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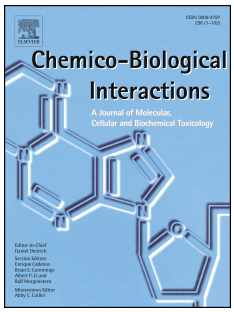

The low-dose benzene debate needs a sharp blade

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The low-dose benzene debate needs a sharp blade.

Over the past decade, a series of papers has been published by a group of researchers at the University of California Berkeley on low-dose effects induced by benzene (e.g. [1, 2]). These papers have raised questions since the published observations are remarkable for several reasons. The papers report a relative increase in the intensity of the observed effects as exposure concentrations get lower, implying that exposure to low concentrations of benzene should be regarded as disproportionally hazardous. Of course, the observation of certain effects at very low dose levels is not remarkable per se, especially if they only relate to gene expression without changes in phenotype. The supralinearity at low dose levels, however, is unexpected and in contrast with the general rule in toxicology that effects usually fade away as exposure concentrations get lower. So, we had a look at the available evidence and the strength of the available data to support the reported benzene low-dose phenomenon.

Quantitative and qualitative differences in metabolism of certain compounds exist at low dose levels as compared to higher dose levels and this could potentially be due to the presence of a high-affinity, low-capacity enzyme. Indeed, the investigators reporting the low-dose phenomenon have postulated such an enzyme [3, 4]. However, this hypothetical enzyme has not been found yet [5, 6]. Typically, such high-affinity, low-capacity enzymes play some crucial role in maintaining homeostasis or some other crucial vital physiological process and is phylogenetically well preserved across species. Nevertheless, to the best of my knowledge, this type of enzyme has never been found for benzene (nor similar dose-dependent metabolism) in any animal species, therefore it doesn't seem very likely that humans would possess it.

Another potential explanation could be found in the exposure assessment itself, that is if the claimed 'low dose' was actually not as low as it was deemed to be. The exposure data in the various publications go all back to a series of studies in China [7-9]. If you have a closer look at the exposure assessments as reported in later studies (e.g. [1, 2, 10]), it is clear that in most of these publications actual exposure measurements were not done. On the contrary, the exposures are based on previously reported studies and essentially there is only one paper that forms the basis for the exposure assessment which is subsequently used in the other