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Copper and its inorganic compounds

Assessment Values in Biological Material – Translation of the German version from 2017

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Copper and its inorganic compounds

BAT Value Documentation

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Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has evaluated copper (CAS No 7440-50-8) in 2016.
Due to the homeostatic regulation of copper there is no correlation between copper exposure in air and copper in blood or urine. Neither increased inhalation exposure higher than the MAK value of 0.01 mg copper/m^3 nor increased oral supply lead to an increase of copper in blood or urine, even if first signs of exposure such as increased C-reactive protein (CRP) are observed. An additional occupational burden cannot be differentiated from physiological levels of copper. Therefore, the evaluation of a biological tolerance value (BAT value) and a biological reference value ("Biologischer Arbeitsstoff-Referenzwert" (BAR)) for copper and its inorganic compounds is not indicated.

Keywords

copper; copper(I) chloride; copper(II) acetate; copper(II) carbonate; copper(II) chloride; copper(II) hydroxide; copper(II) nitrate; copper(II) oxide; copper(II) oxysulfate; copper(II) sulfate; copper(II) sulfate pentahydrate; BAT value; biological reference value (BAR, "Biologischer Arbeitsstoff-Referenzwert"); occupational exposure; biological tolerance value; toxicity

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Copper and its inorganic compounds

BAT (2016)	**not established**
BAR (2016)	**not established**
MAK value (2013)	**0.01 mg copper/m³ R**
Peak limitation (2013)	Category II, excursion factor 2
Absorption through the skin	–
Sensitization	–
Carcinogenicity	–
Prenatal toxicity (2006)	Pregnancy Risk Group C
Germ cell mutagenicity	–
Synonyms	–
Chemical name	Cu
CAS number	[7440-50-8]
Molecular formula	Cu
Molecular weight	63.55 g/mol
Melting point	1083 °C
Boiling point at 1013 hPa	2595 °C
Density at 20 °C	8.94 g/cm³

Substance	CAS number	Molecular formula	Molecular weight [g/mol]	Solubility in water
Copper	7440-50-88	Cu	63.55	insoluble
Copper(I) chloride	7758-89-6	CuCl	99.00	barely soluble
Copper(II) acetate	142-71-2	$Cu(CH_3–COO)_2$	181.64	soluble
Copper(II) carbonate	1184-64-1	$CuCO_3$	123.56	insoluble
Copper(II) chloride	7447-39-4	$CuCl_2$	134.45	soluble
Copper(II) hydroxide	20427-59-2	$Cu(OH)_2$	97.56	insoluble

Substance	CAS number	Molecular formula	Molecular weight [g/mol]	Solubility in water
Copper(II) nitrate	3251-23-8	$Cu(NO_3)_2$	187.56	soluble
Copper(II) oxide	1317-38-0	CuO	79.55	insoluble
Copper(II) oxysulfate	12158-97-3	$Cu_3O_2SO_4$	318.71	barely soluble
Copper(II) sulfate	7758-98-7	$CuSO_4$	159.61	soluble
Copper(II) sulfate pentahydrate	7758-99-8	$CuSO_4 \cdot 5H_2O$	249.68	soluble

For humans, copper is an essential trace element, a constituent of many proteins and enzymes. The daily intake is between 1 and 4 mg, mainly via the diet (Greim 2004, translated).

Next to aluminium, copper is one of the most widely used non-ferrous metals and is commonly found in nature. Copper is used as raw material in the electrical and construction industry and in machine and apparatus construction. In addition, it is used as active ingredient in pesticides and wood preservatives, in antifoulings, feed additives and in colour pigments.

1 Toxikokinetics and Metabolism

Absorption, distribution, elimination

At the workplace the main route of uptake of metallic copper is via the airways. In addition, by swallowing copper-containing dusts and via food and drinking water, oral ingestion of copper and subsequent absorption in the gastro-intestinal tract are possible. The normal daily intake of copper is considered to be between 0.9 and 4 mg (BfR 2004). Dermal absorption is only of minor importance for the uptake of copper or its inorganic compounds.

