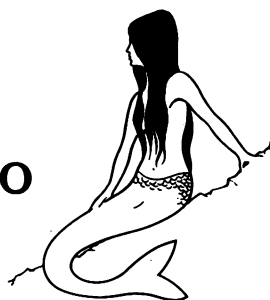


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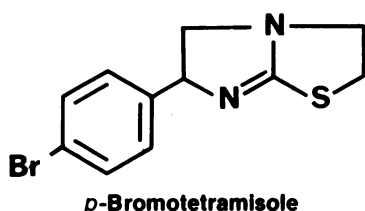
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(-)-*p*-Bromotetramisole: a potent alkaline phosphatase inhibitor



In the process of evaluating the biochemical effects of Tetramisole (*dl*-2,3,5,6-tetrahydro-6-phenylimidazo[2,1-*b*]thiazole hydrochloride), a broad-spectrum anthelmintic,¹ it was discovered that the compound was a potent inhibitor of alkaline phosphatase.² Consequently, similar studies were undertaken on the analogs of Tetramisole. Its levorotatory isomer, Levamisole (R12456, *l*-Tetramisole, *l*-2,3,5,6-tetrahydro-6-phenylimidazo[2,1-*b*]thiazole hydrochloride)²⁻⁴ and R8231 [*dl*-6-(*m*-bromophenyl)-2,3,5,6-tetrahydroimidazo[2,1-*b*]thiazole oxalate]²⁻⁴ proved to be potent, stereospecific, noncompetitive inhibitors of alkaline phosphatase from various tissues, yet showed no inhibition of the intestinal isoenzyme. The *d*-isomers were completely inactive.

l-p-Bromotetramisole (R30402) has been found to be more potent than Levamisole as an inhibitor of alkaline phosphatase.⁵⁻⁷ The inactive *d*-isomer, *d-p*-bromotetramisole (R30401), is useful as an internal control.

The organo- and stereospecificities of these alkaline phosphatase inhibitors have been demonstrated biochemically as well as cytochemically in a variety of tissues and species.^{2-4,6-12} Specific phosphatase activities are not altered by these compounds.^{4,7} Thus, this high degree of specificity allows the differentiation between "true" 5'-nucleotidase, Na-K-ATPase, Mg-

ATPase or glucose-6-phosphatase and non-specific alkaline phosphatase, the latter being totally suppressed upon addition of the inhibitor.^{4,7,13-18}

l-p-Bromotetramisole is reportedly more appropriate for the quantitative determination of the intestinal and placental isoenzymes in human serum than the commonly used L-phenylalanine.⁶

l-p-Bromotetramisole has several advantages over Levamisole and R8231:

1. potency - it is ten times as potent as Levamisole
2. stability - it is more stable in aqueous solution than R8231
3. the availability of both *levo*- and *dextro*-isomers.

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