HEAVY METAL CERTIFIED · RESEARCH ANALYSIS

Total Arsenic Is a Poor Proxy: Why Arsenic Speciation Matters

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Abstract

For decades, food-arsenic risk assessment has rested on the assumption that organoarsenicals — chiefly arsenobetaine, the dominant arsenic species in marine fish and shellfish — are biologically inert and pass through the body unchanged. That assumption is now contested on three independent fronts: biomonitoring studies that read seafood-derived dimethylarsinic acid as if it measured inorganic-arsenic methylation, in vitro digestion work showing organic arsenicals partly convert to inorganic As(V) in the stomach, and a large Japanese cohort in which serum arsenic that is roughly 98 percent arsenobetaine tracked hypertension risk. None of these refutes inertness outright, but together they show that total arsenic is a poor proxy for arsenic risk. The certification consequence is direct: a defensible standard limits speciated inorganic arsenic rather than total arsenic, and reads an arsenic result in the context of its food matrix instead of assuming every organic form is harmless. The full anchor-source evidence base lives on the Heavy Metal Index, the independent literature reference this analysis cites one way.

The Inertness Assumption and Why It Matters

Food-arsenic risk assessment has long rested on a single premise: that organoarsenicals — chiefly arsenobetaine, the dominant arsenic species in marine fish and shellfish — are metabolically inert, pass through the body unchanged, and pose no toxicological concern even at concentrations that would alarm if the arsenic were inorganic. That premise created the structural divide in how agencies treat arsenic in food. Inorganic arsenic is regulated, characterised with dose-response relationships, and the target of maximum levels and reduction initiatives; organic arsenic in seafood is largely excluded from risk characterisation on the grounds that it does not contribute to health risk.

The same premise is what makes the distinction between inorganic arsenic and total arsenic meaningful in practice. A product reporting 200 ppb total arsenic that is almost entirely arsenobetaine is treated as categorically different from one at 200 ppb that is almost entirely inorganic. Eight independent studies published between 2023 and 2024 now test that premise on three fronts at once — metabolism, biomonitoring and epidemiology — across seafood, fungi and algae-derived matrices. None refutes it outright, but together they make one thing clear for anyone certifying a product: total arsenic is a poor proxy for arsenic risk.

The Biomonitoring Confound

The standard way to biomonitor inorganic-arsenic exposure uses the urinary fraction of dimethylarsinic acid (DMA) as an index of methylation efficiency, reading a higher DMA fraction as efficient methylation and therefore a lower retained inorganic-arsenic burden. That reading has a confound. Arsenosugars and arsenolipids from seafood are metabolised to DMA by a route that does not pass through the inorganic-arsenic methylation sequence, so a person who eats a lot of seafood shows an elevated urinary DMA fraction not because they methylate inorganic arsenic well, but because they are excreting DMA derived from arsenosugar catabolism [1].

The practical effect is that studies using urinary %DMA as a methylation index in seafood-eating populations may systematically underestimate those populations' inorganic-arsenic exposure. Agencies that lean on that biomonitoring literature — EFSA's dietary inorganic-arsenic assessments among them — may therefore carry modelled exposure margins that are slightly optimistic, because the seafood-arsenosugar bias in the underlying studies is real and is not corrected for [1].

Speciation Is Not Stable Through Digestion

A second challenge concerns whether organic arsenic survives digestion intact. Using a standardised in vitro gastrointestinal protocol, one study characterised arsenic speciation in crab and scallop before and after simulated digestion and found that organic arsenicals in both matrices underwent a two- to three-fold increase in the inorganic As(V) fraction, attributed to a pH-dependent free-radical oxidation that becomes active under the acidic conditions of the stomach [2]. The speciation measured in the food at the moment of eating — the speciation used to classify a food as predominantly organic and therefore low risk — is not necessarily the speciation present at the point of intestinal absorption.

The result does not settle how much inorganic arsenic is actually absorbed from a seafood portion. In vitro digestion models replicate pH, enzyme activity and transit time imperfectly and do not account for intestinal re-speciation or transporter-mediated selectivity in absorption. What the finding establishes is narrower but still material: the assumption that speciation is stable through digestion is not justified, and the gap between food-measurement speciation and absorbed-fraction speciation has not been closed [2].

An Epidemiological Signal at Dietary Levels

The strongest human-evidence challenge comes not from speciation chemistry but from a prospective cohort. In the J-MICC Daiko study, a community cohort of 2,709 Japanese adults with measured serum arsenic and prospectively adjudicated outcomes, serum total arsenic — estimated at about 98 percent arsenobetaine from population speciation surveys — was associated with dose-dependent hypertension risk that remained significant after adjustment for fish-consumption frequency, age, sex, body-mass index and other cardiovascular risk factors [3].

That result is anomalous under the inertness assumption. If almost all serum arsenic is arsenobetaine and arsenobetaine is inert, serum arsenic should track fish consumption rather than act as an independent vascular risk factor once fish consumption is controlled — yet the association persists. The authors offer three readings: residual confounding by fish constituents the frequency variable does not capture, a biological effect of arsenobetaine or a minor co-metabolite at population-typical concentrations, or misclassification of serum arsenic as predominantly arsenobetaine. None is ruled out, and the cohort is Japanese, where seafood arsenic intake runs unusually high, so the exposure at which the signal appears may not transfer to lower-consuming populations [3]. The study does not demonstrate arsenobetaine toxicity; it is simply inconsistent with treating fish arsenic as toxicologically invisible.