The copper concentration in the body is finely regulated. The central organ of the copper homoeostasis is the liver. It is assumed that homoeostastic regulation takes place over a wide intake range of 0.8 to 5.5 mg/day (Itter and Pabel 2013). Copper is eliminated primarily via the bile and thus with the faeces. Excretion in urine is given to be less than 60 µg/day (Harris 1991). Excess supply, however, can result in an increased urinary excretion (WHO 1998). For the biological half-life of copper 13 to 33 days (Bolt 2012) or 20 to 35 days are reported in literature (BfR 2004).

2 Critical Toxicity

Copper is an essential trace element and constituent of many proteins, among others of more than 20 enzymes. To avoid a deficiency, an oral intake of 1–3 mg/day is regarded as necessary (SCOEL 2014). Intake amounts of up to 5 mg/day are considered tolerable (SCF 2003). After inhalation exposure the acute effects described

include irritation of the airways and flu-like or cold-like symptoms ("metal fume fever-like" symptoms).

After repeated inhalation exposure to high levels of metallic copper dust gastro-intestinal symptoms occurred. Apart from these, neurological symptoms (for example headaches, numbness, poor memory, concentration problems) were described. Inflammation of the airways is regarded as critical toxicity after inhalation exposure. An increased oral intake of copper over a longer period of time leads to liver dysfunction. Regarding the hepatotoxicity of copper children are much more sensitive than adults. For the occurrence of systemic toxicity (for example in the liver) a NOAEL of 10 mg copper/day is given for adults (Itter and Pabel 2013). For further information the reader is referred to the MAK documentations (Greim 2004, translated; Hartwig 2014, translated).

3 Exposure and Effects

After occupational inhalation exposure to 0.64–1.05 mg copper/m^3, the plasma copper concentrations in exposed workers did not differ significantly from those of non-exposed control persons (108 ± 4 µg/dl versus 99 ± 3 µg/dl) (Finelli et al. 1981). From this it can be concluded that no dose-dependently increased internal copper concentrations are to be expected up to an inhalation exposure of about 1 mg copper/m^3 (SCOEL 2014).

If the MAK value of 0.01 mg copper/m^3 (R) is adhered, no increased blood copper concentrations are to be expected in comparison with the general population. The derivation of a BAT value for copper is therefore not indicated.

Similarly, after oral ingestion of copper with the drinking water for 2 months, no relationship between the measured copper concentrations in serum and the level of the oral copper exposure (< 0.01 to 6 mg/l drinking water) was found. Independent of the concentrations in serum (estimated mean value about 18 µmol copper/l or 1.14 mg copper/l), however, there was an increase in gastro-intestinal symptoms with increasing copper concentrations (Araya et al. 2003).

Increased internal exposures compared with control persons were found in a study by Afridi et al. (2009). Here, biological materials (blood, urine, hair samples) from 56 production workers, 35 employees in the quality control and 75 non-exposed employees from a Pakistani rolling mill were investigated. Details of external exposure are not given. In all three matrices, however, increased values were found for the employees classified as exposed. The mean values (or the range of values) in blood were 1.85 (1.63–2.36) mg/l for non-exposed employees, 2.97 (2.24–3.66) mg/l for quality control employees, and 3.84 (3.09–4.63) mg/l for production workers. In urine, the values were 0.19 (0.14–0.25) mg/l for non-exposed employees, 0.37 (0.28–0.49) mg/l for quality control employees and 0.53 (0.46–0.62) mg/l for production workers. In the analyzed hair samples the copper levels were 12.2 (11.1–13.3) µg/g, 15.3 (12.8–17.8) µg/g and 17.9 (15.3–19.6) µg/g, respectively. There are no data available for possible effect reactions resulting from the exposures. With regard to the production workers, the study collective with the highest exposure, the authors point to the high proportion of persons (24 of 56 investigat-

ed) with "kidney problems". In addition, 16 of the 56 test persons were reported to have "abnormal liver function".

