

✓ THE ACTIVITY OF THIA CETAZONE, THIAMBUTOSINE AND THIOCARLIDE IN  
THE CHEMOTHERAPY OF EXPERIMENTAL LEPROSY

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The increasing number of dapsone-resistant strains of M. leprae emphasizes the need for a number of alternative drugs effective in leprosy therapy, either for selective use in patients harboring dapsone-resistant bacilli, or for routine administration in combination with dapsone.

Of the "second line" drugs available, thiacetazone (p-acetylamino-benzaldehyde-thiosemicarbazone, TBI) and thiambutosine (p-butoxy-p'dimethylaminodiphenyl thiourea) have been poorly studied with respect to their activity against M. leprae and their pharmacology.

This paper reports investigations on the activity of thiambutosine, thiacetazone and thiocarlide (Isoxyl) against M. leprae in the mouse foot pad model, with a view to rationalizing their use in clinical therapy.

The minimum effective dose (MED) of thiambutosine and thiocarlide against 5 strains of M. leprae was found to be 0.03% to 0.1%, and of thiacetazone 0.01% to 0.03%. The three compounds were found to be purely bacteriostatic against M. leprae at dietary concentrations up to 0.2%.

The serum levels in mice of thiambutosine were determined using a gas chromatographic method, and of thiacetazone using a radioactive assay procedure, and by relating these to the MED results, thiambutosine was found to have a minimum inhibitory mouse serum concentration of 0.3 µg/ml to 1.0 µg/ml, and thiacetazone of approximately 0.26 µg/ml. These MIC's were related to the serum levels of patients under treatment with the drugs.