Polonium-210 and Sulfhydryl Chelating Agents

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Outline

- Introduction
- Polonium-210
- Sulfhydryl chelating agents
- Distribution of ^{210}Po in rats
- Chelating agents and ^{210}Po
- Summary

Periodic Table of the Elements

- Alkali metals
- Alkaline earth metals
- Transition metals
- Lanthanide series
- Actinide series
- Poor metals
- Nonmetals
- Noble gases

- C Solid
- Br Liquid
- H Gas
- Tc Synthetic

New / Original	1 IA	2 IIA	3 IIIB	4 IVB	5 VB	6 VIB	7 VIIB	8 ——	9 VIIIB	10 ——	11 IB	12 IIB	13 IIIA	14 IVA	15 VA	16 VIA	17 VIIA	18 VIIIA	
1	1 H Hydrogen 1.00794; 1																	2 He Helium 4.002602; 2	K
2	3 Li Lithium 6.941; 2 1	4 Be Beryllium 9.012182; 2 2											5 B Boron 10.811; 2 3	6 C Carbon 12.0107; 2 4	7 N Nitrogen 14.00674; 2 5	8 O Oxygen 15.9994; 2 6	9 F Fluorine 18.9984032; 2 7	10 Ne Neon 20.1797; 2 8	K L
3	11 Na Sodium 22.989770; 2 8 1	12 Mg Magnesium 24.3050; 2 8 2											13 Al Aluminum 26.981538; 2 8 3	14 Si Silicon 28.0855; 2 8 4	15 P Phosphorus 30.973761; 2 8 5	16 S Sulfur 32.066; 2 8 6	17 Cl Chlorine 35.453; 2 8 7	18 Ar Argon 39.948; 2 8 8	K L M
4	19 K Potassium 39.0983; 2 8 8 1	20 Ca Calcium 40.078; 2 8 8 2	21 Sc Scandium 44.955910; 2 8 9 2	22 Ti Titanium 47.867; 2 8 10 2	23 V Vanadium 50.9415; 2 8 11 2	24 Cr Chromium 51.9961; 2 8 13 1	25 Mn Manganese 54.938049; 2 8 13 2	26 Fe Iron 55.8457; 2 8 14 2	27 Co Cobalt 58.933200; 2 8 15 2	28 Ni Nickel 58.6934; 2 8 16 2	29 Cu Copper 63.546; 2 8 18 1	30 Zn Zinc 65.409; 2 8 18 2	31 Ga Gallium 69.723; 2 8 18 3	32 Ge Germanium 72.64; 2 8 18 4	33 As Arsenic 74.92160; 2 8 18 5	34 Se Selenium 78.96; 2 8 18 6	35 Br Bromine 79.904; 2 8 18 7	36 Kr Krypton 83.798; 2 8 18 8	K L M N
5	37 Rb Rubidium 85.4678; 2 8 18 8 1	38 Sr Strontium 87.62; 2 8 18 8 2	39 Y Yttrium 88.90585; 2 8 18 9 2	40 Zr Zirconium 91.224; 2 8 18 10 2	41 Nb Niobium 92.90638; 2 8 18 12 1	42 Mo Molybdenum 95.94; 2 8 18 13 1	43 Tc Technetium (98); 2 8 18 13 2	44 Ru Ruthenium 101.07; 2 8 18 15 1	45 Rh Rhodium 102.90550; 2 8 18 16 1	46 Pd Palladium 106.42; 2 8 18 18 0	47 Ag Silver 107.8682; 2 8 18 18 1	48 Cd Cadmium 112.411; 2 8 18 18 2	49 In Indium 114.818; 2 8 18 18 3	50 Sn Tin 118.710; 2 8 18 18 4	51 Sb Antimony 121.760; 2 8 18 18 5	52 Te Tellurium 127.60; 2 8 18 18 6	53 I Iodine 126.90447; 2 8 18 18 7	54 Xe Xenon 131.293; 2 8 18 18 8	K L M N O
6	55 Cs Cesium 132.90545; 2 8 18 18 8 1	56 Ba Barium 137.327; 2 8 18 18 8 2	57 to 71	72 Hf Hafnium 178.49; 2 8 18 32 10 2	73 Ta Tantalum 180.9479; 2 8 18 32 11 2	74 W Tungsten 183.84; 2 8 18 32 12 2	75 Re Rhenium 186.207; 2 8 18 32 13 2	76 Os Osmium 190.23; 2 8 18 32 14 2	77 Ir Iridium 192.217; 2 8 18 32 15 2	78 Pt Platinum 195.078; 2 8 18 32 17 1	79 Au Gold 196.96655; 2 8 18 32 18 1	80 Hg Mercury 200.59; 2 8 18 32 18 2	81 Tl Thallium 204.3833; 2 8 18 32 18 3	82 Pb Lead 207.2; 2 8 18 32 18 4	83 Bi Bismuth 208.98038; 2 8 18 32 18 5	84 Po Polonium (209); 2 8 18 32 18 6	85 At Astatine (210); 2 8 18 32 18 7	86 Rn Radon (222); 2 8 18 32 18 8	K L M N O P
7	87 Fr Francium (223); 2 8 18 32 18 8 1	88 Ra Radium (226); 2 8 18 32 18 8 2	89 to 103	104 Rf Rutherfordium (261); 2 8 18 32 32 10 2	105 Db Dubnium (262); 2 8 18 32 32 11 2	106 Sg Seaborgium (266); 2 8 18 32 32 12 2	107 Bh Bohrium (264); 2 8 18 32 32 13 2	108 Hs Hassium (269); 2 8 18 32 32 14 2	109 Mt Meitnerium (268); 2 8 18 32 32 15 2	110 Ds Darmstadtium (271); 2 8 18 32 32 17 1	111 Rg Roentgenium (272); 2 8 18 32 32 18 1	112 Uub Ununbium (285); 2 8 18 32 32 18 2	113 Uut Ununtrium (284)	114 Uuq Ununquadium (289)	115 Uup Ununpentium (288)	116 Uuh Ununhexium (292)	117 Uus Ununseptium	118 Uuo Ununoctium	K L M N O P Q

