

Table 2. Variation of temperature ($^{\circ}\text{C}$) with time at stated bed depth.

Depth (mm)*	Time of heating (min)						
	5	10	15	20	40	80	120
3.1	47	55	60	65	87	98	123
9.3	36	44	52	56	74	90	98
15.5	23	28	33	38	46	45	46

* Depth below bed surface.

moisture which on condensation is then available for more solute migration. This circulatory movement should increase with an increase in temperature gradient. This was confirmed by prolonged drying with the base of the bed resting on ice. After 4 h the bottom layer, though still moist, contained a negligible salt content.

Table 2 illustrates that pronounced temperature differences existed within the bed which would be sufficient to cause back diffusion.

Rates of drying obtained from weight loss measurements were also consistent with recirculation. Beds dried by convection in air normally show a constant rate period of drying (Cealgske & Hougen, 1937) which was absent in the present work. Instead there was an initial period when the rate was falling rapidly which corresponded to the rapid drying of the top layers. This was followed by a period at a slowly falling rate when moisture could be moving to the drying plane and recirculating as postulated. Finally, another steep fall in rate was recorded as the plane of drying receded deeper into the bed.

Drying by radiation in a vacuum might bias the vapour pressure gradient towards the surface and would therefore prevent this circulation. Travers (1975) showed that granules suspended in a vacuum oven showed very little intergranular solute migration on drying and this may be partly due to the absence of recirculation.

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REFERENCES

- CEALGSKE, N. H. & HOUGEN, O. A. (1937). *Trans. Am. Inst. chem. Engrs*, **38**, 283-312.
 KING, A. R. & NEWITT, D. M. (1955). *Trans. Instn chem. Engrs*, **33**, 64-69.
 KUZMAK, J. M. & SEREDA, P. J. (1957). *Soil Sci.*, **84**, 291-299, 419-422.
 LEVY, F. L. (1963). *Insulation J.*, **6**, 47-49.
 TRAVERS, D. N. (1975). *J. Pharm. Pharmac.*, **27**, 516-522.

Meso-dimercaptosuccinic acid a chelating agent for the treatment of mercury and lead poisoning

E. FRIEDHEIM†, C. CORVI*, C. H. WAKKER**, 5^e avenue Marc Monnier, Geneva, *Laboratoire Cantonal de Chimie, Institut d'Hygiene, 22 quai Ernest Ansermet, Geneva and **Laboratoire Analix, S.A., 29 rue de Lancy, Geneva, Switzerland

It is known that meso-dimercapto succinic acid (DMS), a water soluble vicinal dithiol, reduces the mercury concentration in organs of mice and guinea-pigs (Friedheim & Corvi, 1975) and rats (Magos, 1976) exposed to mercury dichloride and methylmercuribromide. We now report experimental findings concerning the effect of DMS on repeated exposures to methylmercuribromide in guinea-pigs and to lead acetate in mice.

General procedures. Groups of 5 mice or 2 guinea-pigs were injected intramuscularly with aqueous solutions of salts of the metals and then intraperitoneally with solutions of DMS or D-penicillamine or EDTA, in schedules differing in size, number and spacing of metal compounds and chelating agents, and the interval between metal doses and treatment, and treatment and autopsy. The same organs of each group were pooled, homogenized and dried to constant weight at 110°. Bone was represented by the skull caps. Blood was obtained by heart puncture. Mercury and lead were

† Correspondence.

determined in aliquots of the homogenates by flameless atomic absorption. The results are reported as means of 3-5 analyses in Tables 1 and 2. Individual analysis varied $\pm 3.2\%$ for mercury and 5.4% for lead.

Mercury. The effects of seven doses of DMS, or penicillamine, alternating with seven doses of methylmercuribromide, on the build-up of mercury concentrations in liver, kidneys, brain and blood in guinea-pigs, are reported in Table 1.

DMS or penicillamine, applied alternately with repeated doses of methylmercuribromide, reduced the build-up of mercury concentrations in liver, kidneys and blood, DMS significantly more so than penicillamine. In brain the mercury concentration was reduced to half by DMS, but was increased above the control value by penicillamine.

Lead. The effects of several dose levels of DMS or penicillamine or EDTA on lead concentrations in liver, kidneys, brain, spleen, blood and bone in 9 groups of 5 mice pretreated with lead acetate, are reported in Table 2.

