

A. INGREDIENT NAME:

DIMERCAPTO-1-PROPANESULFONIC (DMPS)

B. Chemical Name:

DL-2, 3-Dimercapto-1-Propanesulfonic

C. Common Name:

DMPS, Unithiol, Dimaval, Mercuval

D. Chemical grade or description of the strength, quality, and purity of the ingredient:

	<i>(Limit-Min/Max)</i>	<i>(Results)</i>
Assay: (Iodometric)	95%	98.2%

E. Information about how the ingredient is supplied:

Fine, white, crystalline powder, odorless

F. Information about recognition of the substance in foreign pharmacopeias:

G. Bibliography of available safety and efficacy data including peer reviewed medical literature:

Aposhian, H.V. DMSA and DMPS— water soluble antidotes for heavy metal poisoning. *Annual Review of Pharmacology and Toxicology*, 1983; 23: 193-215.

Aposhian, H. V., Maiorino, R. M., and Gonzalez-Ramirez, D. Mobilization of heavy metals by newer, therapeutically useful chelating agents. *Toxicology*. 1995; 97(1-3): 23-28.

Chisolm, J. J. BAL, EDTA, DMSA, and DMPS in the treatment of lead poisoning in children. *Clinical Toxicology*, 1992; 30(4): 493-504.

1998-3454B1_02-23-BDL10

Torres-Alanis, O., Garza-Ocanas, L., and Pineyro-Lopez, A. Evaluation of Urinary Mercury Excretion After Administration of 2,3-Dimercapto-1-propane Sulfonic Acid to Occupationally Exposed Men. *Clinical Toxicology*, 1995; 33(6): 717-720.

Aposhian, H. V., Maiorino, R. M., and Rivera, M. Human Studies with the Chelating Agents, DMPS and DMSA. *Clinical Toxicology*, 1992; 30(4): 505-528.

Clarkson, T. W., Magos, L., and Cox, C. Tests of Efficacy of Antidotes for Removal of Methylmercury in Human Poisoning during the Iraq Outbreak. *The Journal of Pharmacology and Experimental Therapeutics*. 1981; 218: 74-83.

Reynolds, J. E. *Martindale - The extra Pharmacopeia* (31st ed.). London, UK: the Royal Pharmaceutical Society. 1996. 997.

Chisolm, J. J. and Thomas D. J. Use of 2,3-dimercaptopropane-1-Sulfonate in Treatment of Lead Poisoning in Children. *The Journal of pharmacology and Experimental therapeutics*, 1985; 235(3): 665-669.

Maiorino, R. M., Gonzalez-Ramirez, D., and Zuniga-Charles, M. Sodium 2, 3-Dimercaptopropane-1-Sulfonate Challenge Test for Mercury in Humans. III. Urinary Mercury after Exposure to Mercurous Chloride. *The Journal of Pharmacology and Experimental therapeutics*, 1996; 277(2): 938-944.

Moore, D. F., O'Callaghan, C. A., and Berlyne, G. Acute arsenic poisoning: absence of polyneuropathy after treatment with 2, 3-dimercaptopropanesulphonate (DMPS). *Journal of Neurology, Neurosurgery, and Psychiatry*, 1994; 57: 1133-1135.

Hurlbut, K. M., Maiorino, R. M., and Mayersohn, M. Determination and Metabolism of Dithiol Chelating Agents XVI: Pharmacokinetics of 2,3-Dimercapto-1-Propanesulfonate after Intravenous Administration to Human Volunteers. *The Journal of Pharmacology and Experimental Therapeutics*. 1994; 268(2): 662-668.

Maiorino, R. M., Xu, Z., and Aposhian, H. V. Determination and Metabolism of Dithiol Chelating Agents. XVII. In Humans, Sodium 2,3-Dimercapto-1-Propanesulfonate is Bound to Plasma Albumin Via Mixed Disulfide Formation and is Found in the Urine as Cyclic Polymeric Disulfides. *The Journal of Pharmacology and Experimental Therapeutics*, 1996; 277(1): 375-384.

Aposhian, H. V., Mershon, M. M., and Brinkley, F. B. Anti-lewisite activity and stability of meso-dimercaptosuccinic acid and 2,3-dimercapto-1-propanesulfonic acid. *Life Sciences*, 1982; 31(19): 2149-2156.

