THE EFFECT OF THIOCHOLESTEROL ON THE ACUTE TOXICITY OF MERCURIC CHLORIDE

BY

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Submitted to the faculty of the Graduate School in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Toxicology from the Department of Pharmacology and Toxicology, Indiana University, May, 1977.

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Date of Approval: May 26, 1977

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Major Subject: Toxicology

Minor Subject: Pharmacology

ABSTRACT

The Effect of Thiocholesterol
on the Acute Toxicity of Mercuric Chloride

James J. Burgun

A single oral dose of thiocholesterol (TC) administered up to 12 hours after a single oral dose of mercuric chloride significantly reduced mortality in mice. Administering TC po in 3 doses 2 hours before, at the same time as, and 2 hours after an intraperitoneal injection of mercuric chloride also afforded a significant degree of protection. Intraperitoneal injection of TC was not effective against mercuric chloride administered orally, nor was it effective against mercuric chloride administered intraperitoneally unless it was given immediately after the mercury. The intraperitoneal administration of TC did not alter mortality caused by the intraperitoneal or oral administration of arsenic trioxide, while orally administered TC increased mortality when given after orally administered arsenic. Thiocholesterol, po, did not protect mice from an ip injection of cadmium chloride. When both were administered ip TC caused a significant reduction in mortality when given up to 1 hour after cadmium. When both were administered po TC reduced mortality when its administration was delayed 2 hours after cadmium; administering TC at shorter intervals failed to provide protection. TC did not change the acute toxicity of thallium sulfate.

BAL, 60 mg/kg ip, given 2 hours after orally administered mercuric chloride increased the LD50 from 55 to 103 mg/kg, whereas TC, 1320 mg/kg po, increased the LD50 to 81 mg/kg. The combination of BAL and TC increased the LD50 to 102 mg/kg. Under these conditions BAL was a more effective antagonist than TC and the combination of the two was no more effective than BAL alone.

Rats were injected via the tail vein with 5 microcuries of 203-mercuric chloride 2 hours after the oral administration of either vehicle or 1 g TC/kg. Animals were sacrificed at intervals up to 14 days after treatment and brain, blood, kidneys, and liver analyzed for Hg. Two additional groups of rats were dosed in the same manner and housed in metabolism cages for 14 days to determine the urinary and fecal excretion of Hg. To evaluate kidney function groups of rats were pretreated with either vehicle or 1 g TC/kg po, 2 hours prior to an iv injection of 1 mg $HgCl_2$/kg. Rats were housed in metabolism cages and sacrificed either 2 days or 4 days after dosing. The 24 hour urine volume was measured and determinations made of total protein, osmolality, creatinine, serum creatinine, and creatinine clearance. One kidney was removed from each rat for histological examination. Thiocholesterol treated rats had a significantly lower concentration of mercury in the liver and blood from day 1 through day 14 compared to control. The TC treated group had less mercury in the kidneys 12 hours after injection but from day 1 through day 14 the levels were no different from control; nor did TC treatment alter brain content of mercury. Control rats excreted 38% of the administered dose of mercury in the urine and 44% of the dose in the feces during 14 days, for a total excretion of 82%. Thiocholesterol treated rats excreted significantly less mercury in the urine (8% of the dose) and significantly more in the

feces (68% of the dose) compared to control. The total amount of mercury excreted after 14 days was 76% of the dose, a slight but statistically significant reduction compared to control. Thiocholesterol treatment reduced the functional and histologic damage done to the kidney by the 1 mg/kg dose of mercuric chloride, even though it did not decrease kidney levels of mercury or promote its urinary excretion.

Thiocholesterol treatment increased the LD50 of mercuric chloride from 55 to 81 mg/kg. Neither phenobarbital nor SKF-525A had significant effects on the ability of TC to antagonize mercuric chloride lethality. The LD50 of mercuric chloride after phenobarbital-TC treatment (86 mg/kg) and after SKF-525A-TC treatment (79 mg/kg) was no different from the LD50 determined after TC treatment alone.

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