FAO/PA/[illegible].2 (a)

WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTÉ

ENGLISH ONLY

JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

SPECIFICATIONS FOR IDENTITY AND PURITY OF FOOD ADDITIVES AND THEIR TOXICOLOGICAL EVALUATION: SOME EMULSIFIERS AND STABILIZERS AND CERTAIN OTHER SUBSTANCES

AND

GENERAL CONSIDERATIONS ON ADDITIVES IN RAW FOOD

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COPPER

by

Dr P.S. Elias
(Consultant)

Biological data

Biochemical aspects

Copper is an essential trace element for man and animals and a physiological constituent of plants, soils and man. The whole human body contains 100-150 mg (Browning, 1969). At subcellular level a number of enzymes contain Cu as part of their structure (tyrosine, lactase, uricase, ascorbic acid dehydrogenase) or require it for proper functioning (catalase, peroxidase, cytochrome oxidase). Somewhat controversial evidence suggests that the metal is an essential co-factor in haemoglobin synthesis and is involved in Fe metabolism. Some animal diseases, especially severe anaemias, are suspected to arise from nutritional copper deficiency. Copper intoxication may cause acute haemolysis in sheep (Anon., 1966). In man the average daily requirement for adults is estimated at 2 mg, for infants and children at 0.05 mg/kg bodyweight (Fd. Std. Cttee, 1956; Browning, 1969). The average daily dietary intake for adults is estimated at 2-5 mg, of which up to 0.7 mg are excreted in the urine (FAO/WHO, 1967; Browning, 1969). 0.8 mg are retained mainly in liver, kidney and intestine, while 1.40 mg are excreted in the faeces. Increased intake appears to have little effect on urinary output but faecal excretion may rise to 10-20 times the urinary excretion. Absorption from the G.I. tracts is limited. Normal human serum levels range from 68-90 mg/ml of which 95% is carried by the α_2-globulin copper oxidase ceruloplasmin. The remainder is bound to albumin or amino acids. In vitro studies on liver and kidney slices using ^{64}Cu-acetate demonstrated intracellular transport by histidine and other amino acids (Neumann and Silverberg, 1956).

Disordered copper metabolism occurs in Wilson's disease, [illegible] syndrome, [illegible], [illegible], but the significance of the abnormal [illegible] acid or urine levels is uncertain. The characteristic signs of [illegible] degeneration are due to abnormal Cu deposition due to [illegible], especially [illegible] copper oxidase activity. A high copper intake [illegible] molybdenosis in animals and, conversely, copper intoxication [illegible] to molybdenum. This activity of molybdenum requires inorganic sul[illegible] (Anon, [illegible]).

Copper catalyses fat oxidation and 2 ppm in milk or butter produces off-flavours. [illegible] amounts inhibit [illegible] (Fd. Std. Cttee, 19[illegible]). [illegible] are highly toxic to unicellular organisms, e.g. algae ([illegible] Std. C[illegible], 1956).

Copper salts are absorbed from the G.I. tract after ingestion and from the lungs after inhalation. They are soluble in gastric juice. The existence of chronic human copper poisoning has not been established (Fd. Std. Cttee, 1956; Bur. Mines Inf., 1953). Excess Cu renders many foods and beverages unpalatable (Fd. Std. Cttee, 1956). The zinc/copper ratio in soil has been [illegible] to be important for the development of gastric cancer in man (Anon, 19[illegible] a).

Acute toxicity

In animals ingestion of 3 ounces of 1% $CuSO_4$ solution produces intense G.I. tract inflammation (Browning, 1969).

Fatal oral human doses :	Basic copper sulphate	200 mg/kg bodyweight
	Copper chloride	"
	Copper carbonate	"
	Copper hydroxide	"
	Copper oxychloride	"
	Copper sulphate	600-900 mg highly toxic
	Copper acetoarsenite	5-10 mg/kg bodyweight

Large doses cause severe mucosal irritation and corrosion, widespread capillary damage, hepatic and renal damage, CNS irritation and depression. Sulphhaemoglobinaemia and haemolytic anaemia have been seen. The acetate and sulphate are very toxic especially the cupric salts while cuprous chloride is the most toxic. Local skin corrosion with eczema and eye inflammation occur. Copper sulphate has been used in suicide attempts. Rapid transfer of absorbed Cu to red cells causes haemolysis. Hepatic necrosis and renal tubular oedema with necrosis are seen (Chuttani et al., 1965; Browning, 1969). Occupational copper poisoning causes greenish hair and urine in coppersmiths and copper colic (Bur. Mines Inf., 1953). Inhalation of dust or vapour causes copper fume fever - brasschills (Bur. Mines Inf., 1953). Contact of food or soft acid water with copper utensils may cause poisoning, but no haemochromatosis or liver disease (Bur. Mines Inf., 1953; Hueper, 1965; Browning, 1969). Skin rashes have occurred from water conducted in copper piping at levels of 7 ppm (P.... , 1968) The existence of chronic copper poisoning in man whether industrial or non-industrial is debatable (Browning, 1969). In mammals injection or inhalation of copper and its compounds leads to haemochromatosis, liver injury or lung injury (Browning, 1969).

Short-term studies

None available.

Long-term studies

None available.

Carcinogenicity

No recorded observations implicate copper as human carcinogen following occupational, dietary or medicinal exposure (Hueper, 1965). Subcutaneous implants of powdered copper oxide, copper sulfide and cupric sulfide into rats failed to induce local sarcomata (Hueper, 1965). However, mice, rats and birds inoculated with copper compounds developed teratomata, seminomata and interstitial cell neoplasms in testes (Hueper, 1965). Critical assessment of these findings do not support any suggestions that medicinal copper preparations constitute a cancer hazard to man.

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