Aposhian, H. V. Biological Chelation: 2,3-dimercapto-propanesulfonic acid and meso-deimercaptosuccinic acid. *Adv Enzyme Regul*, 1982;20: 301-319.

H. Information about dosage forms used:

Capsules

I. Information about strength:

200-400mg

J. Information about route of administration:

Orally

K. Stability data:

Melts at about 230-235°

Stable

L. Formulations:

M. Miscellaneous Information:

transition, but possessed conformational order similar to that of the liquid-crystalline state. These results suggest that DMPC-d54 persists in domains in the outer monolayer while DMPS-d54 is dispersed in the inner monolayer. These experiments are the first to demonstrate that FTIR spectroscopy can be utilized to monitor directly a specific species of lipid molecule from the entire phospholipid population.

AN: 96134839

Record 10 of 27 - MEDLINE EXPRESS (R) 1991 - 1995

TI: Prevention by chelating agents of metal-induced developmental toxicity.

AU: Domingo-JL

SO: *Reprod-Toxicol.* 1995 Mar-Apr; 9(2): 105-113

ISSN: 0890-6238

LA: ENGLISH

AB: Chelating agents such as calcium disodium ethylenediaminetetraacetate (EDTA), 2,3-dimercaptopropanol (BAL), or D-penicillamine (D-PA) have been widely used for the past 4 decades as antidotes for the treatment of acute and chronic metal poisoning. In recent years, meso-2,3-dimercaptosuccinic acid (DMSA), sodium 2,3-dimercapto-1-propanesulfonate (DMPS) and sodium 4,5-dihydroxybenzene-1,3-disulfonate (Tiron) have also shown to be effective to prevent against toxicity induced by a number of heavy metals. The purpose of the present article was to review the protective activity of various chelating agents against the embryotoxic and teratogenic effects of well-known developmental toxicants (arsenic, cadmium, lead, mercury, uranium, and vanadium). DMSA and DMPS were found to be effective in alleviating arsenate- and arsenite-induced teratogenesis, whereas BAL afforded only some protection against arsenic-induced embryo/fetal toxicity. Also, DMSA, DMPS, and Tiopronin were effective in ameliorating methyl mercury-induced developmental toxicity. Although the embryotoxic and teratogenic effects of vanadate were significantly reduced by Tiron, no significant amelioration of uranium-induced embryotoxicity was observed after treatment with this chelator.

AN: 95315648

Record 11 of 27 - MEDLINE EXPRESS (R) 1991 - 1995

TI: Mobilization of heavy metals by newer, therapeutically useful chelating agents.

AU: Aposhian-HV; Maiorino-RM; Gonzalez-Ramirez-D; Zuniga-Charles-M; Xu-Z; Hurlbut-KM; Junco-Munoz-P; Dart-RC; Aposhian-MM

SO: *Toxicology.* 1995 Mar 31; 97(1-3): 23-38

ISSN: 0300-483X

LA: ENGLISH

AB: Four chelating agents that have been used most commonly for the treatment of humans intoxicated with lead, mercury, arsenic or other heavy metals and metalloids are reviewed as to their advantages, disadvantages, metabolism and specificity. Of these, CaNa₂EDTA and dimercaprol (British anti-lewisite, BAL) are becoming outmoded and can be expected to be replaced by meso-2,3-dimercaptosuccinic acid (DMSA, succimer) for treatment of lead intoxication and by the sodium salt of 2,3-dimercapto-1-propanesulfonic acid (DMPS, Dimaval) for treating lead, mercury or arsenic intoxication. Meso-2,3-DMSA and DMPS are biotransformed differently in humans. More than 90% of the DMSA excreted in the urine is found in the form of a mixed disulfide in which each of the sulfur atoms of DMSA is in disulfide linkage with an L-cysteine molecule. After DMPS administration, however, acyclic and cyclic disulfides of DMPS are found in the urine. The Dimaval-mercury challenge test holds great promise as a diagnostic test for mercury exposure, especially for low level mercurialism. Urinary mercury after Dimaval challenge may be a better biomarker of low level mercurialism than unchallenged urinary mercury excretion.

