FY05-LI(51)-130
The Health Implications of the Mercury-Selenium Interaction

Contractor**:** Energy & Environmental Research Center
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PARTICIPANTS

Sponsor		Cost Share
TVA		$20,000
EPRI		$35,000
DOE		$53,846
NDIC		$50,000
	Total Cost	$158,846

Project Schedule - 24 Months

Contract Date – 6/24/04
Start Date – 7/1/04
Completion Date – ~~6/30/06~~
Extension to – ~~12/31/06~~
– ~~3/31/07~~
– ~~9/30/07~~
– 12/31/07

Project Deliverables

Contract Signed: 7/1/04 (✓)
Status Reports: 3/31/05 (✓); 12/31/05 (✓)
Final Report – ~~6/30/06( )~~
– ~~12/31/06( )~~
– ~~3/31/07( )~~
– ~~9/30/07( )~~
– 12/31/07(✓)

OBJECTIVE / STATEMENT OF WORK:
Explore interactions between mercury & selenium in experimental models designed to closely approximate human patterns of exposure. The project will examine the effects of dietary intakes of methylmercury and the protective effects of dietary selenium.

STATUS

Through March 31, 2005. Collaboration was initiated with a Slovenia research group studying mercury and selenium in human brain and pituitary tissues.

Through December 31, 2005. Results from the animal study have been presented at five nationwide meetings. The results demonstrate that the selenium-dependent protective effects against mercury toxicity were quite evident. Tissue analysis of samples from the animal study is underway.

January 1 – March 31, 2006. Results from the animal study have been presented at six nationwide meetings. Results indicate no reliable risk assessment of the potential effects of mercury exposure can be made without concurrent consideration of the selenium status of the exposed individuals. Additional element and enzyme testing will continue.

Final Report. The EERC performed three tasks in the investigation of the hypothesis that selenium (Se) sequestration is the primary molecular mechanism of methylmercury (MeHg) toxicity. Project tasks included 1) a rat study designed to examine the effects of dietary Se and MeHg on the health of growing animals, their tissue Hg and Se concentrations, and the effects of these elements on one another's retention and distribution; 2) a study of the direct interactions between Hg and Se in

animal tissues performed using x-ray absorption fine structure (XAFS); and 3) a study to evaluate the conditions that define the biochemical threshold of MeHg toxicity.

Although the MeHg issue involves fish consumption, previous research studies of Hg–Se interactions performed elsewhere have often used inappropriate methods to administer MeHg and Se and usually tested exceedingly high concentrations that bore little relevance to human exposure. The rat study performed in this project was unique in ensuring that both MeHg and Se were administered via the physiologically appropriate dietary route. To properly reflect the role of dietary Se in the human MeHg exposure issue, this study examined the influence of diets containing Se concentrations reflecting the normal human dietary range. Three levels of dietary Se were used, with the highest level approximating the concentration present in ocean fish. Low, moderate, or high MeHg exposures were used so that Se-dependent effects on growth and tissue Hg accumulation could be assessed throughout the meaningful range of exposures. The primary purpose of this project was to examine the influence of Hg:Se molar ratios in dietary exposures and in tissues of exposed animals in order to assess the potential effects of similar exposures in humans consuming seafood. The feeding study was performed to examine the role of dietary Se in preventing MeHg toxicity and to assess the influence of Se on MeHg distributions and the influence of MeHg on Se distributions. Toxic effects of high MeHg exposures were entirely dependent upon dietary Se intake. Among animals that were exposed to diets with high MeHg concentrations (70 μmol/kg; ~14 ppm), impaired growth became evident in rats fed low-Se (0.25 μmol/kg), high-MeHg diets after 5 weeks, but no impaired growth was evident in rats fed diets containing even moderately higher (0.50 μmol/kg) dietary Se concentrations. Contrary to what would have been expected based on the assumptions the current U.S. Environmental Protection Agency and Food and Drug Administration advisories are based upon, statistical analysis of data from this study indicates that MeHg exposure is not directly related to a risk for adverse effects. Most surprisingly, among rats fed high-MeHg diets and varying dietary Se intakes, tissue Hg concentrations were inversely related to MeHg toxicity as assessed by growth impairment. However, consistent with the expectations of the hypothesized Se sequestration mechanism of MeHg toxicity, toxicity was inversely related to tissue Se. The most readily understood and consistent index of MeHg risk observed in this study was the Hg:Se molar ratio in the diets and tissues. The MeHg:Se molar ratio in diets and tissues was directly proportional to the adverse effects that were observed in the groups exposed to high MeHg, but Hg concentrations were not. The computational model initiated in this study indicates that the MeHg:Se molar ratio in diets and tissues is a far more reliable predictor of health risks associated with MeHg exposure than the current reference dose and risk indicators based on MeHg exposure alone.

The primary finding of this project is that dietary Se status has a pivotal role in health aspects of the Hg issue. Measurements of MeHg exposure are clearly insufficient to establish meaningful assessments of risk. Environmental and human health risk assessments relating to MeHg need to concurrently assess both the relative and absolute amounts of MeHg and Se, otherwise they report exposure without a meaningful basis for assessing actual risk. It is expected that a more sophisticated approach to MeHg risk assessments will evolve from this work that will clarify the major conflicts of the MeHg issue. For example, current epidemiological studies of human MeHg exposure are designed to test the hypothesis that mothers' MeHg exposure during pregnancy is directly proportional to adverse effects observed in their children. Insights from this study indicate that conflicting results of the various human studies conducted around the world require the updated hypothesis, mothers' MeHg exposure in excess of dietary Se intake during pregnancy is directly proportional to adverse effects observed in their children. All of the findings of the major human studies of maternal MeHg exposure are entirely consistent with this updated hypothesis. Since ocean fish are rich in Se relative to MeHg, they are beneficial instead of harmful.