

ISS. THE IMPORTANCE OF KINETICS AND INTERINDIVIDUAL SUSCEPTIBILITY IN TOXICITY AND RISK ASSESSMENT: A HELP FOR FORENSIC TOXICOLOGY

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The quantitative assessment of the extent and time of exposure to chemicals able to induced toxicity including fatal outcome or to impair behavior in humans are essential information also in forensic medicine, which includes detection and identification of the presence of drugs and poisons in body fluids, tissues, and organs. Indeed, postmortem forensic toxicology is used in investigations to establish whether or not drugs were the cause or contributing factor in death; human performance toxicology is used to evaluate the effect of alcohol/drug in driving and at the workplace; forensic medicine can be involved in the evaluation of illegal drug consumption.

Generally, in toxicological risk assessment only the extent of the external exposure is available, although it is recognized that measuring internal exposure is much more relevant for establishing a dose-response relationship. However, in forensic medicine the situation is the other way round, being the internal dose more frequently available. Starting from external exposure, the estimate of the internal one (or vice vice in reverse dosimetry) depends on availability of information about the absorption, distribution in the body, metabolism and excretion (ADME) of a chemical, usually referred to as toxicokinetics (TK). Many of the enzymes and transporters involved in TK processes are genetically polymorphic, that is they are present in different forms among individuals. The activity of specific enzymes can also differ depending on age, gender, pathological conditions and also due to exposure to other chemicals (drugs, alcohol, smoking habits) since many enzymes are inducible or can be irreversibly inhibited, As a consequence any biomarkers of exposure (i.e. alcohol in blood) reflect also the individual's response determined by genetic and acquired factors, making also quite different the time course of elimination from the body of a chemical. This in turn also determined a different individual susceptibility to the action of drug/chemical/poisons. Examples relevant to forensic toxicology will be presented.

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