AN: 95232791

Record 12 of 27 - MEDLINE EXPRESS (R) 1991 - 1995

TI: Sodium 2,3-dimercaptopropane-1-sulfonate challenge test for mercury in humans: II.

Urinary mercury, porphyrins and neurobehavioral changes of dental workers in Monterrey, Mexico.

AU: Gonzalez-Ramirez-D; Maiorino-RM; Zuniga-Charles-M; Xu-Z; Hurlbut-KM; Junco-Munoz-P; Aposhian-MM; Dart-RC; Diaz-Gama-JH; Echeverria-D; et-al

SO: *J-Pharmacol-Exp-Ther.* 1995 Jan; 272(1): 264-74

ISSN: 0022-3565

LA: ENGLISH

AB: The sodium salt of 2,3-dimercaptopropane-1-sulfonic acid (DMPS) challenge test (300 mg p.o. after an 11-hr fast) was given in Monterrey, Mexico to dental and nondental personnel. Urine samples were collected and analyzed for total mercury. The mean mercury urinary excretion (+/- S.E.) for 6 hr before and 6 hr after DMPS administration for 10 dental technicians, who formulate amalgam, was 4.84 micrograms +/- 0.742 and 424.0 micrograms +/- 84.9; for 5 dentists, who use amalgam in their practice, 3.28 micrograms +/- 1.11 and 162.0 micrograms +/- 51.2; and for 13 nondental personnel, 0.783 microgram +/- 0.189 and 27.3 micrograms +/- 3.19. The urinary coproporphyrin levels before DMPS administration, which are indicative of renal mercury content, were quantitatively associated with the urinary mercury levels among the three study groups after DMPS administration. This was not so if the urinary mercury level before DMPS administration was compared with the urinary coproporphyrin concentration. The urinary mercury level after DMPS administration is a better indicator of exposure and renal mercury burden than is the mercury level measured in the urine before DMPS is given. Regression analysis showed that the coefficient of urinary mercury was statistically and adversely associated with complex attention (switching task), the perceptual motor task (symbol-digit substitution), symptoms and mood. The easily performed DMPS-mercury challenge test is useful for monitoring dental personnel for mercury vapor exposure.

AN: 95114894

Treatment with DMPS was started because of very severe poisoning, anuric renal failure and optimistic reports on the "new" chelating agent 2,3-dimercapto-1 propanesulphonic acid (DMPS) in mercury poisoning. DMPS was administered by parenteral route initially and was continued thereafter by oral route, until whole blood and urine mercury concentrations had decreased below a level considered as toxic. Except for a temporary pruritic erythema of the skin, no side effects of DMPS treatment were observed. The clinical course was mild, despite continuing high whole blood mercury concentrations. Recovery was uneventful and complete. DMPS treatment, administered by intravenous and oral route, was shown to be an effective alternative for BAL in life-threatening mercuric chloride intoxication. The pharmacokinetic data presented in this case report suggest that non-renal mercury clearance may considerably exceed renal mercury clearance.

AN: 94257266

Record 17 of 27 - MEDLINE EXPRESS (R) 1991 - 1995

TI: Determination and metabolism of dithiol chelating agents. XVI: Pharmacokinetics of 2,3-dimercapto-1-propanesulfonate after intravenous administration to human volunteers.

AU: Hurlbut-KM; Maiorino-RM; Mayersohn-M; Dart-RC; Bruce-DC; Aposhian-HV

SO: J-Pharmacol-Exp-Ther. 1994 Feb; 268(2): 662-3

ISSN: 0022-3565

LA: ENGLISH

AB: The pharmacokinetics of 2,3-dimercaptopropane-1-sulfonate (DMPS), an effective chelating agent for mercury, were determined in five healthy adults after i.v. administration of 3.0 mg/kg of DMPS. DMPS is rapidly transformed to disulfide forms; 15 min after administration, only 12% of the total DMPS detected in blood was present as the parent drug. DMPS and its metabolites were eliminated primarily by the kidneys. By 96 hr after administration, 12% of the total DMPS found in the urine was excreted as the parent drug (10% of the administered dose) and 88% was excreted as disulfide metabolites (74% of the administered dose). The disposition of parent drug was described by a biexponential equation with an elimination half-life of 1.8 hr. By contrast, the elimination half-life of total DMPS was 20 hr. The oral bioavailability of the parent drug was found in a separate study to be 39%. Mercury excretion in healthy volunteers correlated well with the urinary excretion of both the parent drug ($r^2 = .94$) and the disulfide metabolites ($r^2 = .96$).

