Exploring the Metabolomic Alterations in Diatom *Cyclotella meneghiniana* in Response to Hg(II) and MeHg Exposure

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Mercury pollution in aquatic systems is of significant concern for human and environmental health due to its ability to bioaccumulate and to biomagnify (in particularly as methylated form) within the trophic food web. Phytoplankton, including diatom species, are crucial for primary production and the functioning of global biogeochemical cycles. Located in the basis of aquatic food webs, perturbations in these organisms can pose a significant impact on the entire ecosystem. Despite this, our current understanding of how mercury species, such as Hg(II) and MeHg, affect these organisms is limited. Although previous research has identified certain toxic effects of mercury on phytoplankton, the specifics of metabolomic disturbances in diatoms are not well understood. Therefore, the present work aims to study the metabolic alterations in diatom *Cyclotella meneghiniana* induced by short-term exposure to subletal concentrations of Hg(II) and MeHg. For that, this study employed a combination of targeted metabolomics, biological accumulation, and physiological response assays to elucidate the metabolomic disturbances in diatom *Cyclotella meneghiniana*, following a 2-hour exposure to Hg(II) ($8.3\times10^{-9} \pm 4.4\times10^{-10}$ M and $8.4\times10^{-8} \pm 5.1\times10^{-10}$ M) and MeHg ($6.5\times10^{-9} \pm 6.9\times10^{-10}$ M and $7.9\times10^{-8} \pm 3.3\times10^{-9}$ M).

Findings revealed that Hg(II) and MeHg exposure resulted in metabolism disturbances concerning amino acids, nucleotides, fatty acids, carboxylic acids, and antioxidants, but not carbohydrates. The extent of these alterations was concentration-dependent for Hg(II), with higher Hg(II) concentrations causing more significant metabolomic disturbances. For MeHg treatments, no apparent concentration dependence was found, with both MeHg concentrations inducing metabolomic perturbations.

This research presents the first evidence of the primary metabolomic alteration induced by short-term exposure to Hg(II) and MeHg in the diatom species *Cyclotella meneghiniana*. Our findings highlight the potential advantages of using targeted metabolomic approaches to detect early-stage perturbations caused by metal exposure in the phytoplankton species before physiological endpoint detection.

Keywords: inorganic mercury (Hg(II)), monomethylmercury (MeHg), metabolomic perturbations, diatom species, *Cyclotella meneghiniana*, targeted metabolomic, physiological response assays