I. Introduction

A century of study of the process by which many organisms convert inorganic arsenic into an array of methylated metabolites has answered many questions and has posed some new ones. The capacity of microorganisms to form volatile arsenic compounds was first recognized in the 19th century (Cullen, 2008). This observation prompted Frederick Challenger and his colleagues to study arsenic methylation in microorganisms and to postulate a chemically plausible sequence of reactions in which pentavalent arsenic is reduced to trivalency and the resulting trivalent arsenical is oxidatively methylated (for a historical review see Chasteen et al., 2003). Identification of genes encoding arsenic methyltransferase in the three domains of the tree of life – Bacteria, Archaea, and Eukarya - provide an opportunity to test the chemical plausibility of Challenger's scheme and other alternate schemes for arsenic methylation. Although our understanding of molecular aspects of enzymatically catalyzed methylation of arsenic remains in flux, data are sufficient to assert that conversion of inorganic arsenic to methylated species is a major determinant of the distribution and retention of arsenic among tissues and is an important factor in its actions as a toxicant and carcinogen.

In this chapter, attention first focuses on metabolic processes that convert inorganic arsenic into methylated oxyarsenical species; that is, compounds in which an arsenic atom is bound to one or more methyl groups and one or more oxygen atoms, and on the toxicological significance of the oxidation state of arsenic present in methylated oxyarsenicals. Attention then focuses on methylated thioarsenicals, a class of compounds in which an arsenic atom is bound to one or more methyl groups and one or more sulfur atoms, that are metabolites of inorganic arsenic and on the linkage between metabolic processes involved formation of methylated oxyarsenicals and of methylated thioarsenicals. Finally, attention is focused on evidence linking the metabolism of complex organic arsenicals (e.g., arsenosugars, arsenobetaine, arsenolipids)[1] to the metabolism of methylated arsenicals. Integrating

[1] In this chapter, inorganic arsenic and its methylated metabolites are identified on the basis of the oxidation state of the arsenic atom in the molecule. For oxy-arsenicals, inorganic species are arsenate (As^{V}) and arsenite (As^{III}). Methylated species are monomethylarsonic acid (As^{V}), monomethylarsonous acid (As^{III}), dimethylarsinic acid (As^{V}), dimethylarsinous acid (As^{III}), trimethylarsine oxide (As^{V}), and trimethylarsine (As^{III}). Corresponding thioarsenical species are identified explicitly (e.g., thioarsenate or monomethylmonothioarsenate). Naming of complex organic