previous electron micrographs[19] and those of Evans et al.[20] showed that all of these cell borders are present in typical plasma membrane fractions prepared with the present method.

The present result is of interest in light of the current hypothesis that the HCO_3^--ATPase is involved in the development of pH gradients across cell membranes of secretory organs[5]. In the liver, there are transcellular pH gradients that cannot be explained by a passive distribution of hydrogen or bicarbonate ions, and the liver is also capable of secreting a solution of high bicarbonate ion concentration and high pH[21]. Since this secretion of the liver is similar (in alkalinity) to that of the pancreas, the fact that the liver plasma membrane does not contain a HCO_3^--ATPase while that of the pancreas is thought to[22], is of physiological interest. However, the pancreas results are suspect due to mitochondrial contamination. In conclusion the present results indicate that the HCO_3^--stimulated Mg^{2+}-ATPase is not involved with HCO_3^--secretion into bile since neither rat liver p.m. fragments nor rat liver microsomal vesicles have HCO_3^--ATPase activity.

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Anthelmintic activity of tioxidazole (Sch 21480) against gastrointestinal roundworms

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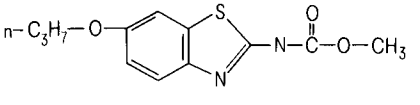
Summary. Methyl-6-propoxybenzothiazole-2-carbamate (tioxidazole) has broad spectrum activity against gastrointestinal nematodes.

We wish to report the discovery of a new anthelmintic agent with broad spectrum activity against gastrointestinal roundworm infections. Tioxidazole is methyl-6-n-propoxybenzothiazole-2-carbamate and has the chemical formula $C_{12}H_{14}N_2O_3S$ (figure). Structural similarity of tioxidazole and benzimidazole anthelmintic compounds should be noted.

Tioxidazole is prepared from 2-amino-6-n-propoxybenzothiazole and methylchlorocarbonate in pyridine as solvent. It is crystallized from ethanol as a stable, white, odorless, powder melting at 178–180 °C. It is insoluble in water and only slightly soluble in most organic solvents. Other methods of preparation have been described[1].

Tioxidazole was effective in mice against *Nematospiroides dubius* and *Syphacia obvelata* when administered at dietary levels of 0.018% to 0.037% or by gavage at 50 mg/kg for 5 days. A single 75 mg/kg oral dose was over 99% effective against a *Trichinella spiralis* infection in mice[2]. Against *Strongyloides ratti* tioxidazole was active by gavage as a single oral dose of 200 mg/kg, 100 mg/kg twice daily, or by 50 mg/kg given for 3 days or 25 mg/kg for 5 days.



Methyl-6-n-propoxybenzothiazole-2-carbamate - (tioxidazole).

In preliminary experiments in dogs, a single oral dose of 200 mg/kg was active against *Toxascaris leonina.* Daily doses of 100 mg/kg for 3 days or 50 mg/kg for 5 days were also effective against hookworms and *Trichuris vulpis.*

Single oral doses of 10–50 mg/kg administered to sheep, naturally or artificially infected, eliminated 87–100% of *Haemonchus spp., Ostertagia spp., Trichostrongylus spp., Marhallagia spp.* or *Cooperia spp.* In critical studies in horses, single oral doses of 5–25 mg/kg were effective in eliminating over 90% of *Parascaris equorum, Oxyuris equi, Strongylus vulgaris, S. edentatus* and a variety of small strongylid worms.

Dose levels up to 100 mg/kg have had no adverse effects in the horse. Further studies to evaluate oral toxicity and teratogenic potential are underway, as are investigations to delineate the compound's safety and field efficiency.

1 U.S. patent No. 4,006,242, issued February 1, 1977 to M.M. Nafissi-V.

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