The metabolism of ethyl, n-propyl, n-butyl and iso-amyl alcohols by the isolated perfused rat liver

R.M. AUTY* & R.A. BRANCH
(introduced by K.D. BHOOLA)

Departments of Medicine and Pharmacology, University of Bristol

Ethanol, n-propanol, n-butanol and iso-amyl alcohol have been added to the fluid perfusing isolated rat livers, and their disappearance from the perfusate with time followed. Livers from young adult female rats (Wistar) weighing 180-240 g were perfused by the portal vein with 100 ml of freshly prepared 20% rat donor blood in Krebs solution equilibrated with 95% O_2, 5% CO_2 at 37°C. The flow rate of the perfusate was 20 ml/minute. The concentrations of the alcohols in the perfusate were assayed by gas-liquid-chromatography (Curry, Walker & Simpson, 1966; Bonnichsen & Linturi, 1962) using 4-methyl-1-pentanol as an internal standard.

As in man (Shumate, Crowther & Zarafshan, 1967) and in the intact animal (Makar & Mannering, 1970), the elimination of ethanol from the perfusate was biphasic. At low concentrations (below 5 mmol L^{-1}) it was exponential with time (half life 13.78 (± 2.28 s.e. mean) min), at higher concentrations it was linear (rate 10.5 (± 0.95 s.e. mean) mmol.h^{-1}). The three higher aliphatic alcohols were eliminated in a similar biphasic manner, though the rates of the linear and exponential phases differed from one alcohol to another, as did the concentration at which the exponential process changed to the linear process. Calculation of the apparent Michaelis constant (K_m) and maximal velocity (V_{max}) for ethanol in the system (Table 1) gave values for these parameters which were in excellent agreement with those already published for a similar isolated perfused liver system (Makar & Mannering, 1970). The apparent K_m and V_{max} values for the higher alcohols were compatible with those obtained with purified alcohol dehydrogenase (ADH) (Theorell & Bonnichsen, 1951; Winer, 1958).

TABLE 1 Apparent Michaelis constants (K_m) and maximal velocities (V_{max}) of ethanol in the isolated perfused rat liver system.

Alcohol added simultaneously with ethanol	*K_m of ethanol Moles*	*V_{max} of ethanol mmol/l/min*
None	2.23×10^{-3}	0.14
n-propanol	5×10^{-3}	0.14
n-butanol	4×10^{-3}	0.14
Iso amyl alcohol	8×10^{-3}	0.14

Simultaneous addition of ethanol (initial concentration 10 mM) and n-propanol (2-3 mM), n-butanol (1.9 mM) or iso-amyl alcohol (1.2 mM) to the perfusate inhibited both the linear and the exponential phases of ethanol elimination. The apparent K_m and V_{max} values for ethanol in this situation reveal that the inhibition is competitive (Table 1).

References

BONNICHSEN, R. & LINTURI, W. (1962). Gas chromatographic determination of some volatile compounds in urine. *Acta Chem. Scand.*, **16**, 1289.

CURRY, A.S., WALKER, G.W. & SIMPSON, G.S. (1966). Determination of ethanol in blood by gas chromatography. *Analyst*, **91**, 742-743.

MAKAR, A.B. & MANNERING, G.J. (1970). Kinetics of ethanol metabolism in the intact rat and monkey. *Biochem. Pharmacol.*, **19**, 2017-2022.

SHUMATE, R.P., CROWTHER, R.F. & ZARAFSHAN, M. (1967). A study of the metabolism rates of alcohol in the human body. *J. Forensic Med.*, **14**, 83-100.

THEORELL, H. & BONNICHSEN, R. (1951). Studies on liver alcohol dehydrogenase I. Equilibria and initial reaction velocities. *Acta Chem. Scand.*, **5**, 1105-1126.

WINER, A.D. (1958). A note on the substrate specificity of horse liver alcohol dehydrogenase. *Acta Chem. Scand.*, **12**, 1695-1696.