Absorption, distribution, metabolism, and excretion (ADME)

In this guide

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Inorganic mercury

14. Inorganic mercury has low bioavailability via the oral route, with an average absorption rate of 7% in human studies and a range of 1.4 – 15.6% based on the amount of inorganic mercury consumed (Tokar et al., 2012).

15. Studies conducted in mice and rats indicate that the predominant site of absorption of inorganic mercury is the small intestine (ATSDR., 2024). There are several absorption mechanisms for Hg^{2+} in the small intestine, including active and passive processes. The formation of thiol S-conjugates of Hg^{2+} produces molecules that can act as homologues of endogenous molecules/polypeptides. Hence, possible routes of uptake include interaction with

plasma membrane amino acids, peptides, drugs, and ion transporters (Bridges and Zalups., 2010; 2018).

16. In human blood, mercuric mercury is divided between plasma and erythrocytes, with more being present in plasma (EFSA., 2012). In plasma, the main sulfhydryls that form S-conjugates with Hg^{2+} are albumin (Ikegaya et al, 2010) and low molecular weight thiols like glutathione, cysteine metallothionine and red blood cell haemoglobin (ATSDR., 2024).

17. Due to their low lipophilicity neither mercurous nor mercuric mercury easily cross the placental or blood-brain barriers. Mercuric mercury distribution in the body is specific to certain organs and cell types within them. The kidney bears the greatest mercuric mercury burden, predominantly in the proximal convoluted renal tubule (EFSA., 2012). The next largest deposition occurs in the liver, with highest concentrations found in the periportal areas. Additionally, the mucous membranes of the intestinal tract, the epithelium of the skin, the interstitial cells of the testes as well as the choroid plexus in the brain are likely to accumulate mercuric mercury (EFSA., 2012).

18. The metabolism of mercury species involves oxidation and reduction processes along with conjugation to glutathione and appears to be similar between humans and experimental animals. Mice studies have provided some evidence that suggests a small amount of mercuric mercury can be reduced to elemental mercury and eliminated as elemental mercury vapour. In contrast, elemental mercury can be readily oxidised by hydrogen peroxide and catalase to mercuric mercury. There is no evidence in the literature that methylated mercury species are synthesised in human tissue (EFSA., 2012).

19. Inorganic mercuric mercury is eliminated through faeces and urine. In a clinical study involving five adults who received a single intravenous dose of $^{203}Hg(NO3)2$ (0.6–2.8 µg Hg), faecal excretion measured over 70 days ranged from 18% to 38% of the administered dose, while urinary excretion ranged from 6% to 35% (Hall et al., 1995). Farris et al. (2008) reanalysed the Hall et al. (1995) data and estimated that, on average, around 30% of the dose was excreted via faeces and 25% via urine. Mercury is also excreted in human sweat and saliva (ATSDR., 2024).

20. The half-life of absorbed mercuric mercury in the human body is approximately 40 days (EFSA., 2012).

Organic mercury

21. Following oral intake, MeHg is absorbed readily by the gastrointestinal tract and enters the systemic circulation, where mercuric ions can be delivered to target organs (ATSDR., 2004). MeHg has a larger oral absorption fraction than inorganic mercuric mercury, and greater accumulation in the brain and the kidneys (ATSDR., 2024).

22. Studies conducted in humans and experimental animals have demonstrated that gastrointestinal absorption of mercury is almost 100% following ingestion of MeHg as the chloride salt or when incorporated into fish or other protein (ATSDR., 2024). Following absorption, it is able to cross the placenta, the blood-brain and blood-cerebrospinal fluid barriers, allowing accumulation in the fetus and brain, respectively (EFSA., 2012). MeHg can also enter the hair follicle which is relevant for biomonitoring purposes (EFSA., 2012).

23. In contrast to mercuric mercury, in human blood >90 % MeHg accumulates in the erythrocytes, where it is bound to the cysteinyl residues of haemoglobin and in plasma, about 99 % MeHg is bound to albumin. By ligand exchange mechanisms, MeHg is transferred from plasma proteins to low molecular weight thiols glutathione and cysteine (EFSA., 2012).

24. MeHg can cross the mammary gland to be excreted in milk and thus children can be exposed during breastfeeding. In human milk, a mean of 26 - 63 % of total mercury has been found as MeHg, however the proportion can rise with increased MeHg intake (Miklavčič et al., 2011).

25. Fetal distribution is similar to maternal distribution, although fetal brain mercury concentration is approximately 5-7 times higher than that in maternal blood (COT, 2004). Cord blood concentrations are also reported at up to twice the maternal blood concentration (Bocca et al., 2019; FAO/WHO., 2007; Lee et al., 2010; Sakamoto et al., 2018; Vigeh et al., 2018).

26. Partial demethylation of MeHg occurs in mammals in the presence of reactive oxygen species. Demethylation occurs predominantly in the liver, intestinal tract, spleen, and to a lesser extent in phagocytic cells and the brain (Suda et al., 1992). Mercuric mercury in the brain is generally the result of either in situ dealkylation of organic mercury species, such as MeHg, or oxidation of elemental mercury. Demethylation of MeHg by intestinal bacteria also contributes to the excretion of inorganic mercuric mercury in faeces (Li et al., 2019).

27. MeHg has a half-life of approximately 70 - 80 days in the human body and steady state is achieved within a year (COT., 2004). Approximately 90 % is excreted by the faecal route as mercuric mercury (EFSA., 2012). Urinary excretion

of MeHg is limited by enterohepatic recycling by metabolism of the S-conjugate of glutathione (CH3Hg-S-CysGlyGlu) and reabsorptive transport of the S-conjugate of cysteine (CH3Hg-S-Cys) (Tanaka et al., 1992; Tanaka-Kagawa et al., 1993).