In an investigation of workers in a Russian copper refinery no association could be established between external copper exposures up to about 2 mg/m³ (inhalable, water soluble fraction) and the urinary excretion of copper (see Figure 1). Depending on the work areas, the mean values in urine samples were 21 µg/l (pyrometallurgy, 71 workers, 267 samples) and 18 µg/l (electrorefinery, 56 workers, 220 samples). There are no data available for possible effect reactions in exposed employees (Nieboer et al. 2007).

As part of an experimental study on the occurrence of signs of systemic inflammation after inhalation of zinc- or copper-containing welding fumes, 15 test persons were exposed to welding fumes containing either zinc, zinc and copper (Zn/Cu) or only copper (Cu) for 6 hours each. An additional physical strain was simulated with the help of a bicycle ergometer (performance 80 W for 10 minutes, once per hour each). Based on the PM_{10} fraction the mean air concentrations of copper in the two exposures involving copper were 0.65 mg/m³ (Zn/Cu) and 0.41 mg/m³ (only Cu). In blood samples of the test persons, taken before and 24 hours after the exposures, the inflammation marker CRP was significantly increased (Markert et al. 2016). In addition, to investigate the internal copper exposure of the test persons, the copper concentrations were determined in spontaneous urine samples obtained before and immediately after the exposure as well as 24 hours after the exposure. Compared with initial mean urinary copper concentrations of 11.6 µg/l ± 7.5 µg/l (exposure to Zn/Cu) and 10.7 µg/l ± 6.2 µg/l (exposure to Cu only) no increase in the internal exposure to copper was found either after 6 hours (mean values 8.6 ± 2.6 and 8.2 ± 4.7 µg/l, respectively) or after 24 hours (10.8 ± 3.2 and 12.1 ± 8.9 µg/l, respectively). With mean values between 5.8 and 6.7 µg/g creatinine, the measured values at the three sampling times and for the different exposure scenarios levelled off even more when related to creatinine (Kraus 2015). The present external copper exposure which, via local effects, is responsible for the increase in the effect marker, is not reflected in an increase in systemic internal exposure (Markert et al. 2016).

4 Selection of the Indicators

The detection of copper is possible in blood, serum or plasma and in urine. The biomarkers copper in serum or copper in urine are used in clinico-chemical examinations to demonstrate pathological disorders in copper storage (for example Morbus Wilson, Menkes syndrome) or diet-related copper deficiency. In addition, increased copper concentrations in serum can occur with various diseases (for example liver cirrhosis, inflammation, diverse tumours).

While, for determinations in blood or urine, a database for an evaluation of the results is in principle available, this applies only to a very limited extent to analytical results in hair samples. The few available studies show a wide variation of copper concentrations in not occupationally exposed persons (SCOEL 2014). Copper is predominantly excreted via the bile. Its renal elimination is estimated to be less than

