Tetrahydroisoquinoline and -carboline alkaloids, possible links between alcohol and opiate addiction, are formed by condensation of endogenous amines with acetaldehyde. In our opinion formaldehyde is a much better reaction partner than acetaldehyde. According to our experimental results chronic alcoholics in contrast to healthy persons eliminate methanol continuously and independent of ethanol. As we could show that this is due to oxidation there must be a long lasting leakage of formaldehyde. We think it possible that exogenous methanol, which is a constituent of all alcoholic beverages, is another source of formation of alkaloids and thus participates in the aetiology of addiction.

INTRODUCTION

Tetrahydro-isooquinoline (TIQ) and-carboline (THBC) alkaloids and their derivatives are possible links between alcohol and opiate addiction (1). They are formed by condensation of endogenous amines with either acetaldehyde or formaldehyde. It is widely accepted that acetaldehyde is derived from exogenous ethanol. But for formaldehyde only endogenous sources are discussed. It is ignored that besides ethanol also methanol is constituent of all alcoholic beverages (2). Thus consumption of alcoholic beverages always means not only to consume ethanol but also methanol.

EXPERIMENTS AND RESULTS

Methanol and ethanol are both metabolized by liver alcohol dehydrogenase. As the affinity of this enzyme system is much higher for ethanol than for methanol, synchronous administration of both alcohols by consumption of alcoholic beverages results in a competitive inhibition of methanol oxidation. This effect is well known and used therapeutically in cases of methanol intoxication to avoid generation of toxic metabolites.

Continuous intake of alcoholic beverages thus will cause accumulation of methanol in the blood. It is obvious that blood levels can be reached which exceed those originating from a one-night drinking excess. We have compared analytical data of chronic alcoholics and of healthy volunteers and found that there are, indeed, remarkable differences (Fig. 1, 2). To our opinion blood-methanol levels above 10 mg/l strongly indicate chronic abuse, and those above 5 mg/l are highly suspicious.

Some of the samples contained up to 180 mg/l. Nevertheless, we expected much higher values. Without any doubt there exist alcoholics who drink for months and possibly for years. Some of them will prefer methanol-rich beverages. In such cases almost infinite values should be produced. But they have not been found until today. The question arose, whether chronic alcoholics possibly are able to eliminate methanol despite high ethanol concentrations.

Such we studied the elimination kinetics of methanol in chronic alcoholics and
compared the results with those of healthy volunteers after a drinking experiment. All alcoholics exhibited a time dependent exponential decrease of blood-methanol levels without any correlation to the actual ethanol concentration. On the contrary all non-alcoholics showed a long lasting methanol plateau as long as the ethanol levels remained somewhat above 0.3 promil (Fig. 3). In comparison to the healthy persons the patients also exhibited higher ethanol elimination rates, and there exists an obvious concentration dependence. Also propanol-1 showed a tendency towards faster elimination.

We were able to subdivide the 63 chronic alcoholics (DSM-III No. 303,9;29) into 4 types by means of clinical-psychiatric and psychophysiological findings. Of these type 1 is marked by heavy withdrawal symptoms or attacks but absence of psychodynamic or social deviations. We supposed that this type of addiction is more likely than the others caused by biochemical disorders. It is interesting that the elimination rates of alcoholics of type 1 are significantly higher than those of the others (Fig. 4).

DISCUSSION

In alcoholics there must exist a different pathway of elimination. As we could not find any differences in expiration or excretion in comparison to healthy persons this effect must be due to metabolism. We think it most probable that the microsomal alcohol-oxidizing system (MEOS) is responsible, which is known to be induced by chronic administration of alcohols. And the degree of induction possibly depends on genetic determinants. Maybe that this is the cause of the observed type differences.

However, oxidation of methanol in chronic alcoholics results in a continuous formation of formaldehyde. As formaldehyde is a much more potent partner for the Pictet-Spengler reaction than acetaldehyde, to our opinion exogenous methanol may be an until today disregarded source for TIQ and THBC formation.

REFERENCES


Fig. 1: Distribution of blood-methanol concentrations (in mg/l) found in 110 known alcoholics

Fig. 2: Distribution of blood-methanol concentrations (in mg/l) found in drinking experiments with non-alcoholics
Fig. 3: Elimination of methanol in 63 chronic alcoholics (----) and 21 healthy volunteers (**). Mean values. The blood ethanol levels were above 0.3 promil.

Fig. 4: Methanol-elimination constants (h⁻¹) of chronic alcoholics belonging to different types of disease. Mean values and standard deviation.