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Environmental Health Risk Assessment of Ambient BTEX Levels in Lisbon, Portugal: A PBPK Study Approach

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Introduction

Health risk associated with exposure to chemicals in the environment is traditionally done on substance by substance bases. However, this approach does not take into account the possible interactions between chemicals which can determine different toxicity of the mixtures than would be expected from the individual chemicals.

Newer assessment methods such as physiologically based pharmacokinetic (PBPK) models coupled with biologically based dose-response (BBDR) models are increasingly used in health risk assessment as they can take into account for the metabolic interaction between chemicals.

The objective of the study is to apply a computational framework based on PBPK/BBDR models for the quantitative heath risk assessment associated to exposure to a quaternary mixture of VOC's (BTEX) measured in Lisbon, Portugal.

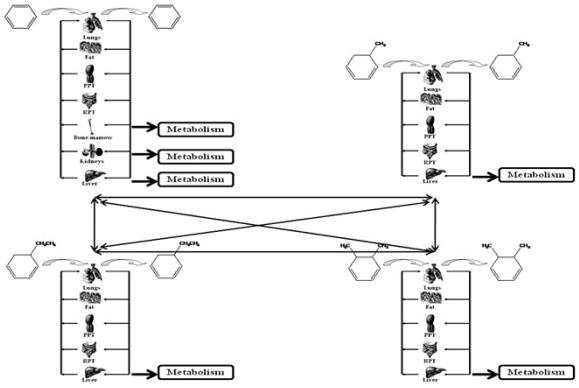

Figure 1: Conceptual representation of a PBPK model for a mixture of BTEX

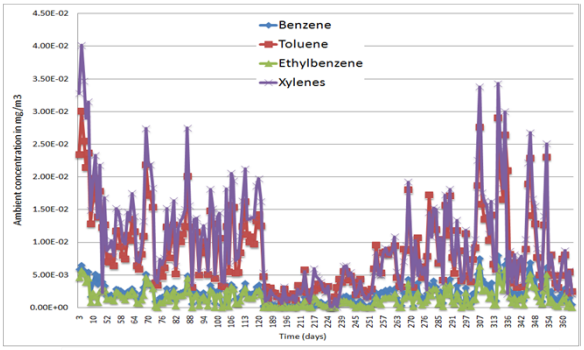

Figure 2: Ambient daily concentrations of BTEX in Lisbon during 2003

Data and methods

An integrated system for exposure modeling has been implemented in the 2 FUN player software to estimate the internal doses and the impact of human health due exposure to xenobiotics. The main component of the platform is a Physiology Based ToxicoKinetic (PBTK) model, coupled wit a Biology Based Dose Response (BBDR) model (figure 1). Uncertainty and variability of the affecting parameters were implemented in each stage through Markov Chain Monte Carlo (MCMC) simulation to estimate and manage the associated uncertainty originated by existing uncertainty or the heterogeneity of physiological-biochemical parameters.

Benzene, toluene, ethylbenzene and xylenes (BTEX) were selected as case study to derive health risks from long-term low level co-exposure to urban ambient BTEX levels in Lisbon. Daily averages were calculated from the hourly dataset for 2003 obtained from the Portuguese Environmental Agency using data from Entrecampos (traffic station) and Beato (urban background) stations. This daily dataset was further process to ensure only days with corresponding readings for all four BTEXs remained in the dataset (figure 2). The annual average concentration of benzene, toluene, ethylbenzene, xylenes was 2.2μg/m^3, 8.7μg/m^3, 1.5μg/m^3, and 10μg/m^3 respectively. The benzene mean annual concentration is well below the national limit value of 5μg/m^3.

The methodology permits the estimation of benzene carcinogenic risks capturing the continuously changing environmental and biological dynamics.

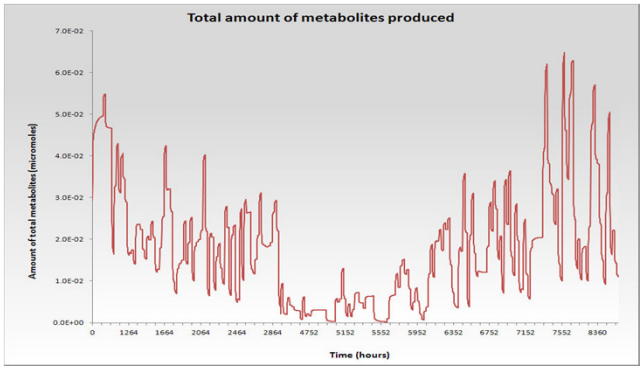

Fig3: Time course of the total benzene metabolites from co-exposure to urban ambient BTEX levels in Lisbon

Results

The integrated modeling platform was applied to a mixture of VOC's (BTEX) exposure data measured in ambient air in Lisbon in 2003. The estimation of health risk due to benzene was much refined when the internal dose of the parent substance and its metabolites was taken into account rather than personal exposure linked to epidemiological relations. This is due to two reasons:

(a) Aggregation of exposure through different microenvironments with continuously changing ambient concentrations provides differences at the daily variation time profile between personal exposure and internal dose, significantly affecting the overall risk estimation.

(b) The presence of co-exposure to the other VOCs in the mixture affects the levels of benzene metabolites through inhibition of benzene metabolism. The extent of the change in tissue dose depends on the concentrations of all mixture components and at typical ambient concentration this interaction effect is very low.

MCM analysis results indicated that the associated risk for cancer (leukaemia) per individual ranges from 1.28^{-5} to 3.11^{-4}, with a median value of 2.13^{-5} under the exposure scenario occurring in Lisbon. These values are within the findings of related epidemiological studies

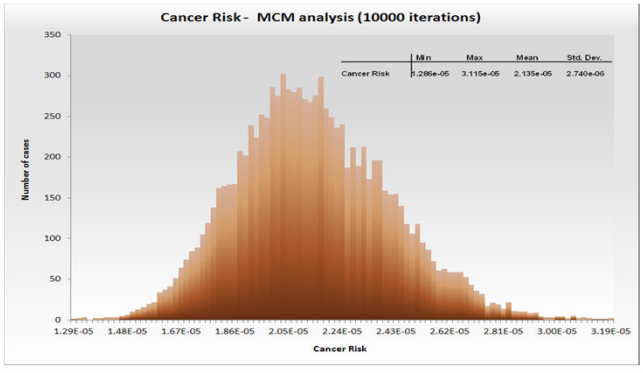

Figure 4: Probability distribution of cancer risk from co-exposure to urban ambient BTEX levels in Lisbon

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