fraction of the total amount of nickel per total amount of nickel loaded, i.e. taking into account the effect of particle loading, show no straightforward tendencies related to particle loading (Fig. 2, dashed lines). The three highest particle loadings (III–V) show an inverse behaviour compared to

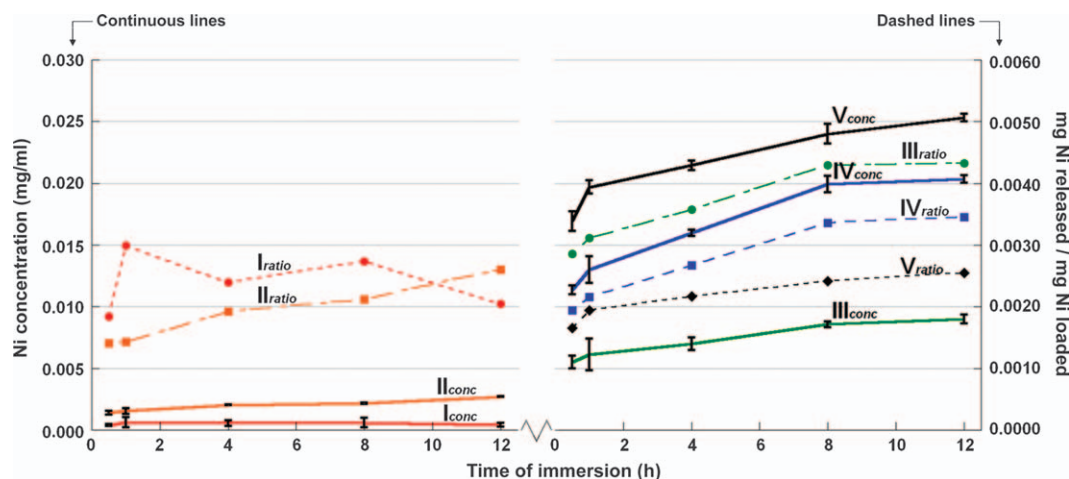


Fig. 2. Total concentration (continuous lines) of nickel released from nickel powder particles immersed in artificial sweat at 30 degree celsius for different time durations for particle loadings, I: 0.1 and II: 0.5 mg/cm^2 (left) and, III: 1, IV: 3 and V: 5 mg/cm^2 (right). Error bars represent the deviation of triplicate samples. The corresponding ratio between the amount of released nickel and the amount of loaded nickel particles are also displayed in each graph (dashed lines).

observations of the nickel concentrations, with the lowest released fraction of nickel for the highest particle loading (Fig. 2, right). For most immersion time intervals, the lowest particle loading (I) resulted in a higher released fraction than the second lowest (II) and the highest particle loading (V) (Fig. 2). For all particle loadings investigated, the results show less than 0.5% of the total amount of loaded nickel to be released into the solution.

Measured release rates of nickel normalized to the surface area of the particles are presented in Fig. 3 (left) for the different loadings of nickel particles immersed in artificial sweat. Generally, the nickel release rate is initially high and decreases with time, reaching a relative steady-state level of $0.1 \mu\text{g}/\text{cm}^2/\text{hr}$ or less for all particle loadings investigated. Loading III ($1 \text{ mg}/\text{cm}^2$) showed the highest release rate throughout the immersion period, in particular during the first hour of immersion. The end-point, in terms of total amount of released nickel, after 12 hr of immersion (Fig. 3, right), clearly shows the range of nickel release from the different particle loadings. The difference in total amount of released nickel is more than 60 times between the lowest (I) and the highest (V) loading.

In order to facilitate comparison and the use of generated data in further risk assessments, nickel release data are compiled in Table 2.

XPS analysis detected oxygen and oxidized nickel in the outermost surface layer on as-received nickel particles, indicative of a nickel oxide surface layer. In addition, the metallic nickel peak was observed, which implies a relatively thin (a few nm) surface oxide layer. The immersion in artificial sweat leads to a slight growth of the oxide film and a possible formation of hydroxides/

oxy-hydroxides. No other contaminants or adsorbed species from the test medium were detected on the surface of the nickel powder.

Discussion

The particle loading, i.e. the amount of nickel powder immersed in artificial sweat, has a significant influence on the released nickel concentration (Fig. 2). The general observation, at a given test volume, is an increasing amount of released nickel with increasing particle loading. This is to be expected because nickel release depends on surface area, which increases with increasing particle loading. As a result, the total surface area available for corrosion-induced release of nickel increases. However, in terms of the released nickel fraction, the highest loadings (III–V) show an inverse trend, i.e. an increasing fraction with decreasing particle loading (Fig. 2, right). For the two lowest particle loadings, there was not a clear trend for nickel release and particle loading. These results suggest that the extent of nickel release relative to the initial loading is influenced by the solution volume to particle surface area ratio. The relative motion/agglomeration of the particles in the artificial sweat is crucial because it influences the available and active surface area of particles in a corrosion-induced metal release process. With higher particle loading, the nickel metal particles may agglomerate, thereby reducing the effective surface area available for release of nickel.

