XXI Congress of the International Academy of Legal Medicine
Lisbon, 28 – 30 May, 2009

The effect of xenobiotics on rat liver alcohol dehydrogenase activity or how medicines can affect the metabolism of alcohol

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Submission date: **28-02-2009**

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Presentation type: **POSTER**

Contents: **It is well documented that serious side effects or toxic interactions may occur after the administration of some drugs and/or medicines with the concurrent use of alcohol (ethanol). Most of these interactions are attributable to pharmacokinetic changes caused by alcohol in the hepatic drug metabolic pathways catalysed by the cytochrome P450 system. What is not so well known is the potential effect of drugs and medicines on the activity of the liver alcohol dehydrogenase (ADH). Liver cytosolic ADH, the major catabolizing enzyme of alcohol, catalyzes the reversible oxidation of ethanol to acetaldehyde with the corresponding reduction of NAD to NADH. The knowledge of ADH-xenobiotics interactions would be very important because if a drug significantly inhibits liver ADH it will prevent ethanol to be eliminated at normal rates and blood alcohol concentration (BAC) would concomitantly increase. In these situations, it should be definitely known by physicians, pharmacists and patients that drugs with that kind of action present an increased risk of slowing alcohol metabolism. This might then result in potentially toxic plasma alcohol concentrations with behavioural impairment and social, legal and forensic implications. In order to evaluate the possible interactions between commonly prescribed medicines and ethanol metabolism, a spectrophotometric method was developed to study the alcohol dehydrogenase activity of rat liver homogenates by monitoring NADH formation at 340 nm in the presence and in the absence of different xenobiotics. Enzyme activity was calculated from the linear increase in A340nm after ethanol addition1 in the presence of tramadol, flunitrazepam, alprazolam and propanonol. 4-Methylpyrazole, a well-known specific inhibitor of ADH, was used as a positive control. Results will be presented that demonstrate the efficiency of the method and the preliminary data of the interaction between ADH and the tested substances.**

References

1. Kägi, J.H.R. and Vallee, B.L. (1960) Journal of Biological Chemistry 235, 3188-3192.