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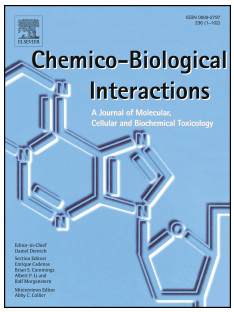

Evidence for non-linear metabolism at low benzene exposures? A reanalysis of data

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Evidence for non-linear metabolism at low benzene exposures? A reanalysis of data

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Abstract (200-300 words)

The presence of a high-affinity metabolic pathway for low level benzene exposures of less than one part per million (ppm) has been proposed although a pathway has not been identified. The variation of metabolite molar fractions with increasing air benzene concentrations was suggested as evidence of significantly more efficient benzene metabolism at concentrations <0.1 ppm The evidence for this pathway is predicated on a rich data set from a study of Chinese shoe workers exposed to a wide range of benzene concentrations (not just "low level"). In this work we undertake a further independent re-analysis of this data with a focus on the evidence for an increase in the rate of metabolism of benzene exposures of less than 1 ppm.

The analysis dataset consisted of measurements of benzene and toluene from personal air samplers, and measurements of unmetabolised benzene and toluene and five metabolites (phenol hydroquinone, catechol, trans, trans-muconic acid and s-phenylmercapturic acid) from post-shift urine samples for 213 workers with an occupational exposure to benzene (and toluene) and 139 controls. Measurements from control subjects were used to estimate metabolite concentrations resulting from non-occupational sources, including environmental sources of benzene. Data from occupationally exposed subjects were used to estimate metabolite concentrations as a function of benzene exposure. Correction for background (environmental exposure) sources of metabolites was achieved through a comparison of geometric means in occupationally exposed and control populations. The molar fractions of the five metabolites as a function of benzene exposure were computed.

A supra-linear relationship between metabolite concentrations and benzene exposure was observed over the range 0.1 to 10 ppm benzene, however over the range benzene exposures of between 0.1 and 1 ppm only a modest departure from linearity was observed. The molar fractions estimated in this work were near constant over the range 0.1 to 10 ppm. No evidence of high affinity metabolism at these low level exposures was observed. Our reanalysis brings in to question the appropriateness of the dataset for commenting on low dose exposures and the use of a purely statistical approach to the analysis.

Keywords: benzene, low dose, linearity, urine, metabolites, specificity

Highlights

- Previous pooling of benzene datasets from different factories was inappropriate.
- No evidence of significant non-linearity was seen over the exposure range 0.1 to 1 ppm benzene and molar fractions were essentially constant.