Biomarkers Of Industrial And Environmental Exposure To 1,3-butadiene

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Abstract

1,3-butadiene (BD) is an industrial chemical also present in high quantities in cigarette smoke and urban air. BD undergoes metabolic activation primarily by CYP 450 2E1 to form 3,4-epoxy-1-butene (EB), 1,2,3,4-diepoxy butane (DEB), hydroxymethylvinylketone (HMVK), and 3,4-epoxy-1,2-butanediol (EBD). These electrophilic species can react with DNA nucleobases to form promutagenic adducts or can be metabolized to the corresponding mercapturic acids and excreted in urine as 1-hydroxy 2-(*N*-acetylcysteinyl)-3-butene (MHBMA), 1,4-*bis*-(*N*-acetylcysteinyl)butane-2,3-diol (*bis*-BDMA), 1,2-dihydroxy-4-(*N*-acetylcysteinyl)-butane (DHBMA), and 1,2,3-trihydroxy-4-(*N*-acetylcysteinyl)-butane (THBMA), respectively. In the present work, we employed isotope dilution HPLC-ESI-MS/MS methodology to determine the metabolic profile of BD in laboratory rats and humans. The relative contribution of individual mercapturic acids in rats were THBMA (46.7%) > DHBMA (36.6%) > MHBMA (15.1%) >> *bis*-BDMA (1.6%). In contrast, humans excreted mostly DHBMA (85%) >> THBMA (11%) > MHBMA (4%) >> *bis*-BDMA (<0.1%), consistent with previous reports that humans metabolize a smaller fraction of BD to DEB. In addition, sensitive nanoLC/ESI^{+}-HRMS^{3} methods were employed to quantify EB-induced DNA adducts, N-7-(1-hydroxy-3-buten-2-yl) guanine (EB-Gua II), in human blood and urine. Adduct levels were increased in occupationally exposed workers as compared to controls and did not correlate with smoking status.