Atomic masses in parentheses are those of the most stable or common isotope.

57 La Lanthanum 138.9055; 2 8 18 18 9 2	58 Ce Cerium 140.116; 2 8 18 19 9 2	59 Pr Praseodymium 140.90765; 2 8 18 21 8 2	60 Nd Neodymium 144.24; 2 8 18 22 8 2	61 Pm Promethium (145); 2 8 18 23 8 2	62 Sm Samarium 150.36; 2 8 18 24 8 2	63 Eu Europium 151.964; 2 8 18 25 8 2	64 Gd Gadolinium 157.25; 2 8 18 25 9 2	65 Tb Terbium 158.92534; 2 8 18 27 8 2	66 Dy Dysprosium 162.500; 2 8 18 28 8 2	67 Ho Holmium 164.93032; 2 8 18 29 8 2	68 Er Erbium 167.259; 2 8 18 30 8 2	69 Tm Thulium 168.93421; 2 8 18 31 8 2	70 Yb Ytterbium 173.04; 2 8 18 32 8 2	71 Lu Lutetium 174.967; 2 8 18 32 9 2
89 Ac Actinium (227); 2 8 18 32 18 9 2	90 Th Thorium 232.0381; 2 8 18 32 18 10 2	91 Pa Protactinium 231.03588; 2 8 18 32 20 9 2	92 U Uranium 238.02891; 2 8 18 32 21 9 2	93 Np Neptunium (237); 2 8 18 32 22 9 2	94 Pu Plutonium (244); 2 8 18 32 24 8 2	95 Am Americium (243); 2 8 18 32 25 8 2	96 Cm Curium (247); 2 8 18 32 25 9 2	97 Bk Berkelium (247); 2 8 18 32 27 8 2	98 Cf Californium (251); 2 8 18 32 28 8 2	99 Es Einsteinium (252); 2 8 18 32 29 8 2	100 Fm Fermium (257); 2 8 18 32 30 8 2	101 Md Mendelevium (258); 2 8 18 32 31 8 2	102 No Nobelium (259); 2 8 18 32 32 8 2	103 Lr Lawrencium (262); 2 8 18 32 32 9 2

