Temporal stability and association with smoking of urinary DNA adducts as biomarkers of exposure to 1,3-butadiene

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1,3-butadiene (BD) is a carcinogenic gas that is used in the polymer industry\(^1\). BD is also present in cigarette smoke\(^2\), and urban air\(^3\). BD is metabolized to reactive epoxides 3,4-epoxy-1-butene (EB), 1,2,3,4-diepoxybutane (DEB), and 1,2-dihydroxy-3,4-epoxybutane (EBD) by cytochrome P450 monooxygenases\(^4\). BD epoxides are detoxified by glutathione S transferases to form monohydroxybutenyl mercapturic acid (MHBMA) and trihydroxybutyl mercapturic acid (THBMA)\(^5,6\). If they are not detoxified, these epoxide metabolites are reactive towards nucleophilic DNA bases to form covalent DNA adducts at the N7 position of guanine. EB can form N7-(2-hydroxy-3-buten-1-yl)guanine (EB-GI) and N-7-(1'-hydroxy-3'-buten-2'-yl)guanine (EB-GII) adducts\(^7\). BD-DNA adducts such as EB-GI and EB-GII are hydrolytically labile and are excreted in urine\(^8\), making them useful as biomarkers of BD exposure to quantify risk associated with BD exposure\(^7\). In the present work, nanoLC-isotope dilution accurate mass spectrometry-based methods for quantitative analysis of EB-GII adducts in human urine were used to evaluate the stability and association with smoking of EB-GII. EB-GII levels were also quantified in groups of smokers and nonsmokers belonging to three different ethnic groups: White, Japanese, and Native Hawaiian.

References
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