Table 1. Effect of 7 doses of meso-dimercaptosuccinic acid (DMS) or D-penicillamine (PA) (in 0.2 ml of a 5% soln per 100 g) alternating with 7 doses of methylmercuribromide (in 0.2 ml of a 0.1% soln per 100 g), on mercury in organs of 3 groups of 2 guinea-pigs (1 group per treatment). Mercury concentrations in treated animals are reported as % of mercury in the controls. The absolute values of mercury concentrations in the controls in ng g⁻¹ dry weight are given in brackets.

	Liver %	Kidneys %	Brain %	Blood %
Controls ng g ⁻¹ dry weight	100 (53.2)	100 (127.6)	100 (14.7)	100 (25.6)
DMS 100 mg kg ⁻¹	26.1	25.6	53.0	29.2
PA 100 mg kg ⁻¹	64.2	81.1	118.0	38.4

Schedule: days 1, 3, 5, 7, 9, 11, 13, 2, 4, 6, 8, 10, 12, 14, 15, 16
 2 mg kg⁻¹ CH₃HgBr (i.m.)
 100 mg kg⁻¹ DMS or PA (i.p.)
 Pause
 Chloroformed,
 necropsy

DMS in doses of 10 and 100 mg kg⁻¹ decreased the lead concentration in liver, kidneys, brain and bone, significantly more so than penicillamine or EDTA. An increase of the dose of DMS to 200 mg kg⁻¹ brought about a further decrease of lead in liver, kidneys and

brain, but not in bone. A further increase of dose to 500 mg kg⁻¹ effected another decrease of lead in liver only. In the spleen, DMS tended to increase the lead concentration, more so with higher doses, as if the complexant were shifting lead to the spleen. Possibly, this is connected with the destruction of lead-charged red blood cells in the spleen. In blood, DMS increased the lead concentration in the lower doses of 10 and 100 mg kg⁻¹, and decreased it sharply with higher doses of 200 and 500 mg kg⁻¹. It may be hypothesized, that the complexant mobilizes lead in the tissues, leading temporarily to higher blood concentrations, which are reduced by larger doses.

Penicillamine or EDTA in doses of 100 mg kg⁻¹ decreased the lead concentration in liver, kidneys, brain and bone, but less so than DMS. In doses of 100 mg kg⁻¹ the lead concentration in the spleen was increased by EDTA and penicillamine, and by penicillamine in the blood, where EDTA had little effect. Thus in the treatment of mercury and lead poisoning DMS proved more effective than either penicillamine or EDTA in mice or guinea-pigs. In the brain DMS significantly reduced mercury and lead concentrations while penicillamine had no, or an adverse, effect.

Table 2. Effect of meso-dimercaptosuccinic acid (DMS) and D-penicillamine (PA) intraperitoneally as 0.1–5.0% solutions on lead in organs of groups of 9 mice (1 group per treatment) dosed with lead acetate intramuscularly in 0.2 ml of a 0.1% solution per 20 g mouse. Lead concentrations in treated animals are reported as % of lead in the controls. The absolute values of lead concentrations in the controls in ng g⁻¹ dry weight are given in brackets.

	Liver			Kidney			Brain		
	DMS	PA	EDTA	DMS	PA	EDTA	DMS	PA	EDTA
Control ng g ⁻¹		100 (51)			100 (91)			100 (8.0)	
mg kg ⁻¹									
10	33	92	88	44	118	79	42	102	47
100	45	55	70	35	55	87	48	65	69
200	43			23			37		
500	29			35			36		
	Spleen			Blood			Bone		
	DMS	PA	EDTA	DMS	PA	EDTA	DMS	PA	EDTA
Control ng g ⁻¹		100 (120)			100 (23)			100 (188)	
mg kg ⁻¹									
10	153	50	100	143	122	82	64	85	74
100	47	104	122	122	160	96	48	83	76
200	291			87			55		
500	313			56			48		

Schedule: days 1–5 lead acetate 10 mg kg⁻¹ (i.m.) daily
 6, 7 pause
 8–10 medication with complexants (DMS, PA, EDTA)
 11, 12 pause
 13 chloroformed, necropsy

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REFERENCES

- FRIEDHEIM, E. & CORVI, C. (1975). *J. Pharm. Pharmac.*, 27, 624–626.
 MAGOS, L. (1976). *Br. J. Pharmac.*, 56, 479–484.