Note: The subgroup numbers 1-18 were adopted in 1984 by the International Union of Pure and Applied Chemistry. The names of elements 112-118 are the Latin equivalents of those numbers.

Polonium-210

- **Naturally occurring radioactive element that emits highly hazardous alpha particles. $T_{1/2}$ = 138.4 days. Can be vaporized! Has 25 known isotopes.**
- **^{210}Po in every human. But *high* doses are deadly. Estimate: minimal lethal dose of ^{210}Po for an 80 kg person is 0.15 GBq (4 millicuries), or 0.89 micrograms. LD50 for 80kg man ~ 1 μg. *250,000* times more toxic than HCN!**
- **The death of the Russian ex-spy Alexander Litvinenko has been linked to the presence of a "major dose" of polonium-210 in his body.**
- **Uses: static control, heat source in satellites, neutron trigger for nuclear weapons.**
- **Present in tobacco!**

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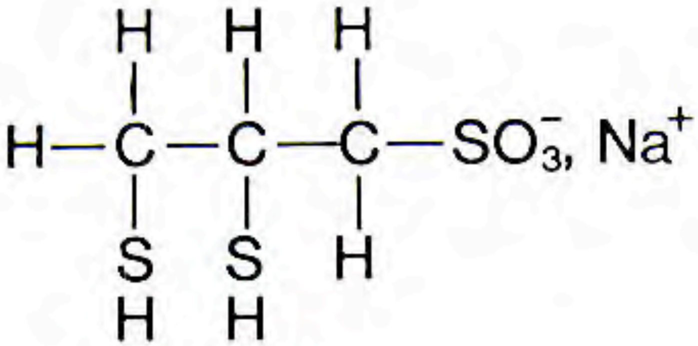
- **Possible bioterrorism scenarios!!**
- **Uses: static control, heat source in satellites, neutron trigger for nuclear weapons.**
- **Present in tobacco!**

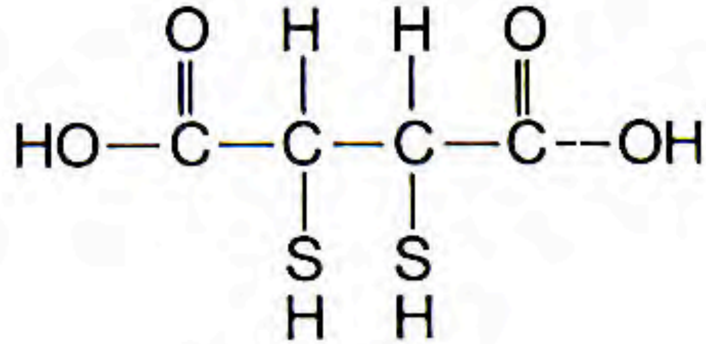


DMPS

(2,3-DIMERCAPTO-1-PROPANE-SULFONIC ACID, Na SALT)

UNITHIOL, DIMAVAL

PETRUNKIN, 1956

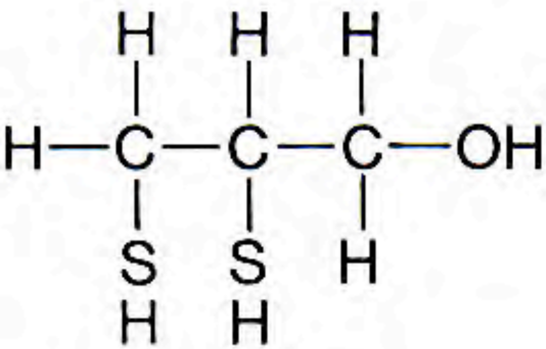


DMSA

(MESO-DIMERCAPTO SUCCINIC ACID)

