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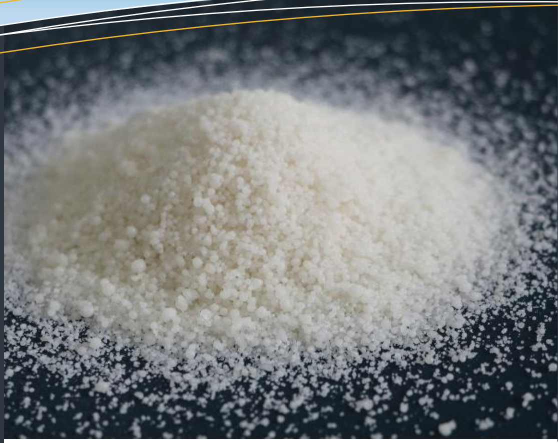
2026

GT
GERMAN SOCIETY OF
TOXICOLOGY

Poison of the month



Arsenic(III) oxide

The proposal to select inorganic arsenic as the Poison of the Month came from the Working Group on Carcinogenesis

… because inorganic arsenic, more than almost any other group of toxicants, links the history of toxicology with modern cancer research and illustrates how profoundly the toxic effects of an element can depend on its chemical form, oxidation state, and duration of exposure.

The Marsh test – arsenic and the history of forensic toxicology

At the beginning of the 19th century, reliable detection of arsenic in biological material was still difficult. This became evident in the John Bodle case in 1832: the chemist James Marsh was able to demonstrate arsenic as the poison in a murder trial, but the precipitate used as evidence was unstable and had deteriorated by the time of the trial. Bodle was acquitted due to the lack of convincing forensic evidence.

Marsh subsequently developed a more sensitive method, which he published in 1836. In this procedure, arsenic compounds are first converted into gaseous arsine (AsH_3). Upon heating, arsine decomposes and elemental arsenic is deposited as a characteristic dark and stable arsenic mirror.

The importance of this method for forensic toxicology became apparent as early as 1840 in the trial of Marie Lafarge, who was accused of poisoning her husband with arsenic. The toxicologist Mathieu Orfila detected arsenic in the body of the deceased, and Lafarge was subsequently convicted of murder.

Inorganic Arsenic – From Historical Poison to Environmental Carcinogen

Few substances are as closely linked to the history of toxicology as inorganic arsenic. Historically, arsenic(III) oxide (As_2O_3), commonly known as arsenic trioxide, became notorious as a homicidal poison. The white, nearly odourless and tasteless powder was relatively easy to obtain and, for a long time, difficult to detect reliably. Acute poisoning typically manifested as severe gastrointestinal symptoms, including vomiting, abdominal pain, and diarrhoea. At high doses, cardiovascular collapse, neurological disturbances, and ultimately multiorgan failure and death could occur.

In the 19th century, inorganic arsenic was not only relevant as an acutely toxic poison but was also used in arsenic-containing compounds in everyday products. One example is the intensely green pigment Schweinfurt green, which was used, among other applications, in wallpapers and paints. This resulted in prolonged, often unnoticed chronic exposure to low concentrations. Exposed individuals suffered from nonspecific symptoms such as weakness and gastrointestinal disturbances and, with continued exposure, also from characteristic skin lesions, peripheral nerve damage, and impairment of additional organ systems.

The numerous cases of arsenic poisoning also promoted the development of forensic toxicology. As analytical methods became increasingly sensitive, reliable detection of arsenic in biological material eventually became possible, representing an important step towards modern forensic toxicology.

Today, toxicological concern focuses primarily on exposure to inorganic arsenic species originating from naturally arsenic-containing minerals in soils and rocks. Arsenic can be released from these geological sources into groundwater and subsequently taken up via contaminated drinking water or foods such as rice and rice-based products. Worldwide, inorganic arsenic is among the most important chemical contaminants of drinking water. The International Agency for Research on Cancer (IARC) has

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classified inorganic arsenic compounds as carcinogenic to humans and assigned them to Group 1.

The toxic effects of inorganic arsenic are strongly determined by oxidation state and chemical species. The toxicologically most relevant oxidation states are As(III), commonly referred to as arsenite, and As(V), commonly referred to as arsenate. As(III) has a high affinity for specific proteins and thereby interferes, among other processes, with key steps of mitochondrial energy metabolism. Due to its structural similarity to phosphate, As(V) can interfere with energy metabolism and impair the formation of adenosine triphosphate (ATP), the principal cellular energy carrier. Both forms can cause severe systemic toxicity at high exposure levels, although As(III) is generally considerably more toxic than As(V).

Long-term exposure to inorganic arsenic results in a different toxicological profile. Characteristic effects include changes in skin pigmentation and hyperkeratosis. More importantly, inorganic arsenic is an established human carcinogen. Chronic exposure is associated with cancers of the skin, lung, and urinary bladder. Arsenic does not primarily act as a directly DNA-reactive carcinogen; rather, it promotes carcinogenesis through several interacting mechanisms, including oxidative stress, altered gene regulation, and impairment of DNA repair.

Because the toxicological significance of arsenic strongly depends on its chemical form, an assessment based solely on total arsenic concentrations cannot adequately reflect the actual health relevance of an exposure. This represents a major challenge for toxicological risk assessment.

By Ute Haßmann

Arsenic is not all the same – why speciation matters

Arsenic provides a particularly illustrative example of how strongly the toxicological effects of an element depend on the chemical form, or species, in which it occurs. Inorganic and organic arsenic species differ markedly in their bioavailability, metabolism, reactivity, and toxic potency. During the biotransformation of inorganic arsenic, methylation can generate particularly reactive intermediates. Trivalent methylated arsenic species can, among other effects, interfere with DNA repair processes and thereby contribute to toxicity. Similar considerations also apply to other elements.

How elemental species determine absorption, distribution, metabolism, and biological effects has been a major focus of the research of Prof. Dr. Tanja Schwerdtle, President of the Max Rubner Institute and recipient of the GT Toxicology Award 2026. Her work further demonstrates that differences in uptake and metabolism can limit the ability of experimental models to adequately reflect the toxicity of individual elemental species in humans.

For a robust risk assessment, it is therefore not sufficient to determine how much of an element is present; it is equally important to know in which chemical form it occurs.

Literature and links:

- Arsenic - an overview | ScienceDirect Topics
- Arsenic
- Visible Proofs: Forensic Views of the Body: Galleries: Cases: Toxicology on trial: Mathieu Orfila and the Lafarge murder case
- Clinician Brief: Arsenic | Environmental Health and Medicine Education | ATSDR
- Reichl, Franz-Xaver. Taschenatlas der Toxikologie. Substanzen, Wirkungen, Umwelt. 3. Auflage (2009) ISBN: 9783131089731
- Foto of XRD Chemical by Unsplash