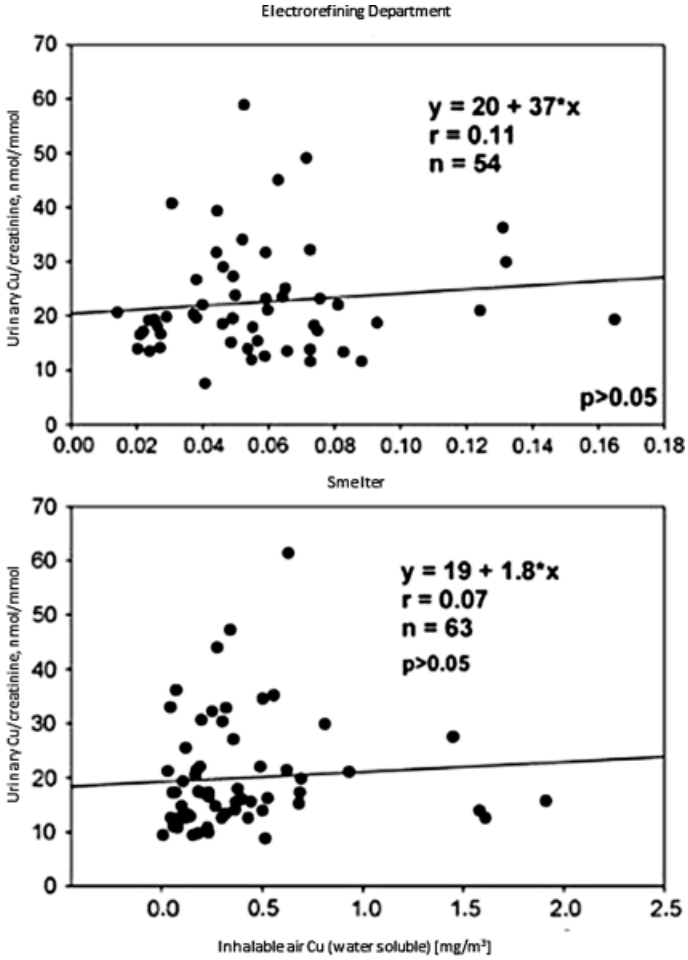

Figure 1 Plots of urinary Cu versus the inhalable water-soluble Cu subfraction for workers in the electrorefinery and smelter departments (from Nieboer et al. 2007 with permission of the Royal Society of Chemistry)

60 µg/day (Harris 1991). Therefore, the urinary copper concentration appears to be suitable to only a limited extent as indicator of internal exposure (WHO 1998). In normal individuals, concentrations in urine are less by a factor of 50–60 than the corresponding concentrations in blood (compare Krause et al. 1996). Because of the described homoeostatic regulation of copper its concentration in blood, and also in urine, should be independent of copper supply.

5 Analytical Methods

Tested methods are available for the analysis of copper in biological materials. Determination is possible with procedures including electrothermal (graphite furnace) atomic absorption spectrometry (GF-AAS) or inductively coupled plasma quadrupole mass spectrometry (ICP/MS) (Angerer et al. 1985; Schramel et al. 2000, translated; Winter et al. 1985). For quality control of the analysis, corresponding control materials are commercially available. External quality assurance is possible for example by participation in the external quality assessment scheme and certification for occupational-medical and environmental-medical toxicological analyses in biological materials (G-EQUAS) of the German Society of Occupational and Environmental Medicine.

6 Background Exposure

There are great variations in the background exposure of the general population (SCOEL 2014). Analytical results for the determination of copper in blood of the general population are shown in Table 1. It has to be taken into consideration that most of the data are mean values and only to a very limited extent suitable for the derivation of a biological reference value (BAR, Biologischer Arbeitsstoff-Referenzwert). Almost all studies show that copper concentration levels in the blood of women are higher than those in the blood of men.

The most reliable data for Germany are from the German Environmental Survey carried out from 1990 to 1992 (n = 3968, Krause et al. 1996). For the 95th percentile of copper exposure in blood 1.5 mg/l was given for women and 1.1 mg/l for men. The analytical results for the determination of copper in the urine of the general population are summarized in Table 2. The values given are mostly in the range up to about 25 µg/l urine. Relatively good agreement was found between the results of the studies by Ohashi et al. (2006), Heitland and Köster (2006) and Krause et al. (1996), which gave mean values of 9–15 µg/l for adults. As was already found for copper concentrations in blood, several studies also revealed a trend toward higher urinary copper levels in women than in men. On the basis of the data from the German Environmental Survey (n = 4002, Krause et al. 1996), the 95th percentile for copper excretion in urine is 24.6 µg/l for women and 20.4 µg/l for men. The creatinine-related values of the 95th percentile are 22.9 µg/g creatinine for women and 13.1 µg/g creatinine for men.