SUCCIMER

LIANG et. al., 1957

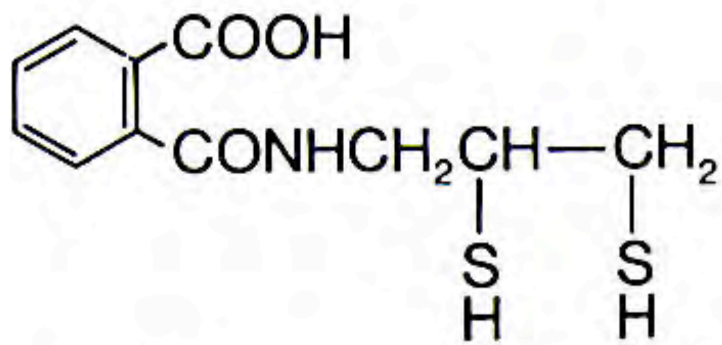


BAL

(BRITISH ANTILEWISITE)

(2,3-DIMERCAPTO-1-PROPANOL)

PETERS et. al., 1945



DMPA

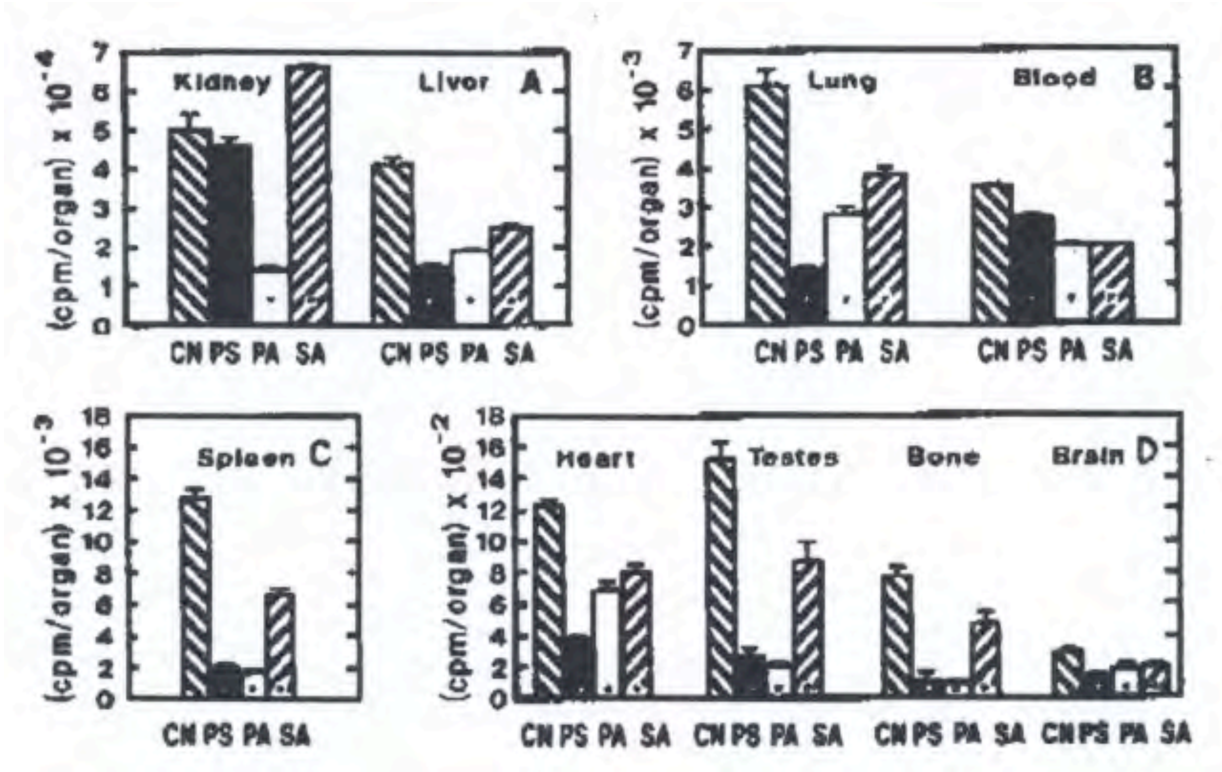
[N-(2,3-DIMERCAPTOPROPYL)-PHTHALAMIDIC ACID]

