Studies on factors suppressing alcohol drinking by rats

Some of the limiting factors in alcohol voluntary consumption were studied with 54 male Long-Evans rats at the Oy Alko Ab central laboratory in Helsinki.

After 48 days of free access to food + H2O and continuous or periodic (every second day) access to 10 % v/v ethanol the rats were divided into six different groups according to their special diet:
1. CANO (n = 9) group continued as before on continuous access (CA) and normal food.
2. CALCY (n = 9) group had 40 mg of cyanamide added per kg of food.
3. CACY (n = 9) group had 200 mg of cyanamide added per kg of food.
4. CACOP (n = 9) group had 500 mg of coprine added per kg of food.
5. PANO (n = 9) continued as before on periodic access (PA) and normal food.
6. PACY (n = 9) group had periodic access and had 200 mg of cyanamide added to each kg of food.

Cyanamide (temposil) and coprine (N5-(hydroxycyclopropyl)-L-glutamine) are very potent aldehyde dehydrogenase (ALDH) enzyme inhibitors.

After eight to ten days of the special diet an intoxication test on the motorized tilting plane was conducted with 1.5 g/kg of 10 % v/v of ethanol + 1 mM 4 MP solution.

The coprine group (CACOP) had a highly significant decrease (p = 0.0006) between their preweek (normal diet week) and postweek (a special diet week) ethanol consumption.

Cyanamide suppressed ethanol consumption just as well in rats with periodic access as continual access. The low cyanamide suppressed ethanol consumption as well as the higher one did.

In the intoxication test ALDH inhibitors did not affect alcohol intoxication. An additional result was that periodic access to ethanol decreased ethanol intoxication. The results suggest that the PANO group had possibly acquired tolerance as a consequence of their previous experience with higher blood alcohol levels and high degrees of intoxication. Animals given 200 mg cyanamide per kg food had a 26.1 % reduction of brain norepinephrine (NE) turnover.

Highly significant cyanamide inhibition of brain norepinephrine release supports the theory that cyanamide and coprine produced suppression of voluntary ethanol consumption acts via inhibition of the brain aldehyde dehydrogenase enzyme. Reduction of ALDH enzyme activity apparently suppresses norepinephrine release which could reduce alcohol intake.