Table 1 Data for copper concentrations in blood

Author	Year	Country	Collective	n	Matrix	Copper concentrations in blood		
						MV ± SD	Range	95th percentile
Karadaq et al. 2004	2004	Turkey	COPD patients	26 ♂ 24/♀ 2	serum	mild COPD (n = 15): 1.02 ± 0.26 mg/l severe COPD (n = 11): 1.13 ± 0.27 mg/l		
			controls	24 ♂ 22/♀ 2		0.92 ± 0.19 mg/l		
Koureme-nou-Dona et al. 2006	2006	Greece	healthy blood donors (18–60 years)	506 ♂ 414 ♀ 92	serum	1.155 ± 0.236 mg/l 1.130 ± 0.220 mg/l 1.268 ± 0.271 mg/l	0.44–2.35 mg/l 0.44–2.02 mg/l 0,67–2.35 mg/l	
Krause et al. 1996	1990–1992	Germany	general population adults (25–69 years)	3968 ♂ 1939 ♀ 2029	blood	0.97 mg/l 0.89 mg/l 1.04 mg/l		1.3 mg/l 1.1 mg/l 1.5 mg/l
Rükgauer et al. 1997	1997	Germany	blood donors (22–75 years)	68	plasma	16.5 ± 4.3 µmol/l *1.05 ± 0.27 mg/l* [1)]	9.2–31.9 µmol/l *0.58–2.03 mg/l* [1)]	
Sánchez et al. 2010	2010	southern Spain	general population	340 ♂ 167 ♀ 173	plasma	1.37 ± 0.48 mg/l 1.31 ± 0.47 mg/l 1.42 ± 0.49 mg/l (♂ vs. ♀; $p < 0.05$)		
Terrés-Martos et al. 1997	1997	Spain	general population	84 ♂ 33 ♀ 51	serum	1.10 ± 0.32 mg/l 1.11 ± 0.25 mg/l 1.09 ± 0.36 mg/l	0.30–2.00 mg/l 0.65–1.76 mg/l 0.30–2.00 mg/l	

[1)] calculated
Abbreviations: MV = mean value; SD = standard deviation

Table 2 Data for urinary copper levels in the general population

Author	Country	n	Copper concentration in urine			Method
			MV ± SD	Range	95th percentile	
Peretz et al. 1989	Belgium	28	0.31 µmol/g crea 19.7 µg/g crea[1)]	0.09–0.78 µmol/g crea 5.7–49.5 µg/g crea[1)]		GF-AAS
Cornelis et al.1975	Belgium	9		11.5–34 µg/day		NAA
Minoia et al. 1990	Italy	507	23 ± 6.9 µg/l	4.2–75 µg/l	reference range 4.2–50 µg/l	GF-AAS, NAA
Kolachi et al. 2011	Pakistan	177				F-AAS
		♂ 82 ♀ 95	160 ± 30 µg/l 170 ± 40 µg/l			
Benes et al. 2002	Czech Republic	1192	21.9 µg/g crea	0.4–331 µg/g crea	94.1 µg/g crea	GF-AAS
		♂ 816 ♀ 376	(significant difference ♂/♀)			
Rodriguez and Diaz 1995	Tenerife/Spain	97 ♂ 46 ♀ 51	22.68 ±0.99 µg/l 23.34 ± 1.63 µg/l 22.02 ± 1.16 µg/l	5.81–47.42 µg/l 5.81–47.42 µg/l 7.21–36.78 µg/l		F-AAS
Ohashi et al. 2006	Japan	1000 only ♀	14.9 µg/l (median) 12.0 µg/g crea (median)	0.58–70 µg/l 0.60–163 µg/g crea		GF-AAS
Heitland and Köster 2006	Germany (west/north)	87 (18–65 years)	9 µg/l	4–30 µg/l	13 µg/l	ICP-MS
Schuhmacher et al. 1994	Spain	434	GM: 26.6 µg/g crea GM: 39.0 µg/l			ICP-AES

Table 2 (continued)

