

Fenofibrate - A lipid-lowering drug - Reduces voluntary alcohol drinking in rats

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The administration of disulfiram raises blood acetaldehyde levels when ethanol is ingested, leading to an aversion to alcohol. This study was aimed at assessing the effect of fenofibrate on voluntary ethanol ingestion in rats. Fenofibrate reduces blood triglyceride levels by increasing fatty acid oxidation by liver peroxisomes, along with an increase in the activity of catalase, which can oxidize ethanol to acetaldehyde. UChB drinker rats were allowed to consume alcohol 10% v/v freely for 60 days, until consumption stabilized at around 7g ethanol/kg/24h. About 1-1.2g ethanol/kg of this intake is consumed in the first 2h of darkness of the circadian cycle. Fenofibrate subsequently administered (50mg/kg/day by mouth [p.o.]) for 14 days led to a 60-70% ($p < 0.001$) reduction of 24-h ethanol consumption. When ethanol intake was determined within the first 2h of darkness, the reduction was 85-90% ($p < 0.001$). We determined whether animals chronically allowed access to ethanol and subsequently treated with fenofibrate, would a) increase liver catalase activity, and b) increase blood acetaldehyde levels after a 24-h ethanol deprivation and the subsequent administration of 1g ethanol/kg. The oral administration of 1g ethanol/kg produced a rapid increase in blood (arterial) acetaldehyde in fenofibrate-treated animals versus controls also administered 1g/kg ethanol (70?M vs. 7?M; $p < 0.001$). Liver catalase activity following fenofibrate treatment was increased 3-fold ($p < 0.01$). Other hepatic enzymes responsible for the metabolism of ethanol (alcohol dehydrogenase and aldehyde dehydrogenase) remained unchanged. No liver damage was induced, as measured by serum glutamic-pyruvic transaminase (GPT) activity. The effect of fenofibrate in reducing alcohol intake was fully reversible. Overall, in rats allowed chronic ethanol intake, by mouth (p.o.), fenofibrate administration increased liver catalase activity and reduced voluntary ethanol intake. The administration of 1g ethanol/kg (p.o.) to these animals increased blood acetaldehyde

levels in fenofibrate-treated animals, suggesting the possible basis for the reduction in ethanol intake. © 2014 Elsevier Inc.

Alcoholism

Catalase

Fenofibrate

Fibrates

Peroxisome proliferator-activated receptor

Treatment

acetaldehyde

alanine aminotransferase

alcohol dehydrogenase

aldehyde dehydrogenase

catalase

fenofibrate

triacylglycerol

acetaldehyde

alanine aminotransferase

alcohol

antilipemic agent

catalase

fenofibrate

alanine aminotransferase blood level

alcohol consumption

alcohol metabolism

animal experiment

animal tissue

Article

controlled study

drinking behavior

drug mechanism

enzyme activity

fatty acid oxidation

male

nonhuman

rat

triacylglycerol blood level

animal

blood

drug effects

drug therapy

enzymology

liver

metabolism

Wistar rat

Rattus

Acetaldehyde

Alanine Transaminase

Alcohol Drinking

Animals

Catalase

Ethanol

Fenofibrate

Hypolipidemic Agents

Liver

Male

Rats

Rats, Wistar