
Lecture: *in vitro* toxicology

Biokinetic considerations in *in vitro* toxicology

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The current practice in toxicological risk assessment is to assess human health or environmental risk of chemicals on the basis of clinical or histopathological endpoints in animal studies. These apical endpoints do normally not take into account the mechanism(s) of toxic action. *In vitro* studies have much better possibilities to study these mechanisms in great detail. Such data are normally expressed as the concentrations giving a certain degree of effect, e.g. the concentration resulting in 50% of the maximal effect (EC_{50}). However, the extrapolation of *in vitro* toxicity data to the *in vivo* situation needs a number of considerations, too. The interpretation of these results in terms of risk requires the “translation” of the data towards the expected exposure in an intact organism. Thus, EC_{50} s, expressed as molar concentrations will need to be converted to the amount (i.e. the dose) to which the organism is exposed.

These biokinetic aspects can now be studied in detail with the help of (physiologically-based) biokinetic (PBBK) models. Such a model allows the calculation of concentrations in tissues given a certain exposure scenario. When used in a reverse way, it thus also allows the calculation of a dose (or exposure scenario) resulting in a concentration in target tissues that would give a toxicologically relevant effect in an *in vitro* system.

Similar models can also be used to study the biokinetic behaviour of compounds in the *in vitro* system, i.e. “biokinetics *in vitro*”. Evaluating the kinetics of a compound in the cell culture is greatly increasing the relevance of the *in vitro* toxicity findings, e.g. by taking into account the actual (free) concentration to which the cells in an *in vitro* system are exposed to. It may also show any relevant differences in the conditions of exposure at a cellular level between the *in vitro* systems and the situation *in vivo*, e.g. in relation to protein binding.

Making use of these models, a conversion was calculated of the EC_{50} values for cytotoxicity to toxic doses (LD_{50} s). It was shown that the correlations with the experimentally determined LD_{50} in rodents improved.

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