

**Exhalation of Trimethylbismuth after oral application of a bismuth salt –
evidence for biomethylation of metals in the human body**

Jens Boertz^{1,2}, Frank Mosel², Margareta Sulkowski¹, Albert W. Rettenmeier²,
Alfred V. Hirner¹

¹Institute of Environmental Analytical Chemistry, University Duisburg-Essen, Universitätsstr.
3-5, 45141 Essen, Germany, alfred.hirner@uni-due.de

² Institute of Hygiene and Occupational Medicine, University Hospital Essen, Virchowstr. 171,
45147 Essen, Germany, a.w.retttenmeier@uk-essen.de

Biomethylation and hydride formation of metals and metalloids is a ubiquitous environmental process that can lead to the formation of chemical species with significantly higher mobility and increased toxicity. While much is known about the interaction of metal(loid)s with microorganisms in environmental settings, little information has been gathered on respective processes inside the human body as yet. Here we study the excretion and biotransformation of bismuth following ingestion of a bismuth-containing pharmaceutical.

Following satisfactory medical screening, 19 male volunteers were given two tablets of bismuth subcitrate. The mass of bismuth ingested by each volunteer was 215 mg. Following ingestion, the concentrations of bismuth and its hydrated and methylated species were monitored in breath, blood, urine and faeces samples over a 56-hour period via ICP-MS or low temperature-gas chromatography- inductively coupled plasma-mass spectrometry LT-GC-ICP-MS.

Most of the inorganic bismuth ingested was excreted via faeces, only 1 % was exported via urine. Faecal bismuth concentrations ranged between 59-2356 mg/kg (wet weight), in comparison bismuth concentrations of urine were between 22-12795 µg/l. Maximum bismuth concentrations in blood were lower in the range of 1.3-158.8 µg/l. Trimethylbismuth was detected via LT-GC-ICP-MS in the breath of all volunteers typically two hours after ingestion. The sigmoid-type profiles observed during the observation period show absolute maxima after eight hours for most of the volunteers, with the concentration maxima being within a concentration range of 0.78 to 458 ng/m³. Trimethylbismuth was also detected in blood up to 2.47 pg/g, but was not found in all cases.

The determination of Trimethylbismuth in breath and blood after oral application of an inorganic bismuth salt, which is predominant exported via faeces, is an evidence for the biomethylation of metals by the intestinal microflora. The toxicological relevance of these findings must be observed in further studies.