BRONZE POWDER

SYNONYMS

Zinc;

Asarco L 15
Blue powder
Emanay zinc dust
Granular zinc
Jasad, LS 2, LS 6
Lead refinery vacuum zinc
Merrillite, Rheinzink
UNII-J41CSQ7QDS
Zinc
Zinc dust
Zinc powder

Copper;

Allbri Natural Copper
Allbri natural copper
Anode copper
Blister copper
C 100 (metal)
C.I. 77400
C.I. Pigment Metal 2
CI Pigment metal 2
CU M3
Cathode copper
Copper
Copper M 1
Copper bronze
Copper powder
Copper slag-airborne
Copper
Cuprum
Cutox 6010
Electrolytic refinery billet copper
Gold bronze

CHEMICAL STRUCTURE

An alloy of copper and zinc (brass), often with impurities of other metals such as aluminium and tin.

CHEMICAL FORMULA

Metallic crystalline lattice structure

IDENTIFIER DETAILS

CAS Number : 7440-66-6 (***zinc***) and 7440-50-8 (***copper***)
CoE Number : -
FEMA : -
EINECS Number : 231-175-3 **(*zinc***) and 231-159-6 (***copper***)
E Number : -

SPECIFICATIONS

Melting Point: Zinc 420ºC and Copper 1083 ºC [Jones & Atkins, 1999]

Boiling point: Zinc 2567ºC and Copper 1083 ºC [Jones & Atkins, 1999]

STATUS IN FOOD AND DRUG LAWS

CoE limits:

Beverages (mg/kg)	Food (mg/kg)	Exceptions (mg/kg)
-	-	-

Acceptable Daily Intake:

ADI (mg/kg)	ADI Set by	Date Set	Comments
0.3-1.0 (*Zinc)*	JECFA	1982	Provisional daily dietary requirement / maximum tolerable daily intake.
0.05-0.5 (*Copper*)	JECFA	1982	Provisional daily dietary requirement / maximum tolerable daily intake

FDA Status: [CFR21]

Section Number	Comments
73	**Listing of colour additives exempt from certification**
73.1646	Bronze powder (under subpart B - Drugs)
73.2646	Bronze powder (under subpart C - Cosmetic)

HUMAN EXPOSURE

Natural Occurrence: Brass is any alloy of copper and zinc; the proportions of zinc and copper can be varied to create a range of brasses with varying properties. Consequently, brass does not occur in nature.

TOXICITY DATA

Zinc

Organism	Test type	Route	Reported dose	Effect	Source
Duck	LDLo	Oral	388mg/kg	AUTONOMIC NERVOUS SYSTEM: OTHER (DIRECT) PARASYMPATHOMIMETIC BEHAVIORAL: ATAXIA BLOOD: CHANGES IN LEUCOCYTE (WBC) COUNT	Journal of Wildlife Diseases. Vol. 36, Pg. 111, 2000.
Human	TCLo	Inhalation	124mg/m3/50M	LUNGS, THORAX, OR RESPIRATION: COUGH LUNGS, THORAX, OR RESPIRATION: DYSPNEA SKIN AND APPENDAGES (SKIN): SWEATING: OTHER	Archiv fuer Hygiene. Vol. 72, Pg. 358, 1910.

[ToxNet, 2009]

Copper

Organism	Test type	Route	Reported dose	Effect	Source
Human	TDLo	Oral	120ug/kg	GASTROINTESTINAL: NAUSEA OR VOMITING	Public Health Reports. Vol. 73, Pg. 910, 1958.
Mouse	LD50	Intraperitoneal	3500ug/kg		"Patty's Industrial Hygiene and Toxicology," 3rd rev. ed., Clayton, G.D., and F.E. Clayton, eds., New York, John Wiley & Sons, Inc., 1978-82. Vol. 3 originally pub. in 1979; pub. as 2n rev. ed. in 1985.Vol. 2A, Pg. 1623, 1981.
Rabbit	LDLo	Subcutaneous	375mg/kg	LIVER: "HEPATITIS (HEPATOCELLULAR NECROSIS), ZONAL" LIVER: OTHER CHANGES KIDNEY, URETER, AND BLADDER: OTHER CHANGES	American Journal of Pathology. Vol. 1, Pg. 117, 1925.

