EFFECT OF TREATMENT WITH NORBOLETHONE ON PARATHION TOXICITY IN MALE RATS

Casey P. Robinson*, P. W. Smith†, Judy K. McConnell*, and B. R. Endecott†

*University of Oklahoma, College of Pharmacy, Health Sciences Center, Oklahoma City, Oklahoma 73190, and
†Civil Aeromedical Institute, Federal Aviation Administration, Oklahoma City, Oklahoma 73125

INTRODUCTION

A number of steroids are classified as "catatoxic" as they oppose the effects of toxic compounds (1). Norbolethone, a clinically useful anabolic steroid, is one of the more potent catatoxic steroids. Its interactions have been studied with carbon tetrachloride (2), indomethacin (3), ethylene glycol (4), L-tyrosine (5), LSD (6), allopurinol (7), bishydroxycoumarin (8), phenyl isothiocyanate (9), haloperidol (10), proscillaridin, (11) methyl salicylate (12), acrylonitrile (13), methaqualone (14), thioacetamide (15), digitoxin (16), aniline (17), cocaine (18), ketamine (19), and pesticides (20, 21).

In this study we report the protective effects of norbolethone against the cholinesterase-inhibiting, organophosphorus insecticide parathion in male rats.

Ninety-three male Holtzman rats weighing between 100-120 g were randomly divided into two groups of 46 and 47 rats. Each rat in one group was fed a suspension of 10 mg of norbolethone in one m*l* of water by oral feeding tube twice daily for three days and once on the fourth day.

A control group was fed 1 m*l* of water on the same schedule. This dose was effective in previous studies with norbolethone and other catatoxic steroids (20, 21). On the fourth day, 2 hours after feeding, four different levels of parathion were injected into either 11 or 12 rats from the control or norbolethone-treated groups. The parathion was dissolved in dimethyl sulfoxide (DMSO) so that each rat received 1 m*l* of DMSO per kg injected i.p. The rats were observed for tremors for one hour, and the LD_{50} values were determined from the number of rats succumbing 24 hours post-injection.

The rats receiving parathion exhibited salivation, piloerection, diarrhea, tremors, or convulsions, signs of cholinergic stimulation typical of poisoning by cholinesterase inhibitors. Norbolethone afforded considerable protection against tremors induced by parathion (Table 1). Most of the control rats had tremors within the first hour even with the lowest dose (2 mg/kg) of parathion. The incidence of tremors at equal doses of parathion (4 or 5 mg/kg) was much lower in norbolethone-treated rats. Mortality was also reduced in norbole-

TABLE 1. *Effect of pretreatment with norbolethone on the incidence of tremors and lethality in male rats given parathion.*

Pretreatment[a]	Dose of parathion[b] (mg/kg)	Fraction of animals having tremors during first hour	LD_{50} (mg/kg) Mean ± S.E.M.
Water sham	2	9/11	3.5 ± 0.28
"	3	11/12	
"	4	12/12	
"	5	12/12	
Norbolethone	4	3/11	5.6 ± 0.24
"	5	6/12	
"	6	9/12	
"	7	9/11	

[a] 10 mg of norbolethone in 1 ml of water (or water alone) by gastric tube twice daily and once on the fourth day.
[b] Intraperitoneally in DMSO (1 ml/kg. body weight) 2 hours after the last dose of norbolethone.

thone-treated rats, with the LD_{50} being 60% higher than that of control rats.

The reduction in toxicity of parathion in male rats following pretreatment with norbolethone was somewhat less than that previously reported for female rats (21). Unlike the case of the catatoxic steroid ethylestrenol (22), no part of this additional protection afforded female rats could be due to androgenic activity since norbolethone is devoid of androgenic activity (23). Catatoxic steroids seem to exert most of their protective effects by induction of liver enzymes (24). Induction of enzymes to a lesser extent in livers from male compared to female rats has been previously reported with another compound (25).

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