PORTNYAGINA & MORGUN, 1966

YONAGA et. al., 1981

Tissue Distribution of ^{210}Po.

Kidney ~50,000; liver ~40,000; spleen ~14,000; lung ~6,000; testes ~1500; heart ~1200; bone ~800; brain ~300.



Intracellular DMPS

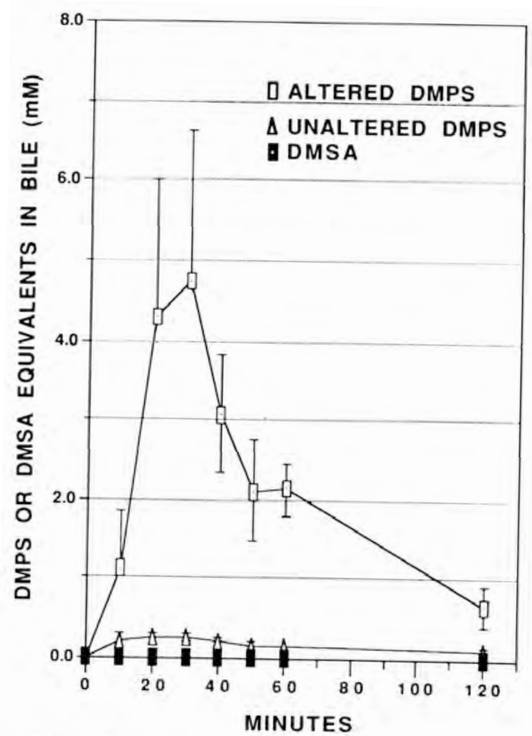


FIG. 4. Determination of DMPS and DMSA in the bile. DMPS and DMSA (0.20 mmol/kg) were administered via the jugular vein at zero time. The method used was the same as that in Fig. 2. There were three rats in each group.

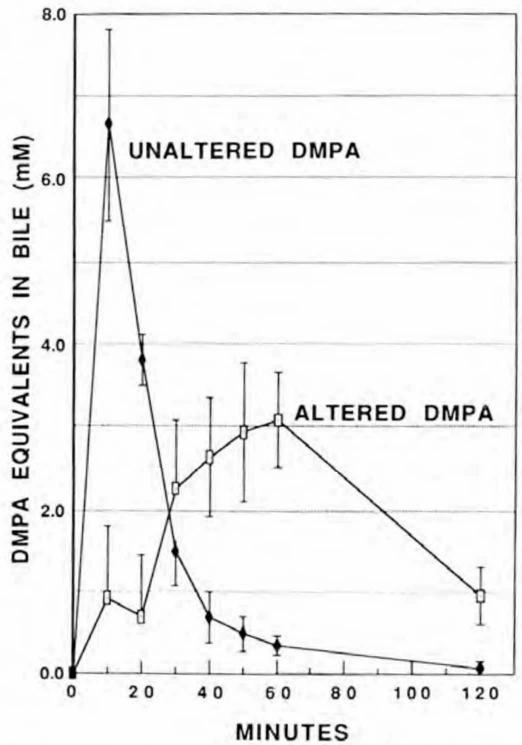


FIG. 3. Unaltered (parent form) and altered (parent form recovered after DTT reduction) DMPA are excreted in the bile. See Fig. 2 legend for method. DMPA was administered at zero time. Altered DMPA was determined by DTT reduction as described in the text. There were three rats in each group. In this and subsequent figures, error bars indicate standard error of the mean.

