The Chemical Form of Mercury in Fish

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The primary dietary source of neurotoxic mercury compounds is via the ingestion of methylmercury species accumulated in fish. Methylmercury from fish has been linked to neurological damage (Minamata disease) (*1*) and increased risk of myocardial infarction (*2*). Despite its importance, the complete chemical identity of the mercury coordination in animal tissue remains unknown. The toxic properties of any element are critically dependant on molecular form; for example, dialkylmercury derivatives are toxic at such low levels that they are considered supertoxic, whereas mercuric selenide has a relatively low toxicity and accumulates as an apparently benign detoxification product in marine mammals (*3*). Knowing the chemical nature of a potential toxicant is, thus, essential to understanding its toxic properties. Mercury is very flexible in its coordination of nonmetallic elements, with structurally characterized species exhibiting coordination numbers between two and eight (*4*). X-ray absorption spectroscopy (XAS) is ideally suited to identification of chemical forms in situ, but it previously has not been much applied to molecular toxicology.

Samples of fresh fish, otherwise intended for human consumption, were obtained from a local fish market. The Hg L_{III} XAS (*5*) of three different fish—swordfish (*Xiphias gladius*), orange roughy (*Hoplostethus atlanticus*), and sand sole (*Psettichthys melanostictus*)—indicated Hg concentrations within the range expected (6.0, 1.2, and 0.4 μM, respectively). The normalized spectra of swordfish and orange roughy were indistinguishable within the noise (sand sole was too "noisy" for comparison), indicating similar or identical chemical forms of mercury. This is notable given their different diets: orange roughy is midway in the food chain, feeding on crustaceans, small squid, and fish, whereas the exclusively fish- and squid-eating swordfish is a top predator.

Figure 1 compares the Hg L_{III} x-ray absorption near-edge spectrum of swordfish skeletal muscle with the solution spectra of selected standard compounds (*6*). Twenty-six different standards were compared overall, including glutathione- and selenium-containing species, and the fish spectra closely resemble only the spectrum of methylmercury cysteine (or structurally related species), which contains linear two-coordinate mercury with methyl and cysteinyl sulfur donors. Thus, the near-edge spectra indicate the coordination of the methylmercury in fish to be completed by an aliphatic thiol. Although XAS cannot unambiguously identify the exact nature of this thiol, cysteine is by a large margin the most likely candidate as the predominant biological thiol, though it is likely part of a larger peptide (e.g., glutathione) or protein.

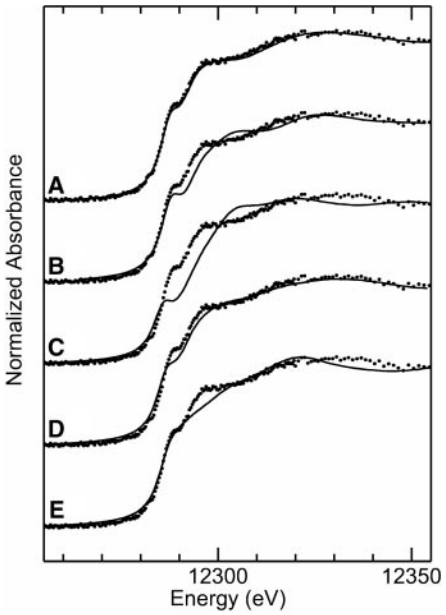

Fig. 1. Comparison of the Hg L_{III} near-edge spectra of swordfish with selected solution spectra. The points show the spectrum of the fish; the solid lines show the spectra of aqueous solutions of standard species, as follows: (**A**) $CH_3HgS(Cys)$, (**B**) CH_3HgCl, (**C**) $Hg^{2+}(Hg(NO_3)_2$ solution), and (**D**) $Hg(SR)_2$, (**E**) $[Hg(SR)_4]^{2-}$.

Our data have implications for the toxic properties expected from human consumption of fish. The most commonly used "model" of methylmercury species in fish is aqueous methylmercury chloride (CH_3HgCl), often erroneously referred to as CH_3Hg^+. The Hg-Cl bond in methylmercury chloride is highly covalent, and our measurements indicate that it remains intact in dilute aqueous solution (*7*). Methylmercury chloride is also fairly hydrophobic and is thus expected to exhibit membrane-crossing properties superior to other methylmercury species, which is expected to correlate with toxic properties (*1*). The acidic high Cl^- conditions in the human stomach may convert methylmercury cysteine species to the chloride, but whether this occurs is, at present, unknown. In at least one model system, methylmercury cysteine proves to be much less toxic than CH_3HgCl; day-old zebrafish larvae tolerate 20-fold the concentration of methylmercury cysteine than CH_3HgCl [supporting online material (SOM) Text]. Considerable publicity has been given to possible health hazards associated with eating fish, but ingestion of a mercury dose through consumption of fish may have quite different toxicological implications than ingestion of the same mercury dose in the form of other methylmercury compounds.

References and Notes

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5. Materials and methods are available as supporting material on *Science* Online.
6. Solution species identity was confirmed by measuring the extended x-ray absorption fine structure. Methylmercury cysteine showed Hg-C and Hg-S bond lengths of 2.06 and 2.35 Å, respectively.
7. Aqueous CH_3HgCl shows Hg-C and Hg-Cl bond-lengths of 2.02 and 2.30 Å, respectively.

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