5.11 Additional Remarks

Type: Biochemical or cellular interactions

Remark: Female F-344 rats received i.m. 0.75 mmol/kg TETA prior to 0.068 or 0.10 mmol/kg nickeldichloride (i.p. or i.m.). In rats killed 6 h after injection of TETA and nickelchloride, Ni concentration in liver, kidney, spleen, lung and heart averaged 3.4, 0.72, 0.27, 0.22, and 0.12 times corresponding Ni concentrations in contol rats that received only nickelchlorid. Ni-induced hyperglycemia and hyperglucagonemia were not prevented. TETA markedly reduced plasma Ni conc. and increased urine Ni excretion during 6 h after injection. Test substance: purified TETA-4Hydrochloride

(99)

Type: Biochemical or cellular interactions

Remark: Norwegian hooded rats received 100 mg TETA per rat with the diet for 3 days and the urine copper concentration was determined. The basal copper excretion of 65.1 nmol/24 h rose after drug application to 305.9 nmol/24 h. Test substance: TETA-2Hydrochloride

(100)

Type: Biochemical or cellular interactions

Remark: Female mixed-breed dogs were administered 150 mg TETA orally in gelantine capsules twice daily for 23 days and serum and 24 h urine were analysed on day 0, 9, 15, and 23. Cu concentration in serum was unchanged but increased in urine from 0.119 to 0.663 mg/24 h. Zn and Fe concentration in plasma and urine were not changed. Predictive value reduced by low number of animals (n=3). Test substance: TETA-4Hydrochloride

(101)

Type: Biochemical or cellular interactions

Remark: Nickel-poisened rats survived at a nickel:TETA ratio of 1:1. Urinary and biliary excretion of nickel was significantly enhanced.

(102)

Type: Biochemical or cellular interactions

Remark: Sodium diethyldithiocarbamate and D- pencillamine are significantly more effective upon acute toxicity of nickel carbonyl in rats than TETA.

(103)

Type: Biochemical or cellular interactions

Remark: The distribution of radioactive nickel, iron, manganese, and tin in plasma was studied in rats which received i.p. injections of their salts with or without i.m. injection of TETA. TETA was most effective in reducing nickel, followed by iron, manganese and tin.

test substance: no data

(104)

Type: Biochemical or cellular interactions

Remark: A single i.p. application of TETA decreased significantly the total body burden of zinc 24 h after i.v. injection of Zn chloride (0.14 mg/kg). Simultaneous peroral administration of TETA with Zn increased whole body burden of Zn, indicating possibly enhanced absorption of zinc.
test substance: TETA-2Hydrochloride

(105)

Type: Biochemical or cellular interactions

Remark: In a comparative study on the effects of 7 chelating drugs on trace metal and biochem. alteration in the rat TETA is one of the drugs producing least effects on the levels of trace metals and biochem. parameters.
test substance: no data

(106)

Type: Biochemical or cellular interactions

Remark: TETA is an effective antidote to acute nickel carbonyl poisoning (4.35 mg/l for 15 min) when it is administered 10 min after and not 10 min before exposure in rats.
test substance: no data

(107)

Type: Biochemical or cellular interactions

Remark: In a comparative study with 16 chelating agents TETA has been shown to be one of the most effective drugs enhancing urinary excretion of copper in the rat.
test substance: no data

(108)

Type: Biochemical or cellular interactions

Remark: 6 daily i.p. injections of 146 mg/kg TETA enhanced significantly excretion of all essential trace metals in rats. In serum levels there were no significant changes indicating redistribution.
test substance: no data

(109)

Type: Biochemical or cellular interactions

Remark: In cadmium preexposed rats 500 mg/kg TETA reduced the hepatic Cd burden but did not elicit any influence on other tissues except pancreas.
test substance: TETA-hydrochloride

(110)