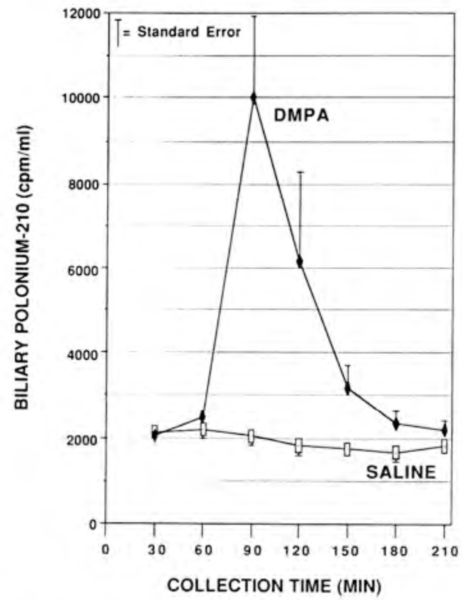
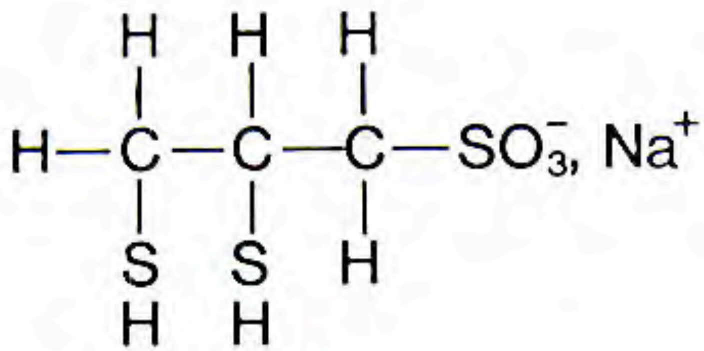


Fig. 5. DMPA increases biliary concentrations of polonium-210. Polonium-210 (3.33×10^7 cpm/kg, intraperitoneal) administered 24 h prior to bile cannulation. Either saline (2 ml/kg, intravenous) or DMPA (0.20 mmol/kg, intravenous) were administered 1 h after bile collection began. Bile was collected in 30-min intervals over 3.5 h. Each point represents the mean ($n = 3$) value. Two-way Anova statistical analysis indicated DMPA curve differs from saline in level ($P = 0.043$) and shape ($P = 0.002$)



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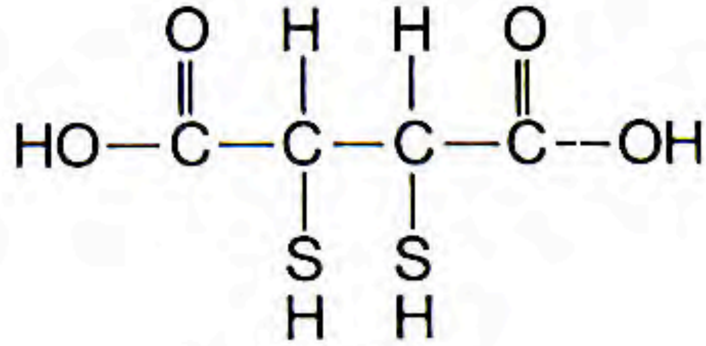

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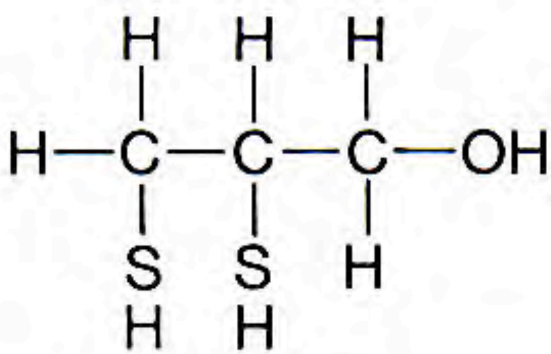