Author	Country	n	Copper concentration in urine			Method
			MV ± SD	Range	95th percentile	
Krause et al. 1996	Germany	4002 (25–69 years)	11.64 µg/l		22.9 µg/l	GF-AAS
		♂ 1955 ♀ 2047	10.48 µg/l 12.75 µg/l		20.4 µg/l 24.6 µg/l	

[1)] calculated
Abbreviations:
MV = mean value
GM = geometric mean
SD = standard deviation
crea = creatinine
GF-AAS = graphite furnace atomic absorption spectrometry
NAA = neutron activation analysis
F-AAS = flame atomic absorption spectrometry
ICP-MS = inductively coupled plasma mass spectrometry
ICP-AES = inductively coupled plasma atomic emission spectroscopy

7 Evaluation

With regard to the studies described in Section 3, it is to be assumed that, due to homoeostatic regulation over a wide exposure range, there is no relationship between external exposure to copper and its concentrations measurable in biological materials. Neither increased inhalation exposure much higher than the currently valid MAK value of 0.01 mg copper/m^3 nor increased oral supply lead to an increase of copper in possible biological exposure indicators. In addition, the main effect is a local toxicity which cannot be demonstrated by a systemic effect (increased copper concentration). It is not possible to differentiate an additional occupational burden from physiological levels of copper by biological monitoring. Therefore, the evaluation of a biological tolerance value (BAT value) and a biological reference value ("Biologischer Arbeitsstoff-Referenzwert" (BAR)) based on the copper concentrations in blood or urine is not indicated.

Neither a BAT value nor a BAR are therefore established for copper and its inorganic compounds.

8 Interpretation of Data

As an essential trace element copper is subject to close homoeostatic regulation. Thereby, increased or reduced supply are balanced. Measurable changes in the copper concentrations in blood or in renal elimination only occur if the adaptability of the organism is not or no longer given. This may be the case with certain diseases; however, it has not been observed to date even in the case of occupational exposure above the valid threshold limit value. Even if, on the basis of the relatively comprehensive data available for copper concentrations in the blood and urine of the German general population, a reference range could be established, this range would hardly be suitable to identify persons with a work-related, increased copper burden.

9 References

Afridi HI, Kazi TG, Kazi NG, Jamali MK, Arain MB, Sirajuddin Kandhro GA, Shah AQ, Baig JA (2009) Evaluation of arsenic, cobalt, copper and manganese in biological samples of steel mill workers by electrothermal atomic absorption spectrometry. Toxicol Ind Health 25: 59–69

Angerer J, Knecht U, Winter L, Fleischer M, Arbeitsgruppe „Analysen in biologischem Material" (1985) Kupfer. Bestimmung in Serum und Harn. Flammenlose Atomabsorptionsspektrometrie. In: Angerer J, Schaller KH, Henschler D (Eds.) Analytische Methoden zur Prüfung gesundheitsschädlicher Arbeitsstoffe, Band 2: Analysen in biologischem Material, 8. Lieferung, VCH, Weinheim

Araya M, Olivares M, Pizarro F, González M, Speisky H, Uauy R (2003) Gastrointestinal symptoms and blood indicators of copper load in apparently healthy adults undergoing controlled copper exposure. Am J Clin Nutr 77: 646–650

Benes B, Spevackova V, Smid J, Cejchanova M, Kaplanova E, Cerna M, Gajewska V, Blatny J (2002) Determination of normal concentration levels of Cd, Pb, Hg, Cu, Zn and Se in urine of the population in the Czech Republic. Cent Eur J Publ Health 10: 3–5

BfR (Bundesamt für Risikobewertung) (2004) Risikobewertung von Kupfer. In: Domke A, Großklaus R, Niemann B, Przyrembel H, Richter K, Schmidt E, Weißenborn A, Wörner B, Ziegenhagen R (Eds.) Verwendung von Mineralstoffen in Lebensmitteln – Toxikologische und ernährungsphysiologische Aspekte, Part II. BfR Wissenschaft, Berlin, 279–291