Type: Toxicokinetics

Remark: The maximal plasma concentration 2 h after a single oral administration of 25 mg/kg was 8 microg/ml in fasted, 3 in nonfasted rats(max after 1h) and 24 microg/ml after

intraduodenal application. Bioavailability 4 h after administration was 6.6, 2.3,and 17.6%, respectively. Plasma levels after i.v. administration of 0.1 mg per rat were 0.0013 mg/ml 10 min. after injection and 0.00045 mg/ml after 4 h. The urinary excretion of unchanged TETA during 24 h was 3.1% of the oral dose and total urinary excretion including not identified metabolites amounted to 35.7% of the dose. Main absorption by permeation across the plasma membrane of intestinal epithelial cells. Binding to the brush border membran was totally inhibited by 0.05 mmol copper.
test substance: TETA-2Hydrochloride

(111)

(1) BUA Report No. 89 "Triethylentetramin", VCH, Weinheim, (1992)

(2) Beilsteins Handbuch der organischen Chemie, Band 4, Springer Ver- lag, Berlin, 255 (1922)

(3) Bayer AG, DIN-Safety Data Sheet Triethylentetramin 18.06.93

(4) Keith, L.H. & Walters, D.B., Compendium of safety data sheets for research and industrial chemicals, Part 3, Verlag Chemie, Wein- heim, 1670-1671 (1985)

(5) Kuehn, R. & Birett, K., Merkblaetter gefaehrlicher Arbeitsstoffe, Band 6, Blatt Nr. T 43, Ecomed Verlag, Landsberg (1982)

(6) Wilson, A.L., Ind. Eng. Chem. 27, 867-871 (1935)

(7) Hommel, G., Handbuch der gefaehrlichen Gueter, Springer Verlag, Berlin, Merkblatt 569 (1988)

(8) Hann, R.W. & Jensen, P.A., Water quality characteristics of ha- zardous materials, Texas A & M University, 3 S. (1974)

(9) Hart, A.W., In: Kirk-Othmer, Encycl. chem. technol., Bd. 7, New York, 22-39 (1965)

(10) Leo, A. et al., Chem. Reviews 71, 525&575 (1971)

(11) Fiedler, H., Chemical and physical properties worksheet (CAS Nr. 112-24-3), unveroeffentlicht (1989)

(12) Calculation Bayer AG, WV-UWS/Produktsicherheit, 1992

(13) Spitz, R.D., Diamines and higher amines, aliphatic, In: Kirk- Othmer, Encyclopedia of chemical technology, Vol.7, 580-602 (1979)

(14) Safety Data Sheet Dow Europe S.A., August 1993

(15) Baldwin, W.C.G, Pr. Roy. Soc. A, 167, 539-554 (1937)

(16) Atkinson, R., Ed., AOP, Rate of hydroxyl radical and ozone reaction from chemical structure, Version SRC 1.31, Syracuse Res. Co. University of California, Riverside, USA (1990)

(17) Hansen, E.B. et al., J. Anal. Toxicol. 9, 167-171 (1985)

(18) Bayer AG data

(19) unpublished report CRL I89039 from AKZO, 1989

(20) DOW Chemical Company, unpublished data (1978)

(21) unpublished report CRL I89044 from AKZO, 1989

(22) Van Wijk, R.J. et al., Environ. Toxicol. Chem. 13, 167-171 (1994)

(23) Dombrowicz, E. et al., Acta Pol. Pharm. 42, 184-191 (1985)

(24) unpublished report CRL F90088 from AKZO, 1990

(25) Schafer, E.W. et al., Arch. Environm. Contam. Toxicol. 12, 355-382 (1983)

(26) Lallier, R., C. R. Acad. Sc. Paris, Ser. D. 262, 1460-1463 (1966)

(27) Chatterjee, M. et al., Int. J. Environm. Stud. 24, 87-95 (1985)

(28) Chemical Hygiene Fellowship, Carnegie-Mellon University, Special Report 39-54 (1976); cited in BG Chemie, Toxikologische Bewertung Nr. 181, Triethylentetramin (1991)

(29) Bayer AG, Untersuchung von E 570 und Haerter T, unveroeffentlichter Bericht (1957)

(30) Smyth, H.F. et al., J. Ind. Hyg. Toxicol. 31, 60-62 (1949)

(31) Stavreva, M., Khig. Zdraveopaz. 22, 179-182 (1979); article in russian, data from TOXLINE abstract

(32) Kowalski, Z. et al., Chem. Abstracts 59, 6889 (1963)

(33) Srivastava, A. et al., Chemosphere 17, 839-844 (1988)