[ToxNet, 2009]

In Vivo Toxicity Status

Carcinogenicity and Mutagenicity

No specific data identified

Dermal Toxicity

No specific data identified

Reproductive and Developmental toxicity

No specific data identified

Inhalation Toxicity

The effects of a single acute exposure to inhaled brass dust on rat pulmonary alveolar macrophages (PAM) were investigated by Anderson et al., (1988). Pulmonary alveolar macrophages lavaged from the lungs of these experimental animals showed both morphological and functional abnormalities. Exposure to brass dust caused a rapid, transient inflammatory response, producing an influx of polymorphonuclear leukocytes into the lavage fluid. Binucleation and multinucleation of PAM were sensitive morphological indicators of pulmonary stress that persisted throughout the 14-day course of the experiment. Pulmonary alveolar macrophages from rats exposed to brass dust were phagocytically activated; both the total numbers of test particulates ingested and the phagocytic index were elevated. Chemotaxis, as measured by direct cellular migration in Boyden chambers, was inhibited for 3 days after exposure, but was markedly stimulated from 7 to 14 days. This was interpreted as a possible consequence of a selective release of lymphokines during the course of the inflammatory response. Some of these results, based on in vivo exposure of PAM to inhaled particulates, differ from those derived from in vitro exposure. The authors suggest that this points to the fact that it is virtually impossible to duplicate the native chemical microenvironment of PAM in vitro and emphasizes the necessity of bringing about PAM-particle interactions in the intact lung in order to obtain more physiologically relevant data.

Donoso et al., (2007) report on a previously healthy 2-year-old female patient who had unintentionally inhaled copper dust, developed respiratory failure a few hours later, and required mechanical ventilation. On hospital day three, the patient developed acute respiratory distress syndrome and was treated with high-frequency oscillatory ventilation for six days. She also developed hemolytic anemia, liver failure, oliguric renal failure, and evidence of acute tubular injury. During her stay in the intensive care unit she received inotropic support, packed red cells transfusion, and diuretics. A sample of bronchoalveolar lavage showed macrophages that stained positive for copper.

Serum and urine copper concentrations were within the normal range after several days. Extubation was successfully achieved after two weeks and the patient was discharged on day 30 without sequelae. This is the first report of acute respiratory distress syndrome secondary to copper aspiration in a pediatric patient. The authors conclude that this is the first case reported of acute respiratory distress syndrome secondary to elemental copper aspiration. Consequently they suggest that it is important for the clinician to be aware of acute respiratory distress syndrome as a differential diagnosis to copper aspiration by treating the patient aggressively in an adequate clinical setting.

Respiratory toxicity of copper was tested by Romeu-Moreno et al., (1994) in Wistar rats by spraying copper sulfate (330 g/l spray) for daily periods of 1 hr in a self-contained chamber for up to 10 days. The respiratory toxicity was compared with that from intraperitoneal administration of 1 mg Cu/mg body weight and with adequate control rats. Analysis of tissue Cu and Zn was done in lung, liver, kidney, and plasma by using atomic absorption spectrophotometry. Similar organ and subcellular distribution of both elements were found between the two treated groups, and only statistically significant higher levels of Cu were found in plasma and liver. The authors reported that following exposure, Cu and Zn were associated with a low-molecular-weight component, which eluted as metallothionein in the postmicrosomal fractions.

In a study conducted by Luo et al., (2009) the inflammatory responses and oxidative stress from metal fume exposure in an automobile plant was investigated. The authors recruited 258 automobile workers and measured the urine zinc, copper, and nickel to determine the exposure level, and examined the white blood cells, and IL-6 as inflammatory responses to the metal fume exposure. We also examined the relationship between glutathione (GSH) and metals exposure. There were significant association between urine metals levels and welding hours. Zinc was significantly associated with blood white cells, interleukin-6, and GSH. Copper was significantly associated with GSH, but nickel was significantly inversely associated with GSH. The authors concluded that automobile welders appear to have significant metals exposure. White blood cells and IL-6 might be involved in inflammatory process of zinc fume exposure with zinc and copper increasing GSH, but nickel depleting it.

Cavallari et al., (2008) reports that there is evidence to suggest that metals play a role in the cardiotoxicity of fine PM (PM2.5) and in exposure-related decreases in heart rate variability (HRV). We examined the association between daytime exposure to the metal content of PM2.5 and night HRV in a panel study of boilermaker construction workers exposed to metal-rich welding fumes. Twenty-six male workers were monitored by ambulatory electrocardiogram (ECG) on a workday while exposed to welding fume and a non-workday (baseline). From the ECG, rMSSD (square root of the mean squared differences of successive intervals) was summarized over the night (0:00-7:00). Workday, gravimetric PM2.5 samples were analyzed by x-ray fluorescence to determine metal content. The authors used linear mixed effects models to assess the associations between night rMSSD and PM2.5