Bolt HM (2012) Toxikokinetische Grundlagen. In: Triebig G, Drexler H, Letzel S, Nowak D (Eds.) Biomonitoring in Arbeitsmedizin und Umweltmedizin, Orientierungshilfe für Betrieb, Praxis und Klinik, Schwerpunktthema Jahrestagung DGAUM 2011, ecomed MEDIZIN, Heidelberg, München, Landsberg, Frechen, Hamburg, 23–27

Cornelis R, Speecke A, Hoste J (1975) Neutron activation analysis for bulk and trace elements in urine. Analyt Chim Acta 78: 317–327

Finelli VN, Boscolo P, Salimei E, Messineo A, Carelli G (1981) Anemia in men occupationally exposed to low levels of copper. In: International Conference Heavy Metals in the Environment, Amsterdam – September 1981, CEP Consultants Ltd, Edinburgh, UK, 475–478

Greim H (Ed.) (2004) Kupfer und seine anorganischen Verbindungen. Gesundheitsschädliche Arbeitsstoffe, Toxikologisch-arbeitsmedizinische Begründungen von MAK-Werten, 39. Lieferung, Wiley-VCH, Weinheim

Hamilton EI, Sabbioni E, van der Venne MT (1994) Element reference values in tissues from inhabitants of the European Community. VI. Review of elements in blood, plasma and urine and a critical evaluation of reference values for the United Kingdom population. Sci Total Environ 158:165–190

Harris ED (1991) Copper transport: an overview. Proc Soc Exp Biol Med 196: 130–140

Hartwig A (2014) Kupfer und seine anorganischen Verbindungen. Gesundheitsschädliche Arbeitsstoffe, Toxikologisch-arbeitsmedizinische Begründungen von MAK-Werten, 57. Lieferung, Wiley-VCH, Weinheim

Heitland P, Köster HD (2006) Biomonitoring of 30 trace elements in urine of children and adults by ICP-MS. Clin Chim Acta 365: 310–318

Itter H, Pabel U (2013) Toxikologie von Blei, Kupfer und Zink. Symposium "Alles Wild?" am BfR, 18.03.2013,
http://www.bfr.bund.de/cm/343/toxikologie-von-blei-kupfer-und-zink.pdf (last accessed on December 5, 2017)

Karadag F, Cildag O, Altinisik M, Kozaci LD, Kiter G, Altun C (2004) Trace elements as a component of oxidative stress in COPD. Respirology 9: 33–37

Kolachi NF, Kazi TG, Afridi HI, Kazi N, Kandhro GA, Shah AQ, Baig JA, Wadhwa SK, Khan S, Shah F, Jamali MK, Arain MB (2011) Distribution of copper, iron, and zinc in biological samples (scalp hair, serum, blood, and urine) of Pakistani viral hepatitis (A–E) patients and controls. Biol Trace Elem Res 143: 116–130

Kouremenou-Dona E, Dona A, Papoutsis J, Spiliopoulou C (2006) Copper and zinc concentrations in serum of healthy Greek adults. Sci Total Environ 359: 76–81

Kraus T (2015) Kammerversuche bei Schweißern. E-Mail an die Kommission vom 06.07.2015 [Email to the Commission dated 6 July 2015]

Krause C, Babisch W, Becker K, Bernigau W, Helm D, Hoffmann K, Nöllke P, Schulz C, Schwabe R, Seiwert M, Thefeld W (1996) Umwelt-Survey 1990/92, Band 1a: Studienbeschreibung und Human-Biomonitoring: Deskription der Spurenelementgehalte in Blut und Urin der Bevölkerung in der Bundesrepublik Deutschland, Umweltbundesamt, WaBoLu-Heft 1/96, Berlin, 135–151 (Kupfer im Blut), 277–306 (Kupfer im Urin)

