

I wish to thank Mr. Sharp of the Wellcome Laboratories of Tropical Medicine for his co-operation and the preparation of the compounds with dimercaprol, Dr. David Trevan for the preparation and examination of the histological preparations of the kidneys and Miss A. Facey for valuable technical assistance.

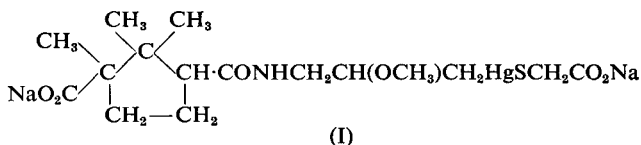
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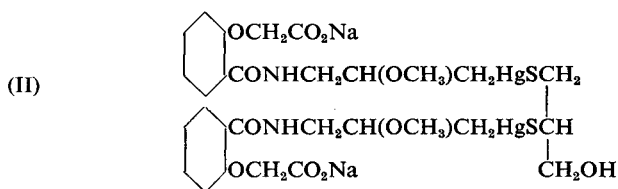
A NOTE ON THE PREPARATION OF COMPOUNDS OF MERCURIAL DIURETICS WITH 2:3-DIMERCAPTOPROPANOL (DIMERCAPROL)

BY T. M. SHARP

LEHMAN¹ has shown that the acute toxicity of mercurial diuretics is greatly reduced by combining the mercury with monothiols such as thioglycollic acid. One of these is now in clinical use in the United States of America under the names thiomerin and mercaptomerin.¹ It was thought that a similar or greater reduction in toxicity might be attained by combining

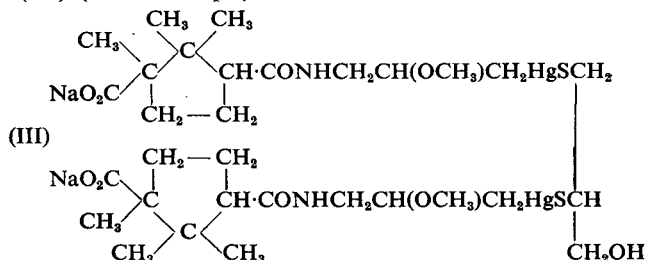


known mercurial diuretics with dimercaprol, 2:3-dimercaptopropanol, which is a well established antidote for heavy metal poisoning. It is now shown that 2 mols. of mersalyl will combine readily in alkaline solution



MERCURIAL DIURETICS WITH DIMERCAPROL

with 1 mol. of dimercaprol to form the disodium salt of 2:3-bis(3'-*o*-carboxymethoxybenzamido-2'-methoxypropylmercurimercapto)-propane-1-ol (II) for which the trivial name *balmersal* is suggested. Similarly γ -hydroxymercuri- β -methoxypropylcamphoramido (mercuriophyllin, U.S.P.) yields 2:3-bis(3'-camphoramido-2'-methoxymercurimercapto)-propane-1-ol (III) (*balmercaph*).



EXPERIMENTAL

Balmersal (II). Salicyl(γ -hydroxymercuri- β -methoxypropylamide)-*O*-acetic acid (19.35 g., 2 mols.) was dissolved in an equivalent amount of N sodium hydroxide. To the strongly alkaline solution 2:3-dimercaptopropanol (2.486 g., 1 mol.) was added slowly with stirring. A slight rise in temperature took place with drop in *pH* to about 8.0. After standing for 1 hour the disodium salt of 2:3-bis-(3'-*o*-carboxymethoxybenzamido-2'-methoxypropylmercurimercapto)-propane-1-ol could be precipitated as a hygroscopic powder by pouring into a large volume of acetone, but it was found preferable to isolate the salt by freeze-drying, when it was obtained as a colourless powder with no definite m.pt.

Found: Hg, 35.9; S, 5.9; $C_{29}H_{36}O_{11}N_2S_2Hg_2Na_2$ requires Hg, 36.5; S, 5.8 per cent.

Balmercaph (III). γ -Hydroxymercuri- β -methoxypropylcamphoramido (4.86 g., 2 mols.) was treated as above with N sodium hydroxide and 2:3-dimercaptopropanol (0.62 g., 1 mol.). The solution was diluted with 4 vol. of water and left in the dark for about a week during which time it slowly deposited a small amount of white insoluble material which was not investigated further. After filtration the solution was freeze-dried to yield the disodium salt of 2:3-bis-(3'-camphoramido-2'-methoxymercurimercapto)-propane-1-ol as a colourless powder with no definite m.pt.

Found: Hg, 35.0; S, 5.92; $C_{31}H_{50}O_9N_2S_2Hg_2Na_2$ requires Hg, 36.3; S, 5.8 per cent.

Mercury was estimated by the U.S.P. method for mercuriophylline, and sulphur by the Carius method.

The author thanks Messrs. K. H. Pratley and A. G. Turner for technical assistance.

SUMMARY

Mersalyl and mercuriophylline combine with 2:3-dimercaptopropanol in the proportion of 2 mols. of the mercury compound to one of the dithiol.

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T. M. SHARP

DISCUSSION

The paper was presented by DR. E. I. SHORT.

MR. A. F. CALDWELL (Singapore) said that as mercury diuretics were frequently used in cases involving kidney damage it would be of great value if the risk of further harm to the kidney could be reduced without affecting the diuretic effect.

VOTE OF THANKS

The Chairman's proposition that a hearty vote of thanks be accorded to all the authors of the papers was carried with acclamation, as was a vote of thanks to the Editor of the *Journal of Pharmacy and Pharmacology* for advance proofs of the papers.

Correction.

THE PURITY OF VITAMIN B₁₂

By J. G. HEATHCOTE.

This Journal, 1952, 4, 643.

TABLE I

For *Cyanocobalamin* (Vitamin B_{12b}) read *Cyanocobalamin* (Vitamin B₁₂).

For *Hydroxycobalamin* (Vitamin B_{12d}) read *Hydroxycobalamin* (Vitamin B_{12b}).