metal exposures both with and without adjustment for total PM2.5. Matched ECG measurements from the non-workday were used to control for individual cardiac risk factors and models were also adjusted for smoking status. To address collinearity between PM2.5 and metal content, we used a two-step approach that treated the residuals from linear regression models of each metal on PM2.5 as surrogates for the differential effects of metal exposures in models for night rMSSD. RESULTS: The median PM2.5 exposure was 650 microg/m3; median metal exposures for iron, manganese, aluminum, copper, zinc, chromium, lead, and nickel ranged from 226 microg/m3 to non-detectable. We found inverse linear associations in exposure-response models with increased metal exposures associated with decreased night rMSSD. A statistically significant association for manganese was observed, with a decline of 0.130 msec (95% CI: -0.162, -0.098) in night rMSSD for every 1 microg/m3 increase in manganese. However, even after adjusting for individual metals, increases in total PM2.5 exposures were associated with declines in night rMSSD. The authors conclude that the results support the cardiotoxicity of PM2.5 metal exposures, specifically manganese. However the metal component alone did not account for the observed declines in night HRV. Therefore, results suggest the importance of other PM elemental components.

In a study conducted by Huang et al., (2008) the effects of white smoke inhalation on lung tissue was investigated. Twenty patients accidentally been exposed to white smoke during military training were the subjects of this study. The authors analyzed clinical manifestations, cytokine changes, and treatment outcomes. All patients initially presented with fever, dry cough, chest tightness, and shortness of breath. Twenty-five percent of these patients had severe acute lung injury requiring artificial ventilation support. Elevation of serum tumor necrosis factor-alpha was observed before treatment with antibiotics and glucocorticoids, but the elevation of transforming growth factor-beta(1) was delayed for 2 to 4 weeks after the accident. All the patients had leukocytosis, which correlated positively to disease severity and negatively to intensive treatments. Ninety-five percent of patients had varying degrees of restrictive ventilation impairment, and 85% of these patients had a significantly reduced diffusion capacity in the lungs. Seventy percent of these patients had transient impairment of liver function, which did not correlate to disease severity. The respiratory sequela of restrictive ventilation impairment developed in the most severely affected patients, whereas other tissue toxicities were mostly transient. Treatment included glucocorticoids, antibiotics, and respiratory therapy. All of the patients survived. The authors conclude that a proper ventilation strategy, early pharmacologic therapy including glucocorticoids, and complication prevention may contribute to good treatment outcomes after white smoke inhalation.

Gilmour et al., (2006) reports that it was recently demonstrated that particulate matter (PM) containing water-soluble zinc produces cardiac injury following pulmonary exposure. To investigate whether pulmonary zinc exposure produces systemic metal imbalance and direct cardiac effects, male Wistar Kyoto (WKY) rats (12-14 wk age) were intratracheally (IT) instilled with saline or 2 micromol/kg zinc sulfate. Temporal analysis was performed for systemic

levels of essential metals (zinc, copper, and selenium), and induction of zinc transporter-2 (ZT-2) and metallothionein-1 (MT-1) mRNA in the lung, heart, and liver. Additionally, cardiac gene expression profile was evaluated using Affymetrix GeneChips (rat 230A) arrays to identify zinc-specific effects. Pulmonary zinc instillation produced an increase in plasma zinc to approximately 20% at 1 and 4 h postexposure with concomitant decline in the lung levels. At 24 and 48 h postexposure, zinc levels rose significantly (approximately 35%) in the liver. At these time points, plasma and liver levels of copper and selenium also increased significantly, suggesting systemic disturbance in essential metals. Zinc exposure was associated with marked induction of MT-1 and ZT-2 mRNA in lung, heart, and liver, suggesting systemic metal sequestration response. Given the functional role of zinc in hundreds of proteins, the gene expression profiles demonstrated changes that are expected based on its physiological role. Zinc exposure produced an increase in expression of kinases and inhibition of expression of phosphatases; up- or downregulation of genes involved in mitochondrial function; changes in calcium regulatory proteins suggestive of elevated intracellular free calcium and increases in sulfotransferases; upregulation of potassium channel genes; and changes in free radical-sensitive proteins. Some of these expression changes are reflective of a direct effect of zinc on myocardium following pulmonary exposure, which may result in impaired mitochondrial respiration, stimulated cell signaling, altered Ca2+ homeostasis, and increased transcription of sulfotransferases. Cardiotoxicity may be an outcome of acute zinc toxicosis and occupational exposures to metal fumes containing soluble zinc. Imbalance of systemic metal homeostasis as a result of pulmonary zinc exposure may underlie the cause of extrapulmonary effects.

