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**Monomethylthioarsenicals are substrates for human arsenic (+3 oxidation state) methyltransferase**

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Methylated thioarsenicals are structural analogs of methylated oxyarsenicals in which one or more oxygen atom bound to arsenic is replaced by a sulfur atom. In sulfide-rich environments, methylated thioarsenicals form from corresponding methylated oxyarsenicals. Thus, monomethylarsonic acid (MMA) is readily converted to monomethylmonothioarsenate (MMMTA), monomethyldithioarsenate (MMDTA), and monomethyltrithioarsenate. The metabolic fate of these methylated thioarsenicals is unknown. Human arsenic (+3 oxidation state) methyltransferase (AS3MT) catalyzes transfer of a methyl group from S-adenosylmethionine (AdoMet) to an arsenical substrate. To date, all identified substrates for AS3MT-catalyzed methylation are oxyarsenicals that contain arsenic in the trivalent oxidation state; oxyarsenicals with arsenic in the pentavalent oxidation state (e.g., MMA) are not substrates for AS3MT-catalyzed methylation. Thus, MMMTA and MMDTA which contain arsenic in the pentavalent oxidation state are unlikely candidates for AS3MT-catalyzed methylation. Using anaerobic conditions to prevent oxidation of thioarsenicals, MMMTA or MMDTA were added to reaction mixtures containing AS3MT, AdoMet, and the non-thiol reductant TCEP. Reaction products were separated by ion-exchange chromatography and detected by ICP-MS. Incubation of MMMTA with AS3MT yields dimethylmonothioarsenate (DMMTA) as the primary metabolite and of MMDTA with AS3MT yields dimethyldithioarsenate (DMDTA) as the primary metabolite. The absence of other metabolites in reaction mixtures suggests that MMMTA and MMDTA are substrates for AS3MT-catalyzed reactions which add a methyl group to substrates to produce DMMTA and DMDTA. If MMMTA and MMDTA are substrates for AS3MT-catalyzed reactions, then interconversion of oxy- and thio-arsenicals occurs not only by exchange of oxygen and sulfur moieties but also by direct competition for enzymatically-catalyzed methylation. (This abstract does not represent the policy of the U.S. Environmental Protection Agency.)