



## Toxicology

## Toxicity of organic and inorganic mercury species in differentiated human neurons and human astrocytes



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## ABSTRACT

Organic mercury (Hg) species exert their toxicity primarily in the central nervous system. The food relevant Hg species methylmercury (MeHg) has been frequently studied regarding its neurotoxic effects in vitro and in vivo. Neurotoxicity of thiomersal, which is used as a preservative in medical preparations, is to date less characterised. Due to dealkylation of organic Hg or oxidation of elemental Hg, inorganic Hg is present in the brain albeit these species are not able to readily cross the blood brain barrier. This study compared for the first time toxic effects of organic MeHg chloride (MeHgCl) and thiomersal as well as inorganic mercury chloride (HgCl<sub>2</sub>) in differentiated human neurons (LUHMES) and human astrocytes (CCF-STTG1). The three Hg species differ in their degree and mechanism of toxicity in those two types of brain cells. Generally, neurons are more susceptible to Hg species induced cytotoxicity as compared to astrocytes. This might be due to the massive cellular mercury uptake in the differentiated neurons. The organic compounds exerted stronger cytotoxic effects as compared to inorganic HgCl<sub>2</sub>. In contrast to HgCl<sub>2</sub> exposure, organic Hg compounds seem to induce the apoptotic cascade in neurons following low-level exposure. No indicators for apoptosis were identified for both inorganic and organic mercury species in astrocytes. Our studies clearly demonstrate species-specific toxic mechanisms. A mixed exposure towards all Hg species in the brain can be assumed. Thus, prospectively coexposure studies as well as cocultures of neurons and astrocytes could provide additional information in the investigation of Hg induced neurotoxicity.

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## 1. Introduction

Organic mercury (Hg) compounds are important neurotoxicants capable of damaging the developing and adult nervous system [1]. Due to its accumulation in the aquatic food chain, chronic exposure to methylmercury (MeHg) via seafood intake still poses a risk to human health [2]. Ethylmercury (EtHg) containing thiomersal, used as a preservative in medical preparations including vaccines, is of

particular concern since it has been linked to autism [3]. Although organic Hg compounds, especially methylmercury (MeHg), have been extensively studied, the mechanisms of Hg species mediated neurotoxicity remain not completely understood [4]. Inorganic Hg<sup>2+</sup> does not readily cross the blood brain barrier. Probably therefore effects of inorganic Hg<sup>2+</sup> species on brain cells are not well characterized [5]. Nevertheless, it should be noted that inorganic Hg is present in the brain due to dealkylation of organic species or an oxidation of elemental Hg, which originates e.g., from the outgassing of amalgam fillings [6,7].

In the literature only a few in vitro studies exist, either comparing effects of one Hg species, especially MeHg, in different brain associated cells or comparing different Hg species in one cell type. Sanfeliu et al. performed in vitro cytotoxicity studies in primary proliferating human astrocytes and neurons, indicating an enhanced sensitivity of neurons towards MeHg as compared to astrocytes [8]. In vitro studies in primary proliferating astrocytes and neurons from murine cerebella confirmed these results [9].

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