(34) Pletscher, A. et al., Z. Unfallmed. Berufskrankh. 47, 163-176 (1954)

(35) Maisey, J. et al., Contact Dermatitis 18, 133-137 (1988)

(36) Thorgeirsson, A., Acta Derm. Venereol. 58, 332-336 (1978)

(37) Markicevic, A. et al., Chem. Abstracts 61, 16688 (1964)

(38) Ormerod, A.D. et al., Contact Dermatitis 21, 326-329 (1989)

(39) Van Putten, P.B. et al., Contact Dermatitis 10, 146-150 (1984)

(40) Krajewska, D. and Rudzki, E., Contact Dermatitis 2, 135-138 (1976)

(41) Rudzki, E. and Krajewska, D., Contact Dermatitis 2, 311-313 (1976)

(42) Rudzki, E., Contact Dermatitis 4, 53 (1978)

(43) Balato, N. et al., Contact Dermatitis 15, 263-265 (1986)

(44) Jolanki, R. et al., Acta Derm. Venereol., S 134, 90-94 (1987)

(45) Camarasa, J.G. and Serra-Baldrich, E., Contact Dermatitis 20, 382 (1989)

(46) Oshima, H. et al., Contact Dermatitis 24, 138-139 (1991)

(47) Tosti, A. et al., Contact Dermatitis 19, 220-222 (1988)

(48) Welcker, A., Dermatol. Wochenschr. 132, 871-876 (1955)

(49) Grandjean, E., Brit. J. Industr. Med. 14, 1-4 (1957)

(50) Grandjean. E., Z. Praeventivmed. 2, 77-98 (1957)

(51) Fawcett, I.W. et al., Clinic. Allergy 7, 1-14 (1977)

(52) Rudzki, E. et al., Med. Pr. 32, 59-62 (1981); article in polish, data from TOXLINE abstract

(53) Greenman D.L. et al., Fundam. Appl. Toxicol. 29, 185-193 (1996)

(54) Dobryszycka, W. et al., Arch. Toxicol. 33, 73-80 (1974)

(55) Woyton, J. et al., Toxicol. Appl. Pharmacol. 32, 5-10 (1975)

(56) Dobryszycka, W. et al., Arch. Immunol. Therap. Exp. 23, 867-870 (1975)

(57) Szacki, J. et al., Arch. Immunol. Therap. Exp. 22, 123-128 (1974)

(58) Hedenstedt, A., Mutat. Res. 53, 198-199 (1978)

(59) Hulla, J. E. et al., Environ. Mutagen. 3, 332-333 (1981)

(60) Warren, G. et al., Mutat. Res. 88, 165-173 (1981)

(61) Heinz, N. and Schroeder, H.F., Drug Res. 31, 950-953 (1981)

(62) Mortelmans, K. et al., Environ. Mutagen. 8, S7, 1-119 (1986)

(63) Union Carbide Corporation, Bushy Run Res. Center, Report 50-43 (1987)

(64) Union Carbide Corporation, Bushy Run Res. Center, Report 50-9 (1987); cited in BG Chemie, Toxikologische Bewertung Nr. 181, Triethylentetramin (1991)

(65) Union Carbide Corporation, Bushy Run Res. Center, Report 43-127 (1981); cited in BG Chemie, Toxikologische Bewertung Nr. 181, Triethylentetramin (1991)

(66) Union Carbide Corporation, Bushy Run Res. Center, Report 44-11 (1981); cited in BG Chemie, Toxikologische Bewertung Nr.181, Triethylentetramin (1991)

(67) Union Carbide Corporation, Bushy Run Res. Center, Report 50-99 (1987); cited in BG Chemie, Toxikologische Bewertung Nr. 181, Triethylentetramin (1991)

(68) National Toxicology Program, Annual Plan for Fiscal Year 1986, report NTP-86-086, 72 (1986)

(69) Union Carbide Corporation, Bushy Run Res. Center, Report 50-122 (1987)

(70) Depass, L.R. et al., Fundam. Appl. Toxicol. 9, 807-811 (1987)

(71) Young, J.T., Grandjean, M. and Swaim, L.D., unpublished report of the DOW Chemical Corporation (1986)

