INFORMATION PROFILE FOR NIEHS NOMINATIONS OF CHEMICALS TO THE NATIONAL TOXICOLOGY PROGRAM

Nominator: EPA **Date:** 6/27/96

Phone: 1-3440

Address: NIEHS

CHEMICAL IDENTIFICATION

Common Name:
Dibromoacetic acid

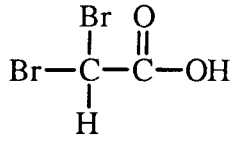
Chemical Name:
Acetic acid, dibromo (9CI)

CAS Number:
631-64-1

Molecular Weight:
218.9

Chemical Formula:
$C_2H_2Br_2O_2$

Chemical Structure:



Rationale for Nomination:
Disinfection by-product in drinking water

Chemical and Physical Properties:
Physical state: white, deliquescent crystals
Boiling point: 218°C (decomposes)
Melting point: 49°C
Vapor pressure: NA
Solubility: very soluble in water and ethanol, soluble in ether
Stability: NA; pKa = 1.48 @ 25°C
Density/Specific Gravity: NA

Name of Supplier(s):
Several

USE AND EXPOSURE

Uses:
Organic synthesis.

US Production and Import Quantities: NA

Regulatory Status:
On TSCA inventory, not otherwise regulated.

Levels of Human Exposure:
Occupational: NA

Environmental:
1989, US surface, lake, reservoir and groundwater, 0.9-19 ug/l (1).
1989 US surface water, 0.7-11 ug/l (2).

Ozonation of natural waters containing bromide ion leads to the formation of inorganic hypobromite and bromate and many brominated organic by-products, only a few of which have been identified. The study described here identified bromoform, bromoacetonitriles, bromoacetone, bromoacetic acids, and a group of labile compounds referred to as bromohydrins. These by-products are reactive toward most quenching agents used for their stabilization. Dissolved organic bromide (DOBr) formation was favored by a low pH, low alkalinity, and low ammonia concentration and increased as a function of bromide concentration in the raw water. A mass balance of bromide indicates that, in some cases, <10% of the DOBr content has been identified (3).

The effects of bromide ion, pH and reaction time on the formation of four trihalomethanes, nine haloacetic acids and total organic halogens in chlorinated drinking water have been investigated. In this extensive study, the relationships of total trihalomethanes and total haloacetic acids with total organic halogen have been evaluated. The study determined the concentration range of nine haloacetic acids and four trihalomethanes as percentage of total organic halogen. The results showed that the percentage of total organic halogen made up of total trihalomethanes plus total haloacetic acids significantly increases with increasing bromide ion concentrations and pH. These observations suggest that both a higher bromide concentration and pH cause the formation of mainly brominated trihalomethanes with the reduction of haloacetic acids which could be identified and quantified by current U.S. Environmental Protection Agency methods (4).

TOXICOLOGY DATA

Genetic Toxicity: NA
Selected by the NTP for genetic toxicology testing.

Subchronic Toxicity: NA

Chronic Toxicity: NA

Carcinogenicity:
An overview of recent developments regarding the reproductive effects of dichloroacetic acid, trichloroacetic acid, dibromoacetic acid, bromoacetic acid, as well as other disinfection by-products (5).

Reproductive/Developmental Effects:
Halogenated acetic acids are major disinfection by-products of water chlorination and ozonation. Limited data in experimental animals indicate that repeated doses of dichloroacetic acid (DCA) or single doses of dibromoacetic acid (DBAA) cause testicular damage. In the present study, spermatotoxic effects were investigated in rats given oral doses of 0, 10, 30, 90, or 270 mg DBAA/kg/day for 14 days. In rats dosed with 270 mg/kg/day, there were marked effects on epididymal sperm motility and

morphology including the flagellar fusion of 2 or more sperm. Testis weight, epididymis weight, and testicular sperm head counts were mildly reduced relative to control, whereas epididymal sperm counts were sunstantially decreased. Histological changes in the testis included retention of Step 19 spermatids in Stages IX to XIII, abnormal development of late spermatids, and the formation of atypical structures resembling residual bodies that were observed predominantly in Stages X to XIV and I of the cycle of the seminiferous epithelium. At the dose of 90 mg/kg/day, effects on spermiation, spermatid development, epididymal sperm counts, sperm motility, and sperm morphology were less severe than at the higher dosage. Reduced caput sperm counts and mild effects on spermiation also occurred at 30 and10 mg/kg/day. These studies indicate that subchronic exposure to DBAA has the potential to affect reproductive outcome in the rat. Compared to previous studies of DCA, DBAA, on a molar basis, appears to be a stronger testicular toxicant than the dichloro analogue (6).

