Impact of selenium co-administration on methylmercury exposed zebrafish: Changes in bioaccumulation and gene expression

P. CABEZAS-SANCHEZ[1], J. SANZ-LANDALUZE[1], J.L. LUQUE-GARCIA [1], S. RAINIERI[2], C. CÁMARA[1]

[1] Dpto. Química Analítica, Facultad CC. Químicas, Universidad Complutense, Avda. Complutense s/n, 28040, Madrid, Spain. jsanzlan@ucm.es
[2] Food Research Division, AZTI-Tecnalia, Parque Tecnológico de Bizkaia, Astondo Bidea 609, 48160 Derio, Spain.

Contamination of ecosystems and exposure to toxic metals is a major concern all over the world. Among heavy metals, mercury is a ubiquitous environmental contaminant that biomagnifies in aquatic food chains, mainly in the form of methylmercury (MeHg) [1]. Selenium is an essential dietary element required for the expression of several Se-dependent proteins, including key enzymes with antioxidant functions such as glutathione peroxidase, and proteins involved in redox signaling, thyroid hormone metabolism, and protein folding pathways. Previous studies have shown that Hg and Se interactions are normally antagonistic, although additive and synergistic toxic effects have also been observed in some studies. These contradictory results, show the extremely complexity of the interaction between Se and Hg compounds [2]. The aim of the present study was to verify the protective role of Se(IV) against methylmercury toxicity using zebrafish as in-vivo model. With this purpose, we studied differences in methylmercury bioaccumulation in zebrafish embryos and in four organs (liver, brain, intestine and skeletal tissue) of adult fish co-exposed to Se(IV). Additionally, we also evaluated changes observed in the gene expression of different organs when comparing adult fish exposed to MeHg alone or with co-administration of Se(IV) over a period of 72 h.

Bioaccumulation studies were carried out using a previously developed protocol for zebrafish eleutheroembryos exposed to chemicals, which is based on a toxicokinetic model that calculates the bioaccumulation factors (BCFs) [3]. Zebrafish embryos were exposed to either MeHg alone or MeHg and Se(IV) (molar ratio MeHg:Se(IV) 1:1) at two concentrations (1% and 0.1% the LC_{50}) during 48 h. Subsequently, the embryos were transferred to clean media during 24 h to simulate a depuration process. About 8-10 mg (20 eleutheroembryos) and media samples were taken at different times to analyze the concentration of methylmercury. Adult fish were exposed to similar concentrations during 72 h. Exposure media was refreshed every 24 h.

A time-dependent accumulation of MeHg was observed in zebrafish embryos and in all the analyzed organs of adult fish. In the last case, intestine and liver showed the highest concentrations of MeHg at the tested exposure times. After co-exposure to MeHg and Se(IV), a significant decreased in the bioaccumulation of MeHg was observed in zebrafish embryos, and mainly in the intestine and the skeletal tissue of adult fish. The higher protective effect of Se(IV) against MeHg accumulation was already detected after 24h of exposure.

The exposure to MeHg produced gene expression patterns that were markedly different in the case of brain and liver in comparison to intestine and skeletal tissue. Moreover, most of the genes tested were induced in the intestine and skeletal tissue and repressed in liver and brain. The co-administration of Se(IV) altered the expression pattern of most genes in all the organs tested. Specifically, Se(IV) was able to reduce or even reverse several of the MeHg-induced changes in gene expression to the level of the untreated samples. Noteworthy is the case of the *gpx1* gene, encoding for one of the most important antioxidant enzyme that was repressed in the brain by MeHg and reversed to the levels of the control after co-exposure to Se(IV). In conclusion, we observed that co-exposure to Se(IV) can significantly modify the toxic response of zebrafish to MeHg in terms of MeHg bioaccumulation and gene expression.

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