(72) Ciba-Geigy Ltd., Report on TK 10458, report No. 830035 (1984), cited in BG Chemie, Toxikologische Bewertung Nr. 181, Triethyl- tetramin (1991)

(73) Cohen, N.L. et al., Fed. Proc. Fed. Am. Soc. Exp. Biol. 41, 944 (1982)

(74) Keen et al., Inflammatory Dis. Copper (Proc. Symp.) 109-121 (1982)

(75) Keen, C.L. et al., Lancet I, 1127 (1982)

(76) Keen, C.L. et al., Proc. Soc. Exp. Biol. Med. 173, 598-605 (1983)

(77) Cohen, N.L. et al., Drug-Nutr. Interactions 2, 203-210 (1983)

(78) Hurley, L.S. et al., Teratology 25, 51A (1982)

(79) Keen, C.L. et al., Teratology 25, 53A (1982)

(80) Union Carbide Corporation, Bushy run research center, Project report 50-127 (1988); cited in BG Chemie, Toxikologische Bewer- tung Nr. 181, Triethylentetramin (1991)

(81) Korhonen, A. et al., J. Appl. Toxicol. 3, 112-117 (1983)

(82) Bachmann, H. et al., Eur. Neurol. 29, 301-305 (1989)

(83) Brewer, G.J. et al., Semin. Neurol. 7, 209-219 (1987)

(84) Dubois, R.S. et al., J. Pediat. Gastroent. Nutr. 10, 77-81 (1990)

(85) Fromtling, R.A., Drugs of Today 23, 507-508 (1987)

(86) Haslam, R.H.A. et al., Dev. Pharmacol. Ther. 1, 318-324 (1980)

(87) Scheinberg, I.H. et al., New Engl. J. Med. 317, 209-213 (1987)

(88) Walshe, J.M., Lancet II, 1401-1402 (1969)

(89) Walshe, J.M., Lancet II, 643-647 (1982)

(90) Walshe, J.M., Prog. Clin. Biol. Res. 34, 271-280 (1979)

(91) Walshe, J.M., Quart. J. Med. 42, 441-452 (1973)

(92) Epstein, O. and Sherlock, S. Gastroentrology 78, 1442-1445 (1980)

(93) Pletscher, A. et al., Z. Unfallmed. Berufskrankh. 47, 163-176 (1954)

(94) Yano, E., Toxicol. Letters 37, 27-32 (1987)

(95) Zielhuis, R.L., J. Occup. Med. 3, 25-29 (1961)

(96) Burrows, D. et al., Contact Dermatitis 15, 55-57 (1986)

(97) Miyazaki, K. et al., Chem. Pharm. Bull. 38, 1035-1038 (1990)

(98) Loessner, S.R. et al., Acta Neurol. Scand. 83, 364-366 (1991)

(99) Sunderman, F.W. et al., Toxicol. Appl. Pharmacol. 38, 177-188 (1976)

(100) Gibbs, K. and J.M. Walshe, Clinic. Sci. Mol. Med. 53, 317-320 (1977)

(101) Allen, K.G.D. et al., Am. J. Vet. Res. 48, 28-30 (1987)

(102) Athar, M. et al., Fundam. Appl. Toxicol. 9, 26-33 (1987)

(103) Baselt, R.C., et al., Res. Communic. Chem. Pathol. Pharmac., 18, 677-689 (1977)

(104) Dwivedi,R.S. et al., Chemosphere 11, 925-932 (1978)

(105) Eybl, V. et al., Arch. Toxicol. Suppl. 13, 370-372 (1989)

(106) Misra, M. et al., Bull. Environm. Contam. Toxicol. 41, 172-184 (1988)

(107) Mitchell, J. et al., Clinical Toxicol. 12, 606-607 (1978)

(108) Planas-Bohne, F., Toxicol. Appl. Pharmacol. 50, 337-345 (1979)

(109) Tandon, S.K. et al., Environm. Res. 35, 237-245 (1984)

(110) Tewari, P.C. et al., Clin. Exp. Pharmacol. Physiol. 15, 71-75 (1988)

(111) Kobayashi, M. et al., Yakugaku Zasshi 110, 759-763 (1990)