Nephrotoxic potential of *N*-(3,5-dichlorophenyl)glutarimide and *N*-(3,5-dichlorophenyl)glutaramic acid in Fischer 344 rats

Ginny L. Kellner-Weibel[a], Ruy Tchao[b] and Peter J. Harvison[b],

[a] Department of Chemistry, Philadelphia College of Pharmacy and Science, 600 South Forty-third Street, Philadelphia, PA 19104-4495, USA
[b] Department of Pharmacology and Toxicology, Philadelphia College of Pharmacy and Science, 600 South Forty-third Street, Philadelphia, PA 19104-4495, USA

...Knoxville, TN). The Pallas software package (**CompuDrug**, Rochester, NY) was used to calculate...suggested that cytochrome P450-mediated **metabolism** in the succinimide ring was involved...However, even if NDPG undergoes oxidative **metabolism** by P450, the glutarimide ring has I...

Abstract

The agricultural fungicide *N*-(3,5-dichlorophenyl)succinimide (NDPS) produces kidney damage in rats. Although many NDPS analogues have been screened as possible nephrotoxicants, the one-carbon homologue, *N*-(3,5-dichlorophenyl)glutarimide (NDPG), has not been evaluated. This study examined the nephrotoxic potential ofNDPG and a putative metabolite, *N*-(3,5-dichlorophenyl)glutaramic acid (NDPGA). Male Fischer 344 rats (*N* = 3–4 per group) were administered a single i.p. injection in corn oil of NDPG or NDPGA (0.4 or 1.0 mmol/kg), NDPS (0.4 mmol/kg), or corn oil alone. Renal function was monitored for 48 h. In contrast to NDPS, NDPG and NDPGA did not significantly alter renal function or kidney morphology when compared to corn oil-treated controls. These experiments show that replacement of the succinimide ring in NDPS with a glutarimide ring abolishes toxicity.
Author Keywords: Glutarimide; Glutaramic acid; Kidney; Rat; Nephrotoxicity; Succinimide

Toxicology Letters
Volume 80, Issues 1-3 , October 1995, Pages 123-129