

Pharmacokinetics of Ethanol — Issues of Forensic Importance

REFERENCE: Jones AW: Pharmacokinetics of ethanol — Issues of forensic importance; *Forensic Sci Rev* 23:91; 2011.

ABSTRACT: A reliable method for the quantitative analysis of ethanol in microvolumes (50–100 μL) of blood became available in 1922, making it possible to investigate the absorption, distribution, metabolism, and excretion (ADME) of ethanol in healthy volunteers. The basic principles of ethanol pharmacokinetics were established in the 1930s, including the notion of zero-order elimination kinetics from blood and distribution of the absorbed dose into the total body water. The hepatic enzyme alcohol dehydrogenase (ADH) is primarily responsible for the oxidative metabolism of ethanol. This enzyme was purified and characterized in the early 1950s and shown to have a low Michaelis constant (k_m), being about ~ 0.1 g/L. Liver ADH is therefore saturated with substrate after the first couple of drinks and for all practical purposes the concentration-time (C-T) profiles of ethanol are a good approximation to zero-order kinetics. However, because of dose-dependent saturation kinetics, the entire postabsorptive declining part of the blood-alcohol concentration (BAC) curve looks more like a hockey stick rather than a straight line. A faster rate of ethanol elimination from blood in habituated individuals (alcoholics) is explained by participation of a high k_m microsomal enzyme (CYP2E1), which is inducible after a period of chronic heavy drinking. Owing to the combined influences of genetic and environmental factors, one expects a roughly threefold difference in elimination rates of ethanol from blood (0.1–0.3 g/L/h) between individuals. The volume of distribution (V_d) of ethanol, which depends on a person's age, gender, and proportion of fat to lean body mass, shows a twofold variation between individuals (0.4–0.8 L/kg). This forensic science review traces the development of forensic pharmacokinetics of ethanol from a historical perspective, followed by a discussion of important issues related to the disposition and fate of ethanol in the body, including (a) quantitative evaluation of blood-alcohol curves and the factors influencing the peak concentration in blood (C_{max}) and the time of its occurrence (t_{max}), (b) biological variations in the ADME of ethanol, including the apparent volume of distribution (V_d or ρ), the disappearance rate from blood (β or k_0), and the disposal rate by the entire body in 1 h (B_{60}), and (c) questions about ADME of ethanol often arising during the prosecuting of accused drunken drivers.

KEY WORDS: Alcohol, analysis, blood concentration, ethanol, forensic science, legal medicine, pharmacokinetics, toxicology.