It is reported by Riley et al., (2003) that the inhalation of combustion-derived particulate matter can have a variety of negative impacts on human health. Metals are known to play a substantial role in these effects, however, the interactions between cellular responses caused by multiple metals is not well understood. The impact of metals (Zn, Cu, Ni, V, and Fe) individually and in combination on a rat lung epithelial cell line (RLE-6TN) was evaluated. Quantifications involved measurement of inhibition of cell culture metabolism (mitochondrial succinate dehydrogenase activity), cell death, mechanisms of cell death, and cytokine secretion. The ranking of metal toxicity based on TC(50) values is V>Zn>Cu>Ni>Fe. Interactions were observed for exposures containing multiple metals: Zn+V, Zn+Cu, Zn+Fe, and Zn+Ni. Zn appears to diminish the negative impact of V and Cu; has an additive effect with Ni, and has no substantial effect on Fe toxicity.

Other Relevant Studies

In a study conducted by Unsal et al., (2008) the protective effects of zinc on halothane induced hepatotoxicity was investigated. Forty-five male Sprague-Dawley rats were divided into three groups. The halothane group received normal drinking water and diet; the zinc-halothane group received 227 mg L(-1) zinc sulphate in the drinking water and diet for 2 weeks; and the control group received normal diet and water. At the end of 2 weeks, rats were housed in an anaesthesia box and 1 MAC (minimum alveolar

concentration)halothane was administered at 6 L min(-1) in room air for 2 h. This was repeated 48 h later. After the rats were sacrificed, we measured alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, gammaglutamyl transpeptidase, glutathione-S-transferase, serum electrolytes and bilirubin in samples. The degree of liver toxicity was assessed by light microscopic examination. The authors demonstrated a reduction of alanine aminotransferase, aspartate amino transferase, glutathione-S-transferase levels and a reduction in liver damage in the zinc-halothane group. The authors conclude that zinc has the potential to alleviate the toxic effects of halothane in rat liver.

Behavioural Data

No data identified.

In Vitro Toxicity Status

Carcinogenicity and Mutagenicity

Copper

Test system	Strain indicator	Metabolic activation	Method	Dose	Results
Ames Salmonella Typhirium	TA98	None	Standard plate	160-220 ppm	NEGATIVE
Ames Salmonella Typhirium	TA102	None	Standard plate	160-220 ppm	NEGATIVE
Ames Salmonella Typhirium	TA1535	None	Standard plate	160-220 ppm	NEGATIVE
Ames Salmonella Typhirium	TA1537	None	Standard plate	160-220 ppm	NEGATIVE
Ames Salmonella Typhirium	TA98	Rat, liver S-9, phenobarbitol	Standard plate	160-220 ppm	NEGATIVE
Ames Salmonella Typhirium	TA102	Rat, liver S-9, phenobarbitol	Standard plate	160-220 ppm	NEGATIVE
Ames Salmonella Typhirium	TA1535	Rat, liver S-9, phenobarbitol	Standard plate	160-220 ppm	NEGATIVE
Ames Salmonella Typhirium	TA1537	Rat, liver S-9, phenobarbitol	Standard plate	160-220 ppm	NEGATIVE

[CCRIS, 2009]

Zinc

Test system	Strain indicator	Metabolic activation	Method	Dose	Results
Ames Salmonella Typhirium	TA98	None	Standard plate	120-160 ppm	NEGATIVE
Ames Salmonella Typhirium	TA102	None	Standard plate	120-160 ppm	NEGATIVE
Ames Salmonella Typhirium	TA1535	None	Standard plate	120-160 ppm	NEGATIVE
Ames Salmonella Typhirium	TA1537	None	Standard plate	120-160 ppm	NEGATIVE
Ames Salmonella Typhirium	TA98	Rat, liver S-9, phenobarbitol	Standard plate	120-160 ppm	NEGATIVE
Ames Salmonella Typhirium	TA102	Rat, liver S-9, phenobarbitol	Standard plate	120-160 ppm	NEGATIVE
Ames Salmonella Typhirium	TA1535	Rat, liver S-9, phenobarbitol	Standard plate	120-160 ppm	NEGATIVE
Ames Salmonella Typhirium	TA1537	Rat, liver S-9, phenobarbitol	Standard plate	120-160 ppm	NEGATIVE
UDS Human Amnion FL cell line	THY INCORP	None	Liquid scintillation counting	0.1-10umol/L	NEGATIVE

[CCRIS, 2009]

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