For the low particle loadings (I and II) with a small amount of particles immersed in the artificial sweat solution, agglomeration is less pronounced or negligible. A higher particle loading includes a larger amount of particles, which may

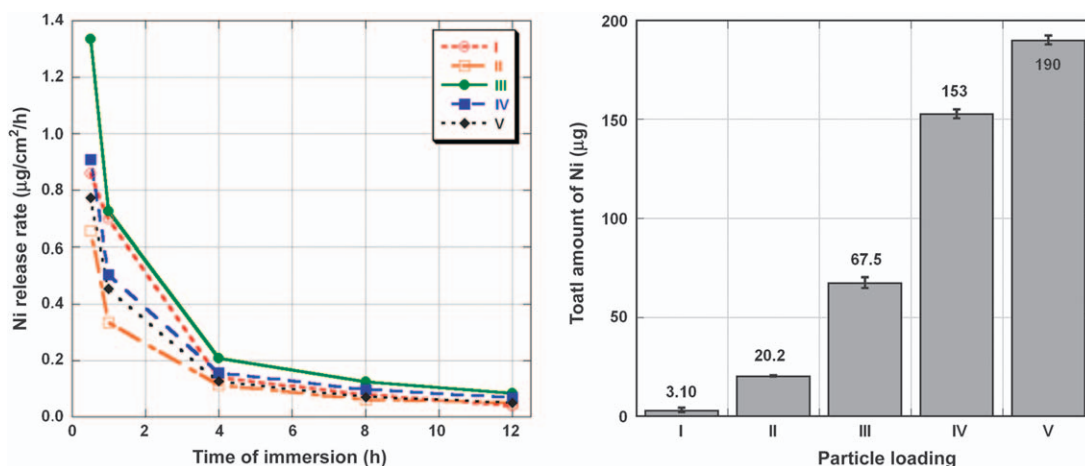


Fig. 3. Release rates of nickel normalized to the surface area of immersed nickel particles for particle loadings, I: 0.1, II: 0.5, III: 1, IV: 3 and V: 5 mg/cm^2 , during immersion in artificial sweat during 12 hr (left). Total amounts of released nickel after 12 hr of immersion in artificial sweat for different particle loadings (right). Error bars represent the deviation between triplicate samples.

Table 2. Released nickel from different particle loadings expressed in terms of concentration, amount of nickel released per bottom surface area of the test vessel and amount of nickel released per surface area of the loaded particles, after 12 hr of immersion in artificial sweat

Particle loading	I	II	III	IV	V
Ni concentration (mg/ml)	0.00041 ± 0.00014	0.00270 ± 0.00004	0.00900 ± 0.00034	0.02037 ± 0.00031	0.02533 ± 0.00031
Ni released bottom area test vessel (mg/cm ²)	0.00021 ± 0.00007	0.00136 ± 0.00002	0.00452 ± 0.00017	0.01023 ± 0.00015	0.01273 ± 0.00015
Ni released particles surface area (mg/cm ²)	0.00048 ± 0.00017	0.00061 ± 0.00004	0.00101 ± 0.00003	0.00081 ± 0.00001	0.00060 ± 0.00001

be more representative for the powder in terms of particle size and other physical/chemical properties. Relatively high levels of total amounts of released nickel from the highest particle loadings (III–V) make the results less sensitive to variations within the powder sample, i.e. particle size and other experimental errors. This may explain the relatively low deviation between the higher particle loadings (III–V). In contrast, for the low particle loadings (I and II) any variation within the powder sample and/or other experimental errors becomes more pronounced in terms of metal release (larger deviation between replicates) because the amount of particles loaded is very small.

Surface area is an important parameter for determining nickel release from nickel powder particles. If it is assumed that the entire surface area of the particles was immersed in the artificial sweat solution and evenly contributed to the released nickel, the amount of nickel released per surface area of the particles should be the same and be independent of particle loading. In reality, the active surface area for nickel release from particles is different from the measured surface area, and depends not only on particle size and surface condition, but also on mixing conditions during the immersion. The initial nickel release rate per surface area of particles, as shown in Fig. 3 (left), differs between different particle loadings. However, the 12-hr nickel release rate is not significantly different for the different loadings.

The surface area also has to be taken into account when comparing nickel release from powders with nickel release from massive sheet surfaces. Increasing particle size results in a decreasing surface area available for corrosion-induced release of nickel. For massive nickel (i.e. sheets, cathodes, etc.), the surface area is small compared to that of nickel particles for the same weight. This difference in release rates for metals as massive sheet or powder form has been acknowledged by the European Union Classification System (23) and United Nations Globally Harmonized System for Classification of Chemicals (24) by allowing for separate environmental classification of massive sheet and powders of the

same metal. Moreover, the composition and thickness of surface films on particles may vary with particle size and differ from that of massive sheet.

The nickel release process is time dependent and approaches a steady-state level (Fig. 3), similar to findings for massive sheet of nickel in artificial rain (25) and in artificial lung fluid (unpublished data). All particle loadings showed initially high release rates that declined towards a lower steady-state level less than 0.1 µg/cm²/hr after 12 hr of immersion. It should be noted that less than 0.5% of the total amount of nickel loaded was released for all particle loadings. Release rates of nickel are in the same order of magnitude as results previously gained for nickel release testing of massive items of different metals and alloys in media mimicking human bodily fluids (16, 17, 26). An important remark is that the alloys have totally different physicochemical properties compared to pure nickel metal.

The nickel oxide surface layer influences the nickel release process. XPS analyses indicate a slow growth of the nickel oxide layer with increasing time of immersion, which partly explains the gradual reduction of release rates with time. No detectable adsorption of species of the artificial sweat solution was seen.

The results of this study can be used in the risk assessment process for direct and prolonged exposure to nickel metal powder, as may be found in certain occupational scenarios (e.g. nickel-producing and nickel-using facilities). The nickel release data can be used to estimate the amount of released nickel available for a given measured dermal exposure to nickel metal powder. This value can then be compared with the dermal nickel elicitation threshold to determine the risk of dermal nickel allergic contact dermatitis in nickel-sensitized individuals in that specific workplace.

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