AN: 94157765

Record 18 of 27 - MEDLINE EXPRESS (R) 1991 - 1995

TI: Human studies with the chelating agents, DMPS and DMSA.

AU: Aposhian-HV; Maiorino-RM; Rivera-M; Bruce-DC; Dart-RC; Hurlbut-KM; Levine-DC; Zheng-W; Fernando-Q; Carter-D; et-al

SO: J-Toxicol-Clin-Toxicol. 1992; 30(4): 505-28

ISSN: 0731-3810

LA: ENGLISH

AB: Meso-2,3-dimercaptosuccinic acid (DMSA) is bound to plasma albumin in humans and appears to be excreted in the urine as the DMSA-cysteine mixed disulfide. The pharmacokinetics of DMSA have been determined after its administration to humans po. For the blood, the t_{max} and $t_{1/2}$ were $3.0 \text{ h} + 0.45 \text{ SE}$ and $3.2 \text{ h} + 0.56 \text{ SE}$, respectively. The C_{max} was $26.2 \text{ micromol} + 4.7 \text{ SE}$. To determine whether dental amalgams influence the human body burden of mercury, we gave volunteers the sodium salt of 2,3-dimercaptopropane-1-sulfonic acid (DMPS). The diameters of dental amalgams of the subjects were determined to obtain the amalgam score. Administration of 300 mg DMPS by mouth increased the mean urinary mercury excretion of subjects over a 9 h period. There was a positive correlation between the amount of mercury excreted and the amalgam score. DMPS might be useful for increasing the urinary excretion of mercury and thus increasing the significance and reliability of this measure of mercury exposure. DMSA analogs have been designed and synthesized in attempts to increase the uptake by cell membranes of the DMSA prototype chelating agents. The i.v. administration of the monomethyl ester of DMSA, the dimethyl ester of DMSA or the zinc chelate of dimethyl DMSA increases the biliary excretion of platinum and cadmium in rats.

AN: 93059546

Record 19 of 27 - MEDLINE EXPRESS (R) 1991 - 1995

TI: BAL, EDTA, DMSA and DMPS in the treatment of lead poisoning in children.

AU: Chisolm-JJ Jr

SO: J-Toxicol-Clin-Toxicol. 1992; 30(4): 493-504

ISSN: 0731-3810

LA: ENGLISH

AN: 93059545

Record 20 of 27 - MEDLINE EXPRESS (R) 1991 - 1995

TI: Protective effects of thiol compounds on chromate-induced cytotoxicity in HeLa cells.

AU: Susa-N; Ueno-S; Furukawa-Y

SO: J-Vet-Med-Sci. 1992 Apr; 54(2): 281-3

ISSN: 0916-7250

LA: ENGLISH

AB: The effects of several thiol compounds on the cytotoxicity induced by chromate (potassium dichromate) were examined. HeLa cells were incubated in Eagle's minimum essential medium (MEM) with or without the chromate alone, or with both chromate and any one of L-cysteine ethyl ester (LCysEE), L-cysteine methyl ester (LCysME), N-acetyl-L-(+)-cysteine, 2,3-dimercaptosuccinic acid (DMSA), 2,3-dimercapto-1-propanesulfonic acid (DMPS), or dithiothreitol. After a given period of incubation, the number of viable cells was counted using the trypan blue exclusion test and the chromium content of the cells was estimated by atomic absorption spectrophotometry. The results obtained were as follows. 1) Chromate-induced cytotoxicity evaluated by inhibition of cell growth at 3 days of

DIMERCAPTO-1-PROPANESULFONIC ACID

Its toxicological properties have not been thoroughly investigated. Ten weeks and 6-month studies in beagle dogs showed no pathological changes attributed to drug.

Has produced nausea, taste impairment, allergic reactions, vertigo, pruritis, necrosis at the injection site and can produce hypotension if given as a bolus.

Has been used as a metal chelator.