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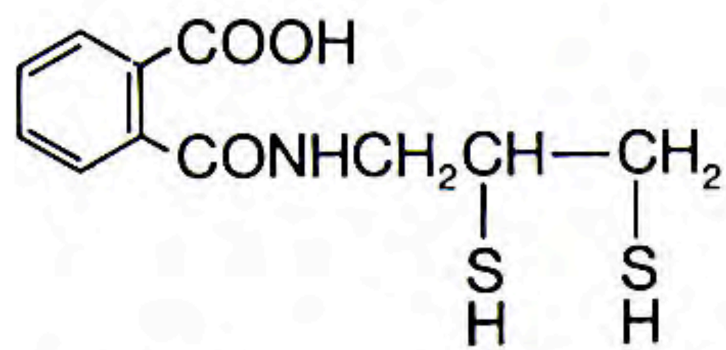

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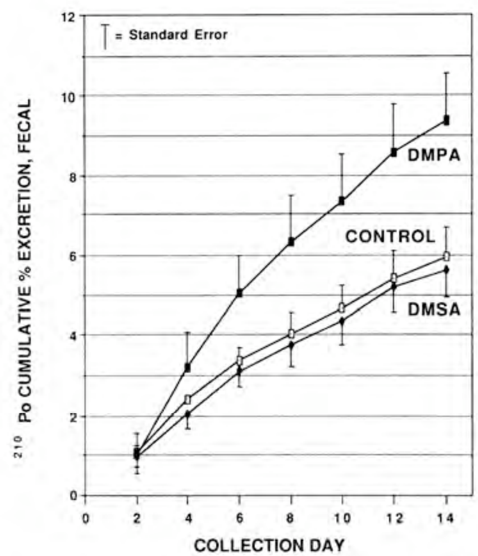


Fig. 2. DMPA increases the fecal excretion of polonium-210. Polonium-210 given at day 0 (3.33×10^7 cpm/kg, intraperitoneal) was followed 1 h later with one of three treatments: 5% sodium bicarbonate control (2 ml/kg, subcutaneous), DMPA or DMSA (0.20 mmol/kg, subcutaneous). Treatments were given once daily for 12 days. Feces were collected, digested and analyzed for polonium-210 content every 2 days. Each point represents the mean ($n = 4$) value. Two-way Anova statistical analysis indicated DMPA ($P < 0.032$) was significantly different from DMSA and control groups

