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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 FOR EVALUATION OF SOME ANTIMICROBIALS, ANTIOXIDANTS AND EMULSIFIERS

AND

GENERAL CONSIDERATIONS CONCERNING RESIDUES IN FOOD

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ACETONE

by

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Biological Data

Biochemical aspects

Acetone ($CH_3CO.CH_3$) is readily absorbed by solution into the blood after inhalation (Hagen, 1924) and progressive accumulation in tissues has been noted after 6 hours inhalation (Haggard et al., 1944). Skin absorption occurs only slowly in animals (Lazarew et al., 1931) and probably none through intact human skin (Cesaro and Pinerolo, 1947). Large oral doses are mostly excreted unchanged through the lungs (40-70%) and the kidneys (15-30%) but small amounts are metabolized slowly to formate and acetate within 24 hours (Williams, 1959). Dogs excrete in their urine some 1-4% of acetone when administered orally at rates of 0.2-1.6 g/kg. Some 60% is excreted through the lungs (Schwarz, 1898). Small doses (1.7 mg/kg body weight) are oxidised mainly to CO_2 (53%) while some 7-14% is exhaled unchanged (Price and Rittenberg, 1950; Sakami and Lafaye, 1950). Some 10% of inhaled acetone is excreted through human skin (Parmeggiani and Sassi, 1954).

Acetone labelled with C^{14} in the methyl group was shown to be converted by rats to liver glycogen, serine, choline and methionine via formate and acetate (Sakami and Lafaye, 1950), while another metabolic pathway involved direct conversion to pyruvate in the liver (Sakami and Lafaye, 1951). Acetone injected into dogs produced high hepatic levels of β-hydroxybutyric acid (Valdignie, 1935). Of 1 g. administered to man some 2% are excreted through the lungs (Rothkopf, 1936). I.v. injection into rabbits markedly increased acetoacetic acid and

β-hydroxybutyric acid and glucose levels in their blood ([illegible], 1937). After i.v. injection at constant rate of [illegible] acetone into man over 2 hours some [illegible] mg were lost through the lungs (1 normal, 5 diabetic subjects). Total urinary acetone excretion did not rise significantly in 7 fasting normal subjects but some 360 mg acetone were excreted in 24 hours by this route. 12 normal subjects maintained high blood levels of acetone for 4 hours after injection but almost all had disappeared from the blood after 24 hours. [illegible] levels rose [illegible] in the blood and [illegible] elevated for 4 hours after injection. No β-hydroxybutyric acid appeared. Simultaneous i.v. glucose or i.v. insulin did not affect blood acetone levels in 7 normal fasting subjects. i.v. injection of acetone into 12 diabetics showed similar levels as in 19 normal subjects. Hence no impairment in ability to destroy acetone occurs in diabetics. The rate of breakdown is so slow, however, as to preclude that more than a small part of normal fat metabolism passes through an acetone stage (Koehler et al., 1941).

Acute toxicity

Animal	Route	LD_{50} mg/kg bodyweight	LD_{100} mg/kg bodyweight	References
Mouse	inhalation	-	46000 ppm	Schultze, 1932
Rat	oral	10700	-	(Smyth et al., 1962 (Shell Chemical Co., 1969
		9700	-	Spector, 1956
	i.v.	-	6-8 ml/kg	Walton et al., 1928
	inhalation	-	32000 ppm/ 4 hrs	(Smyth et al., 1962 (Shell Chemical (Co., 1969
Rabbit	intragastric	5340	-	Spector, 1956
		-	5-10 ml/kg	Walton et al., 1928
	i.v.	-	6-8 ml/kg	Walton et al., 1928
	percutaneous	> 20 ml/kg	-	(Smyth et al., 1962 (Shell Chemical (Co., 1969
Dog	intragastric	-	8 g/kg	Albertoni, 1884

The acute effects of acetone are essentially that of a fairly strong anaesthetic (Elkins,). It also causes moderate inhibition of cholinesterase in vitro and in cats in vivo as shown by increased chemical action potentials in the carotid body nerve after intra-arterial administration (Landgren et al., 1953). Repeated intragastric administration of 8 ml to rabbits for 5-22 days or 8-10 ml to dogs for 8-35 days produced albuminuria and epithelial necrosis of convoluted renal tubules (Albertoni and Pisenti, 1887). Daily administration of 1-2.5 g/kg acetone intragastrically to 5 dogs for 9-19 days produced nephritis with tubular destruction (Poliak, 1925). Intragastric administration to cats caused local irritation of the digestive tract (Taylor and Frodsham, 1943).

Dermatitis from frequent sustained skin contact and irritation of eyes and the nasal mucosa have been observed in man (Brennan, 1918). Reversible renal effects in man have been reported (Browning, 1965). The TWL is 1000 ppm (Sax,). 15-20 g given orally daily to man over several days produced only slight drowsiness but no other ill effects (Albertoni, 1884). Acute massive intoxication in man has caused collapse and possible liver and kidney injury (Cook, 1940; Smith and Mayers, 1944; Harris and Jackson, 1957). Little absorption occurs through the skin after contact with liquid acetone (Browning, 1965).

Special tests

Mouse

Acetone was painted on the clipped dorsal skin of 60 female mice three times a week for 447 days (64 weeks) as part of another experiment. No local papillomata or carcinomata were seen (van Duuren et al., 1965).

Rat

The single injection of 0.1 ml, as part of another experiment, into one or both salivary glands of 35 male and 7 female rats produced local necrosis and complete regenerative repair after 3 weeks. Animals observed for 8 months showed no local or distant tumour formation either macroscopically or histologically (Chaney and Glücksmann, 1965).

Chicken

Injection of acetone into the yolk sac of fresh fertile chicken eggs had little adverse effect on hatchability (80% of normal) and produced no teratogenic lesions (McLaughlin et al., 1964). In another experiment only 37% of embryos survived, the remainder being killed by coagulation due to acetone. Surviving embryos developed normally (Walker, 1967).

Observations in man

Widespread industrial use over many years (e.g. 2000 ppm inhaled for 15 years) only yielded a few cases of mild intoxication but no reports of permanent haematological or organ damage (Browning, 1965; Rowe and Wolf, 1963; Patsett, 1963).

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