REFERENCES

1. Aposhian HV, Mershon MM, Brinkley FB, et al. Anti-lewisite activity and stability of meso-dimercaptosuccinic acid and 2,3-dimercapto-1-propanesulfonic acid. *Life Sciences* 1982; 31(19):2149-56.
2. Aposhian HV. Biological chelation: 2,3-dimercapto-propanesulfonic acid and meso-dimercaptosuccinic acid. *Adv Enzyme Regul* 1982; 20:301-19.
3. Stenman S, Grans L. Symptoms and differential diagnosis of patients fearing mercury toxicity from amalgam fillings. *Scand J Work Environ Health* 1997; 23 Suppl 3:59-63.
4. Garza-Ocanas L, Torres-Alanis O, Pineyro-Lopez A. Urinary mercury in twelve cases of cutaneous mercurous chloride (calomel) exposure: effect of sodium 2,3-dimercaptopropane-1-sulfonate (DMPS) therapy. *J Toxicol Clin Toxicol* 1997; 35(6):653-5.
5. Muckter H, Liebl B, Reichl FX, et al. Are we ready to replace dimercaprol (BAL) as an arsenic antidote? *Hum Exp Toxicol* 1997; 16(8):460-5.
6. Aposhian HV, Arroyo A, Cebrian ME, et al. DMPS-arsenic challenge test. I. Increased urinary excretion of monomethylarsonic acid in humans given dimercaptopropane sulfonate. *J Pharmacol Exp Ther* 1997; 282(1):129-200.
7. Moore DJ, Sills RH, Mendelsohn R. Conformational order of specific phospholipids in human erythrocytes: correlations with changes in cell shape. *Biochemistry* 1997; 36(3):660-4.
8. Kruszewska S, Wiese M, Kolacinski Z, et al. The use of haemodialysis and 2,3 propanesulphonate (DMPS) to manage acute oral poisoning by lethal dose of arsenic trioxide. *Int J Occup Med Environ Health* 1996; 9(2):111-5.
9. Maiorino JS, Gonzalez-Ramirez D, Zuniga-Charles M, et al. Sodium 2,3-dimercaptopropane-1-sulfonate challenge test for mercury in humans. III. Urinary mercury after exposure to mercurous chloride. *J Pharmacol Exp Ther* 1996; 277(2):938-44.
10. Maiorino JS, Xu ZF, Aposhian HV. Determination and metabolism of dithiol chelating agents. XVII. In humans, sodium 2,3-dimercapto-1-propanesulfonate is bound to plasma albumin via mixed disulfide formation and is found in the urine as cyclic polymeric disulfides. *J Pharmacol Exp Ther* 1996; 277(1):375-84.
11. Domingo JL. Prevention by chelating agents of metal-induced developmental toxicity. *Reprod Toxicol* 1995; 9(2):105-13.
12. Aposhian HV, Maiorino RM, Gonzalez-Ramirez D, et al. Mobilization of heavy metals by newer, therapeutically useful chelating agents. *Toxicology* 1995; 97(1):23-38.
13. Gonzalez-Ramirez D, Maiorino RM, Zuniga-Charles M, et al. Sodium 2,3-dimercaptopropane-1-sulfonate challenge test for mercury in humans: II. Urinary mercury, porphyrins and neurobehavioral changes of dental workers in Monterrey, Mexico. *J Pharmacol Exp Ther* 1995; 272(1):264-74.
14. Moore DF, O'Callaghan CA, Berlyne G, et al. Acute arsenic poisoning: absence of polyneuropathy after treatment with 2,3-dimercaptopropanesulphonate (DMPS). *J Neurol Neurosurg Psychiatry* 1994; 57(9):1133-5.