Markert A, Baumann R, Gerhards B, Gube M, Kossack V, Kraus T, Brand P (2016) Single and combined exposure to zinc- and copper-containing welding fumes lead to asymptomatic systemic inflammation. J Occup Environ Med 58:127–132

Minoia C, Sabbioni E, Apostoli P, Pietra R, Pozzoli L, Gallorini M, Nicolaou G, Alessio L, Capodaglio E (1990) Trace element reference values in tissues from inhabitants of the European community. I. A study of 46 elements in urine, blood and serum of Italian subjects. Sci Total Environ 95: 89–105

Nieboer E, Thomassen Y, Romanova N, Nikonov A, Odland JØ, Chaschin V (2007) Multicomponent assessment of worker exposures in a copper refinery. Part 2: Biological exposure indices for copper, nickel and cobalt. J Environ Monit 9: 695–700

Ohashi F, Fukui Y, Takada S, Moriguchi J, Ezaki T, Ikeda M (2006) Reference values for cobalt, copper, manganese, and nickel in urine among women of the general population in Japan. Int Arch Occup Environ Health 80: 117–126

Peretz A, Neve J, Famaey JP (1989) Effects of chronic and acute corticosteroid therapy on zinc and copper status in rheumatoid arthritis patients. J Trace Elem Electrolytes Health Dis 3: 103–108

Rodriguez E, Diaz C (1995) Iron, copper and zinc levels in urine: relationship to various individual factors. J Trace Elem Med Biol 9: 200–209

Rükgauer M, Klein J, Kruse-Jarres JD (1997) Reference values for the trace elements copper, manganese, selenium, and zinc in the serum/plasma of children, adolescents, and adults. J Trace Elem Med Biol 11: 92–98

Sánchez C, López-Jurado M, Aranda P, Llopis J (2010) Plasma levels of copper, manganese and selenium in an adult population in southern Spain: influence of age, obesity and lifestyle factors. Sci Total Environ 408: 1 014–1 020

Schramel P, Dunemann L, Caroli S, Emons H, Arbeitsgruppe „Analysen in biologischem Material" (2000) Aluminium, Chrom, Cobalt, Kupfer, Mangan, Molybdän, Nickel, Vanadium. Bestimmung in Harn. Inductively Coupled-Plasma-Quadrupol-Massenspektrometrie (hochauflösend). In: Angerer J, Schaller KH, Greim H (Eds.) Analytische Methoden zur Prüfung gesundheitsschädlicher Arbeitsstoffe, Band 2: Analysen in biologischem Material, 14. Lieferung, Wiley-VCH, Weinheim

SCF (Scientific Committee on Food) (2003) Opinion of the Scientific Committee on Food on the tolerable upper intake level of copper. SCF/CS/NUT/UPPLEV/57 Final

Schuhmacher M, Domingo JL, Corbella J (1994) Zinc and copper levels in serum and urine: relationship to biological, habitual and environmental factors. Sci Total Environ 148: 67–72

SCOEL (Scientific Committee on Occupational Exposure Limits) (2014) Recommendation from the Scientific Committee on Occupational Exposure limits for copper and its inorganic compounds. SCOEL/SUM/171

Terrés-Martos C, Navarro-Alarcón M, Martín-Lagos F, López-G de la Serrana H, López-Martínez MC (1997) Determination of copper levels in serum of healthy subjects by atomic absorption spectrometry. Sci Total Environ 198: 97–103

WHO (World Health Organisation) (1998) Copper. Environmental Health Criteria 200, Geneva http://www.inchem.org/documents/ehc/ehc/ehc200.htm (last accessed on December 5, 2017)

Winter L, Schaller KH, Arbeitsgruppe „Analysen in biologischem Material" (1985) Kupfer. Bestimmung im Serum. Atomabsorptionsspektrometrie. In: Angerer J, Schaller KH, Henschler D (Eds.) Analytische Methoden zur Prüfung gesundheitsschädlicher Arbeitsstoffe, Band 2: Analysen in biologischem Material, 8. Lieferung, VCH, Weinheim

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