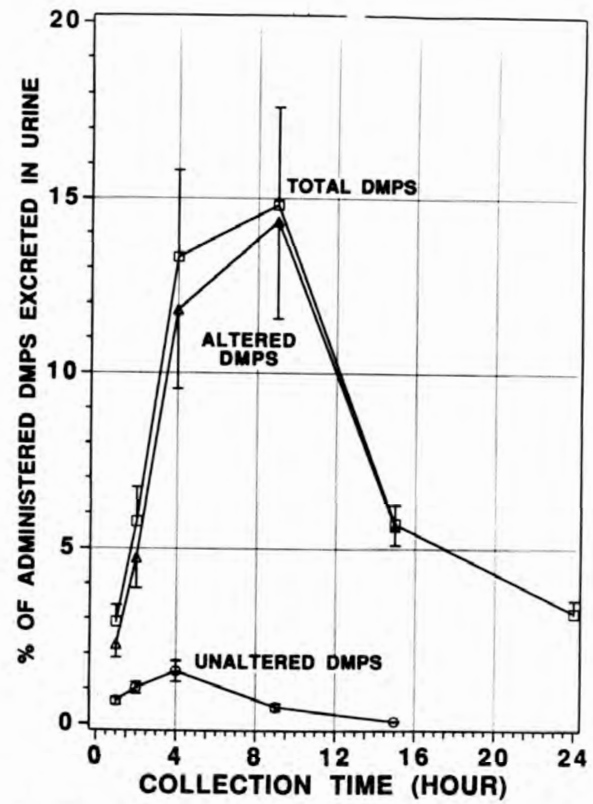


Fig. 10. Urinary excretion of total DMPS, altered DMPS and unaltered DMPS by 10 fasted males given DMPS (300 mg) p.o. Urine samples were treated immediately with mBBr for unaltered DMPS. Total DMPS was determined by treatment with DTT followed by mBBr derivatization. Altered DMPS is total DMPS minus unaltered DMPS. Each point represents the mean ± SE (Maiorino et al., 1991).

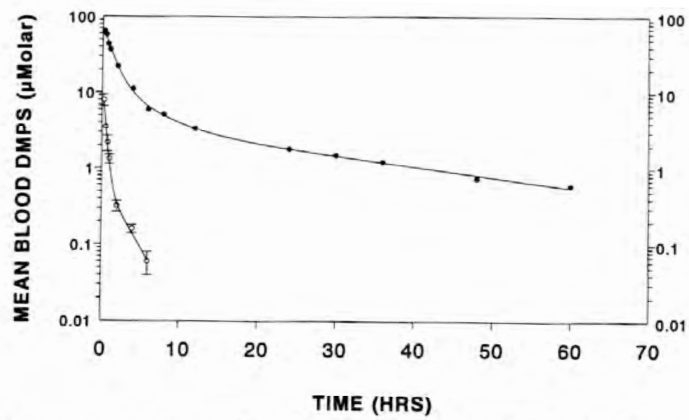


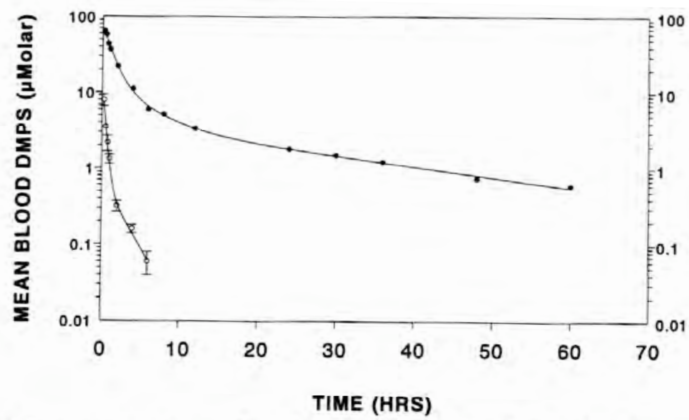
Fig. 11. Mean (± SE) blood concentration-time profiles of total (●) and unaltered (O) DMPS in five subjects given Dimaval, i.v. Unaltered DMPS was detected until the 2-h time point in one subject, until the 4-h time point in another, until the 6-h point in two subjects and until the 8-h point in one subject (Hurlbut et al., 1994).

Scientific Monograph

Dimaval®

(DMPS)

Heyltex Corporation



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- **Chelation increases metal excretion but may not be curative.**
- **Other properties of thiol-containing chelating agents:**
  - **antioxidant**
  - **reducing agents**
  - **cysteine binding and excretion**
    - **DMSA > DMPS**
    - **DMPA???**

If ^{210}Po is a potential terrorist weapon, is there a need to stockpile antidotes? If so, which one(s)?

- Experience with DOD
- Extensive knowledge re DMPS pharmacology in humans. Therapeutic quality readily available.
- Scarcity of everything re DMPA

Summary

- ^{210}Po is an alpha emitter. It is dangerous and lethal in humans. The scenarios can be horrific.
- DMPA or DMPS, but not DMSA, will mobilize ^{210}Po in rats and increase its excretion.
- There is considerable published knowledge regarding DMPS and DMSA in humans.
- DMPA knowledge is limited, especially in humans. A priority as to its chemical synthesis and pharmacological properties needs consider-ation.