15. Domingo JL. Metal-induced developmental toxicity in mammals: a review. *J Toxicol Environ Health* 1994; 42(2):123-41.
16. Sallsten G, Barregard L, Schutz A. Clearance half life of mercury in urine after the cessation of long term occupational exposure: influence of a chelating agent (DMPS) on excretion of mercury in urine. *Occup Environ Med* 1994; 51(5):337-42.
17. Toet AE, van Dijk A, Savelkoul TJ, et al. Mercury kinetics in a case of severe mercuric chloride poisoning treated with dimercapto-1-propane sulphonate (DMPS). *Hum Exp Toxicol* 1994; 13(1):11-6.
18. Hurlbut KM, Maiorino RM, Mayersohn M, et al. Determination and metabolism of dithiol chelating agents. XVI: Pharmacokinetics of 2,3-dimercapto-1-propanesulfonate after intravenous administration to human volunteers. *J Pharmacol Exp Ther* 1994; 268(2):662-8.
19. Aposhian HV, Maiorino RM, Rivera M, et al. Human studies with the chelating agents, DMPS and DMSA. *J Toxicol Clin Toxicol* 1992; 30(4):505-28.
20. Chisolm JJ Jr. BAL, EDTA, DMSA and DMPS in the treatment of lead poisoning in children. *J Toxicol Clin Toxicol* 1992; 30(4):493-504.
21. Susa N, Ueno S, Furukawa Y. Protective effects of thiol compounds on chromate-induced cytotoxicity in HeLa cells. *J Vet Med Sci* 1992; 54(2):281-8.
22. Aposhian HV, Brunce DC, Alter W, et al. Urinary mercury after administration of 2,3-dimercaptopropane-1-sulfonic acid: correlation with dental amalgam score. *FASEB J* 1992; 6(7):2472-6.
23. Maiorino RM, Dart RC, Carter DE, et al. Determination and metabolism of dithiol chelating agents. XII. Metabolism and pharmacokinetics of sodium 2,3-dimercaptopropane-1-sulfonate in humans. *J Pharmacol Exp Ther* 1991; 259(2):808-14.
24. Molin M, Schutz A, Skerfving S, et al. Mobilized mercury in subjects with varying exposure to elemental mercury vapour. *Int Arch Occup Environ Health* 1991; 63(3):187-92.
25. Heise H, Bayerl T, Isenberg G, et al. Human platelet P-235, a talin-like actin binding protein, binds selectively to mixed lipid bilayers. *Biochim Biophys Acta* 1991; 1061(2):121-31.
26. Duffy DM. Silicone: a critical review. *Adv Dermatol* 1990; 5:93-107; discussion 108-9.
27. Aaseth J, Benov L, Ribarov S. Mercaptodextran—a new copper chelator and scavenger of oxygen radicals. *Chung Kuo Yao Li Hsueh Pao* 1990; 11(4):363-7.
28. Playford RJ, Matthews CH, Campbell MJ, et al. Bismuth induced encephalopathy caused by tri potassium dicitrate bismuthate in a patient with chronic renal failure [see comments]. *Gut* 1990; 31(3):359-60.
29. Kew J, Morris C, Aihie A, et al. Arsenic and mercury intoxication due to Indian ethnic remedies. *Br J Med* 1993; 306(Feb 20):506-7.
30. Portnyagina VA, Fedorova IP, Pochinok TV, et al. Microcapsules of sodium 2,3-dimercaptopropane sulfonate (unithiol). *Farmatsiya Moscow* 1991; 40(2):24-7.
31. Campbell JR, Clarkson TW, Omar MD. Therapeutic use of 2,3-dimercaptopropane-1-sulfonate in two cases of inorganic mercury poisoning. *JAMA* 1986; 256(Dec 12):3127-30.

32. Piomelli S, Rosen JF, Chisolm JJ, et al. Management of childhood lead poisoning. *J Pediatr* 1984; 105(Oct):523-32.
33. Lund ME, Banner W, Clarkson TW, et al. Treatment of acute methylmercury ingestion by hemodialysis with N-acetylcysteine (Mucomyst) infusion and 2,3-dimercaptopropane sulfonate. *J Toxicol Clin Toxicol* 1984; 22(1):31-49.
34. Szinicz L, Wiedmann P, Haring H, et al. Effects of repeated treatment with sodium 2,3-dimercaptopropane-1-sulfonate in beagle dogs. *Arzneim Forsch* 1983; 33(6):818-21.
35. Planas-Bohne F, Gabard B, Schaffer EH. Toxicological studies on sodium 2,3-dimercaptopropane-1-sulfonate in the rat. *Arzneim Forsch* 1980; 30(8):1291-4.
36. Catsch A, Harmuth-Hoene AE. New development in metal antidotal properties of chelating agents. *Biochem Pharmacol* 1975; 24(Sep 1):1557-62.