Chlorine and bromine can react with natural organic substances in source waters to form haloacetic acids, major disinfection by-products of water chlorination. Several toxic effects including testicular damage have been attributed to the chloroacetic acids but little information is available on the bromine analogues. In this report the authors present the results of acute toxicity and acute spermatotoxicity studies of monobromoacetic acid (MBAA) and dibromoacetic acid (DBAA). In adult male rats the acute oral toxicity of MBAA was 10-fold that of DBAA (LD_{50} 177 vs 1737 mg/kg). No reproductive-related endpoints were affected in rats given a single dose of 100 mg MBAA/kg or 14 daily doses of 25 mg MBAA/kg/day. In rats dosed with DBAA, serum testosterone fell to 17% of control 2 days after a single dose of 1250 mg/kg but returned to control levels by day 14. Marked effects on sperm motion were seen on post-treatment days 14 and 28. Degenerative flagellar changes in cauda sperm were present on day 14 while abnormal sperm head shapes and flagellar degeneration were observed in both caput and cauda sperm on day 28. Histopathology indicated altered spermiation at all timepoints as evidenced by retention of Step 19 spermatids beyond Stage VIII of the cycle of the seminiferous epithelium. Disorganization, distortion, and degeneration of late spermatids were also observed. On day 14 structures resembling residual bodies were rarely seen in the testis but were numerous in the epididymis. Caput sperm counts were decreased on day 2 and cauda sperm counts were decreased on day 14 and 28. The data indicate that DBAA is a testicular toxicant in the rat with late and elongating spermatids being particularly susceptible germinal cells (7).

The authors recently demonstrated with short-duration tests that dibromoacetic acid (DBAA), a commonly occurring by-product of water disinfection, alters sperm morphology and motility in the male rat. These results suggested that the effects of DBAA on sperm quality were likely to compromise reproductive competence of the male rat early in subchronic exposure. The present studies were undertaken to investigate the dose response and time course of alterations in fertility and sperm quality. Proven breeder male rats were gavaged daily with 0, 2, 10, 50, or 250 mg DBAA/kg for up to 79 days; interim and terminal measurements of sperm quality and reproductive outcome were made. Because of the known neurotoxicity of the analogue, dichloroacetic acid, both natural breeding and artificial inseminations were evaluated in untreated females to distinguish between possible behavioral and spermatogenic effects. DBAA compromised male fertility during the second treatment week in naturally bred rats dosed with 250 mg/kg. The early antifertility effect appeared to be the result of behavioral changes since females artificially inseminated with sperm collected on day 9 successfully produced offspring. However, sperm morphology and motility also were rapidly affected by DBAA treatment so that no offspring via natural insemination and only one litter via artificial insemination were produced subsequent to day 15. Through 31 days, substantial effects on sperm motility, sperm morphology, and epididymal sperm numbers were observed, but there was no

demonstrable effect on serum testosterone or sperm production. Because severe toxicity developed in the group given 250 mg/kg, exposure of these animals was prematurely terminated after 42 doses and their recovery was monitored through a 6-month post treatment period; decreased testis weights and only limited recovery of reproductive performance were observed. Exposure to 50 mg/kg resulted in moderate changes in sperm morphology and motility and moderate decreases in epididymal sperm counts in rats dosed for 31 or 79 days. However, these males remained fertile, litter size was unaffected, and no paternally mediated developmental defects were noted in their offspring. No effects on sperm quality were detected at dosages of 2 or 10 mg/kg. However, compared to controls, naturally bred DBAA-treated rats tended to have fewer inseminations, fewer copulatory plugs, and fewer multiple litters, suggesting that DBAA may have altered mating behavior at dosages as low as 10 mg/kg (8).

Immunotoxicity: NA

Neurotoxicity: NA

Metabolism/Disposition: NA

Structure Activity Relationships:
Re: other haloacetic acids and esters. Expected to be a strong corrosive and irritant.

Other Biological Effects: NA

SOURCES SEARCHED

Chapman & Hall Chemical Database
Chemical Abstracts
Chemical Economic Handbook
Chem Sources International
Chem Sources USA
EMIC
Handbook of Chemistry and Physics
Hazardous Substances Database
IARC Monograph # 52: Chlorinated Drinking Water, etc. (1991)
Kirk-Othmer Encyclopedia of Chemical Technology (third edition)
Medline
Merck Index
RTECS
Safety of Water Disinfection (ILSI Press)
Suspect Chemical Sourcebook
Synthetic Organic Handbook
Toxline/Toxlit

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2. Jacangelo, J. G., Patania, N. L., Reagan, K. M., Aieta, E. M., Krasner, S. W., McGuire, M.

J. Ozonation: assessing its role in the formation and control of disinfection by-products. *J. Am. Water Works Assoc.*, 81:74, 1989.

3. Glaze, W., H., Weinberg, H. S, Cavanagh, J. E. Evaluation the formation of brominated DBPs during ozonation. *J. Am. Water Works Assoc.*, 85(1):96, 1993.

4. Pourmoghaddas, H., Stevens, A., A. Relationship between trihalomethanes and haloacetic acids with total organic halogen during chlorination. *Water Research*, 29(9):2059, 1995.

5. Klinefelter, G. R., Linder, R. E. Recent Reproductive Effects Associated with Disinfection By-Products. Workshop on Disinfection By-products in Drinking Water: Critical Issues in Health Effects Research, Chapel Hill, NC, October 1995.

6. Linder, R. E., Klinefelter, G. R., Strader, L. F., Suarez, J. D., Roberts, N. L., Dyer, C. J. Spermatotoxicity of dibromoacetic acid in rats after 14 daily exposures. *Reprod. Tox.*, 8(3):251, 1994.

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8. Linder, R. E., Klinefelter, G. R., Strader, L., F., Narotsky, M. G., Suarez, J. D., Roberts, N. L., Perreault, S. D. Dibromoacetic acid affects reproductive competence and sperm quality in the male rat. *Fund. Appl. Toxicol.*, 28(1):9, 1995.