WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTÉ

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

[illegible] OF FOOD

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METHANOL
(Methyl Alcohol)

by

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Biological Data

Biochemical aspects

Methanol is only slowly eliminated after ingestion or inhalation. In the rat excretion is mainly by the lungs as CO_2 (65%) and unchanged methanol (14%). In the urine appears 3% unchanged methanol and 3% formate (Bartlett, 1950). In the rabbit 10%-20% is excreted unchanged in the urine and in the dog 15% methanol is excreted in the lungs, 10% in the urine as methanol and 20% as urinary formate (Voltz and Dietrich, 1912). The rabbit forms methylglucuronide (Kamil et al., 1953).

Man excretes methanol and formate in the urine after oral dosing. The urinary formate reaches a peak 2-3 days after ingestion (Williams, 1959). Other urinary metabolites are choline and methylglucuronide (Browning, 1965). There is argument whether ethanol, given simultaneously with methanol, decreases the latter's toxicity by depressing the oxidation of methanol and causing increased excretion of unchanged methanol. But in mice ethanol increases the toxicity of methanol (Browning, 1965).

Methanol is rapidly distributed to all tissues and body water (Yant and Schrenk, 1937). Methanol is probably oxidised by catalase and hydrogen peroxide and any formaldehyde is converted to methylformate by alcohol dehydrogenase of the liver and this slowly hydrolyses (Kendal and Ramanathan, 1952). As the oxidative processes in the cells are poisoned, organic acids accumulate with extreme acidosis (Patty, 1958).

[illegible]

Animal	Route	LD_{100}	LD_{50} mg/kg	Reference
mouse	intragastric	10.5 - 12 mg/kg	-	Moore, 1928
	inhalation	[illegible]	-	[illegible], 1927
rat	inhalation	3.71 - 12.[illegible] g/kg	-	Loewy & van der Heide, [illegible]
	oral	-	12900	Spector, 1956
cat	i.v.	5.9 ml/kg	-	[illegible], 1900
	inhalation	65 700 ppm	-	Lehmann & Flury, 1943
rabbit	intragastric	19 ml/kg	14200	Lund & [illegible], 1925
	i.v.	4.2 g/kg	-	Spector, 1956
monkey	inhalation	1 000 ppm	-	McCord & Cox, 1931

The acute effects are irritation of mucous membranes, depression and drowsiness followed by death from respiratory paralysis. The narcotic effect of methylalcohol is weaker than ethylalcohol but the toxic effect of accumulated doses is greater because of slow elimination. 30-50000 ppm exposure for 30 to 60 minutes may be dangerous to man (Patty, 1958). Acute poisoning in man is followed often by blindness. Symptoms occur after a latent period with dizziness, stupour, G.I. disturbances (Wood and Buller, 1904; Browing, 1965). 5-10 mg are considered toxic but many individuals tolerate more (Lehmann and Flury, 1943). Ingestion of 60-90 g has been reported as causing death in man (AIH.) but other reports quote less than 1 g/kg (Williams, 1959). Poisoning with blindness has also occurred after inhalation. But many reports exist of long exposure without symptoms (Browning, 1965). The MAC value is 200 ppm (Patty, 1958). Apparent penetration of the skin can occur in monkeys, dogs and man (Patty, 1958).

Short-term studies

Rat

Groups of 10 rats received 2.5% methanol with or without 0.9% salt or sodium formate for 210-225 days. 3 rats from each group were given C^{14} labelled methanol on the 120-150th day. Body weights were comparable with controls. Measurements of $^{14}CO_2$ showed no difference in oxidation rate between methanol and ethanol. All methanol-treated rats showed greater oxygen uptake of liver slices and increased catalase activity but no change in alcohol dehydrogenase activity (Wartburg & Roethlisberger, 1961).

Special studies

Repeated inhalations in animals cause small haemorrhages in the gastric mucosa, oedema and retinal ganglionar degeneration, blindness, increased haemopoiesis, oedema and necrosis of cardiac muscle, parenchymatous degeneration with focal necrosis in the liver and kidney, pulmonary inflammation, oedema and patchy neuronal degeneration (Browning, 1965). Dogs were exposed for 379 days to 500 ppm methylalcohol for 8 hours per day without any ill effects on weight, vision, haematology or histopathology (Sayers et al., 1942).

Skin absorption was tested on 9 rats, 12 rabbits and 2 monkeys. All animals died within a few days, rabbit being the least susceptible. Methylalcohol could be recovered from all organs and optic atrophy was noted. About 0.5 ml/kg body weight applied four times per day is the lowest dose causing adverse effects (McCord, 1951).

In man occurs conjunctivitis, headache, giddiness, G.I. disturbances and failure of vision. The optic nerve and retina show oedema and degeneration secondary to metabolites, e.g. formaldehyde or formic acid (Fink, 1943). Methanol can be absorbed through the skin and cause eye lesions. Individual susceptibility and pre-existing nervous disease predispose to toxic effects of methanol (Browning, 1965). Repeated eight hour exposures to 3000 ppm would lead to an increasing concentration of methanol in the human body (AIHA).

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