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JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

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

AND

GENERAL CONSIDERATIONS ON ADDITIVES IN BABY FOOD

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CARBON DISULFIDE

by

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Biological Data

Biochemical aspects

Most of carbon disulfide (CS_2) absorption occurs through the lungs after inhalation but some can be absorbed through the skin. 70-80% are absorbed from the air within 15 minutes but the rate falls rapidly to 40% during longer exposure. 5-13% is eliminated unchanged through the lungs and 0.1-0.3% in the urine, 85-95% is metabolised. Blood becomes saturated quickly but there is slow diffusion to the tissues which may take some weeks to achieve saturation in animals (Büsing et al., 1953; Patty, 1958). CS_2 acts as universal enzyme inhibitor and cellular poison by interference with oxidative phosphorylation and with fat metabolism. This produces hypercholesterolaemia and hyperlipaemia (Simon, 1961) with eventual increases in free plasma cholesterol, phospholipids, neutral fat and β-lipoprotein (Ambrosio et al., 1957; Paterni et al., 1958) and decreased lipolytic activity of vessel walls (Simon, 1961). CS_2 in tissues binds to N-containing compounds to form dithiocarbamates etc., some of which decompose to H_2S with subsequent oxidation to sulphate. Thus urinary excretion of sulphate is increased (Giovine, 1957). Guinea pigs show similar increases in dithiocarbamic acids after CS_2 inhalation (Soucek and Madlo, 1956). Rabbit liver detoxicates CS_2 with concomitant signs of changes in capillary permeability (Michalova et al., 1959). Other evidence of hepatic damage appears as increased urinary loss of Zn and Mg with decreased alkaline phosphatase activity. This may be the result of chelation by dithiocarbamate and thiazolidone, the reaction products of CS_2 with free aminoacid groups. Similar chelation of Cu may cause specific CNS lesions (Scheel et al., 1960).

Acute toxicity

Animal	Route	LD_{100}	Reference
Cat	Inhalation	35 [illegible] ppm (45 min.)	Lehmann, 1884
Man	Inhalation	4 855 ppm (30 min.)	Flury and Zernik, 1931

Acute poisoning in animals produces vomiting and death from respiratory failure. Exposure to high concentrations in man has an [illegible] effect with headache, nausea, [illegible] [illegible] [illegible] [illegible], [illegible] [illegible] [illegible], a fall in blood pressure [illegible] [illegible] [illegible] [illegible] [illegible], [illegible] delirium, paralysis and respiratory failure have been reported; [illegible] severe poisoning caused vomiting, paralysis, mental confusion and psychosis ([illegible], 1954). Poisoning from drinking causes rapid loss of consciousness and [illegible] while small oral doses may only cause headache, vomiting and diarrhoea ([illegible], [illegible]). Permanent dementia and other CNS manifestations can occur unless exposure is terminated [illegible]. Diffuse lesions of cortical neurons and scattered perivascular haemorrhages were seen at autopsy (Quensel, 1904). The MAC value is 20 ppm ([illegible], 195[illegible]; [illegible], 1967).

Short-term studies

Rat.

Intermittent exposure over 12 months produced glomerulonephrosis (Isler, 1954).

Rabbit.

Inhalation over 5 months produced excitement, cramps, tachycardia, weight loss and hepatic fatty degeneration as well as cortical cell destruction in the CNS with gliosis (Ranaletti, 1931). Exposure for 23 weeks produced interstitial nephritis and adrenocortical hyperplasia (Cohen et al., 1959).

Dog.

Chronic exposure caused ganglion cell damage especially in the cerebellar area, vascular endothelial proliferation and peripheral axon demyelination (Alpers and Lewey, 1940). There was some evidence of anaemia on chronic exposure (Binet and Bourlière, 1944).

Monkey.

Chronic exposure produced neuronal lesions in the basal ganglia and prominent atherosclerotic vascular changes (Brieger, 1961).

Human observations

Chronic industrial exposure has produced diverse effects on the CNS, GI tract, renal tract and blood vessels. Damage in the CNS predominates and results from primary lesions of the nerve cells as well as induced atherosclerosis. Encephalopathy, presenile cerebral atherosclerosis with loss of memory, insomnia, irritability and visual disturbances have occurred. A progressive Parkinsonian syndrome with permanent damage and mental disability due to striate or striato-

[illegible] (Horvath and Michalova, 1956; Zeglio, 1942). [illegible] (Zeglio, 1946). [illegible] have been reported (Auffret, 1946). [illegible] (Saita and Cattoni, 1957; [illegible]). [illegible] (Browning, 1953). [illegible] (Browning, 1953) and possibly [illegible] (Schwartz et al., 1957).

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