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PRELIMINARY COMMUNICATION

ELEVATION IN BLOOD ACETALDEHYDE BY PARGYLINE DURING ETHANOL ADMINISTRATION

Gerald Cohen, Dana MacNamee and Dorothy Dembiec
Department of Neurology, Mount Sinai School of Medicine
Fifth Avenue and 100th street, New York, N.Y. 10029

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We report that pargyline, a popular monoamine oxidase inhibitor, markedly elevates blood acetaldehyde levels in ethanol-intoxicated mice and rats. This observation is important to investigators who use pargyline in experiments concerned with ethanol-catecholamine interactions.

Male Swiss-Webster mice (25–30 gms) and male Sprague-Dawley rats (350–400 gms) received i.p. injections of pargyline hydrochloride (gift of Abbott Laboratories), 100 mg/kg in distilled water; this dose is commonly used to inhibit monoamine oxidase[1,2]. Control animals received an equivalent volume (0.5 ml) of distilled water. Two hours later, ethanol 4 gm/kg (25% v/v in saline) was injected i.p. One hour later, the animals were decapitated and blood from the neck was collected onto Parafilm (Fisher Scientific); a 50 μl sample was taken immediately and added to 250 μl of distilled water in a 17.5 ml test tube. The tube was sealed with a screw cap containing a rubber septum and was inserted into a water bath at 55°C. Thirty minutes later, one ml of head gas was withdrawn with a plastic syringe and injected immediately into a Hewlett-Packard gas chromatograph (Model 5750, flame ionization detector, Poropak N column, 160°C, helium zero gas as carrier, flow rate 30 ml/min). Acetaldehyde was eluted from the column in 2.8 minutes. The peak height was linearly related to the amount of acetaldehyde injected and the sensitivity was 94 scale divisions (range 1, attenuation 2) for 2.0 μg acetaldehyde per ml (aqueous standard). Recovery from blood lysates was 85%. This procedure was

BLOOD ACETALDEHYDE LEVELS ONE HOUR AFTER ADMINISTRATION OF ETHANOL (4 GM/KG)

Treatment	Dose	Blood Acetaldehyde (μg/ml, Mean ± SEM)
	Swiss-Webster Mice	
None		0.79 ± 0.08 (N=25)
Pargyline	100 mg/kg (1X)	20.66 ± 0.94 (N=28)
DDC	230 mg/kg (2X)	7.46 ± 3.49 (N=5)
DDC	1 gm/kg (2X)	10.42 ± 0.44 (N=4)
	Sprague-Dawley Rats	
None		1.02 ± 0.74 (N=7)
Pargyline	100 mg/kg (1X)	12.41 ± 2.22 (N=7)

a modification of a standard method[3]. There was no generation of acetaldehyde when ethanol was added to blood lysates from control or pargyline-treated animals under these conditions.

For comparison, diethyldithiocarbamate (DDC, Eastman Organic Chemicals), the water soluble monomer (thiol) of disulfiram (a disulfide), was injected into mice. Deitrich and Erwin[4] have shown that DDC and disulfiram are equally effective inhibitors of liver aldehyde dehydrogenase *in vivo*. DDC was administered in 0.05 M phosphate buffer, pH 7.4, at two dose levels: 230 mg/kg (equimolar, in terms of disulfiram, to the pargyline dose) and 1 gm/kg. These injections were given 18 hours beforehand and, again, one hour before the ethanol.

Results of these experiments (Table) showed that pargyline elevated the blood acetaldehyde levels 22-fold in mice (from 0.8 to 20.7 μg/ml) and 12-fold in rats (from 1.0 to 12.4 μg/ml). In comparison, the mean acetaldehyde levels in mice after two injections of DDC were lower (7.5 μg/ml and 10.4 μg/ml for the low and high doses, respectively) than that seen after a single injection of pargyline. In other experiments, in which the same doses of DDC were injected, but only once, at one hour prior to ethanol, blood acetaldehyde levels were approximately one-half those seen after two doses of DDC. In

control experiments, no acetaldehyde was observed in mice receiving pargyline alone. Blood ethanol levels in these experiments were (mg/ml, mean ± S.E.M.): mice, control 3.79 ± 0.10 and pargyline-treated 4.19 ± 0.04; rats, control 3.81 ± 0.14 and pargyline-treated 4.03 ± 0.12.

Some mice were given ethanol 18 hours after pargyline. These animals did not show the elevation in blood acetaldehyde. Since monoamine oxidase is inhibited at this time[1], it appears that the effect of pargyline on acetaldehyde levels is unrelated to monoamine oxidase inhibition, per se.

In other control experiments, replicate blood samples were lysed in water containing 10^{-2}M sodium bisulfite (an aldehyde-binding agent). This treatment eliminated the measured peak, thereby confirming its identity as acetaldehyde. Sodium bisulfite likewise eliminated the peak from authentic acetaldehyde samples, but had no effect on the measurement of ethanol. The addition of 25 mM thiourea, which has been reported by Sippel[5] to prevent artifactual formation of acetaldehyde from ethanol in tissue extracts, had no effect on the acetaldehyde peak. Therefore, the observed acetaldehyde was not formed during the assay procedure, but was present in the circulating blood.

Acetaldehyde is a pharmacologically active agent[6]. Much of the symptomatology of the alcohol-antabuse reaction in man has been attributed to elevated acetaldehyde levels[6]. Additionally, acetaldehyde releases catecholamines from body stores[6,7], it affects the pathways of catecholamine metabolism[8,9], and it condenses with catecholamines to form tetrahydroisoquinoline derivatives[10]. For these reasons, the remarkable elevation in blood acetaldehyde levels in animals treated with pargyline could be either a source of concern or an experimental tool for investigators studying behavioral or pharmacologic aspects of the interaction of catecholamines with ethanol and acetaldehyde.

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