Beyond Marine Fish: Algae, Mushrooms and Kelp

The concern is not confined to the marine matrices where arsenobetaine dominates. In the model green microalga Chlamydomonas reinhardtii, about 57 percent of total arsenic was found to exist as arsenolipids, including the first report of the arsenosugar phospholipid AsSugPhytol in any organism [4]. The implication is both analytical and commercial: standard acid-digestion protocols may not quantitatively recover arsenolipid fractions, so a total-arsenic figure for spirulina, chlorella, algae protein or algae oil can understate recoverable arsenic and leaves uncharacterised species unaccounted for. This finding should be treated as organism-specific until replicated in commercial algae ingredients, but it is

directly relevant to protein powders, functional foods and infant nutrition that increasingly use algae-derived material.

Two further studies widen the picture. A novel arsenobetaine amide was identified in four mushroom species, extending known organoarsenical diversity to terrestrial fungi and reopening the question of whether arsenobetaine itself is the only bioactive species in its structural class [5]. And a validated HPLC-ICP-MS method found that the kelp Laminaria digitata carries more than 50 percent of its total arsenic as inorganic arsenic — an occurrence fact, not a metabolic conversion, but one that shows the reflex "seaweed arsenic is organic and therefore low risk" is simply wrong for a commercially important genus [6]. The EU's Regulation (EU) 2023/915 now sets specific inorganic-arsenic limits for seaweed products, the regulatory leading edge of a narrowing organic-arsenic exemption [7].

Matrix	Dominant arsenic profile	What a total-arsenic result misses
Marine fish and shellfish	Mostly arsenobetaine	Overstates the toxic fraction; the inorganic share is small
Kelp (Laminaria digitata)	Inorganic arsenic over half of total	Understates risk if read as "organic, low risk"
Microalgae (spirulina, chlorella)	Arsenolipids up to ~57% in a model species	Uncharacterised species that acid digestion may under-recover

The common thread is that the same total-arsenic number carries a different meaning in each matrix. Only speciation, read with category context, tells you what a result means. See the Heavy Metal Certified seaweed and kelp standard for how the inorganic-arsenic limit is set for that category.

What this means for certification

The certification consequence is specific, and Heavy Metal Certified already builds to it. The certified arsenic analyte is inorganic arsenic, quantified as speciated inorganic arsenic by HPLC-ICP-MS; a total-arsenic result is not interchangeable with it. That choice is exactly what this evidence supports. Total arsenic overstates the toxic fraction in arsenobetaine-dominated marine fish, and it can understate risk where the inorganic fraction is high, as in kelp, or where uncharacterised arsenolipids make up much of the total, as in algae-derived ingredients.

How the number is set follows the program's general rule. The default limit for any product and analyte is the strictest maximum level set by a credible government regulator, converted to the product's own basis. Inorganic arsenic is one of the four Tier-1 toxics — with lead, cadmium and methylmercury — so for arsenic the standard may set the stricter of that government limit and the cleaner end of the occurrence evidence, rather than the government floor alone.

The harder discipline the finding demands is what not to assume. Contesting the inertness of arsenobetaine does not license treating every organic arsenic form as dangerous, any more than the old view licensed treating them all as safe; the honest posture is that speciation and matrix context are what make an arsenic result meaningful. For a matrix whose organoarsenical profile is poorly characterised — a new algae-protein ingredient, say, tested only for total arsenic — the defensible response is to flag the uncertainty and require speciated data, not to wave the product through on the strength of an "organic, therefore harmless" label. The finding does not say seafood is dangerous or that fish should be avoided; high fish consumption remains a net benefit for most people. It says the number that certifies arsenic has to be the inorganic fraction, read in the context of the food it came from.

Frequently asked questions

Is the arsenic in fish and shellfish harmless?

Most arsenic in marine fish and shellfish is arsenobetaine, which has long been assumed biologically inert, and high fish consumption remains a net benefit for most people. But that inertness assumption is

now contested on several fronts. A total-arsenic result overstates the toxic fraction in fish, yet it does not prove the organic fraction is entirely without effect.

Why is total arsenic a poor measure of risk?

Total arsenic pools the inorganic form — an IARC Group 1 human carcinogen — with organic forms of very different toxicity. In arsenobetaine-dominated fish it overstates risk, while in kelp or microalgae it can hide a large inorganic or uncharacterised arsenolipid fraction. Only speciated testing resolves the health-relevant inorganic fraction, which is why it is the meaningful measurement.

Does organic arsenic stay organic once you eat it?

Not entirely. In an in vitro digestion study, organic arsenicals in crab and scallop showed a two- to three-fold increase in the inorganic As(V) fraction after simulated gastric digestion. That establishes that speciation at the moment of eating is not necessarily the speciation at absorption. It does not, by itself, quantify how much inorganic arsenic is actually absorbed from a seafood portion.

Is seaweed a low-arsenic food?

Not reliably. A validated HPLC-ICP-MS method found that the kelp Laminaria digitata carries more than half of its total arsenic as inorganic arsenic, so the assumption that seaweed arsenic is organic and therefore low risk is wrong for this commercially important genus. The EU's Regulation (EU) 2023/915 now sets specific inorganic-arsenic limits for seaweed products in recognition of this.

How should a certification standard test arsenic?

By limiting speciated inorganic arsenic rather than total arsenic, since total arsenic overstates risk in fish and can understate it in kelp or algae ingredients. The certified analyte is inorganic arsenic, measured by HPLC-ICP-MS, and the limit adopts the strictest maximum level set by a credible government regulator. Because inorganic arsenic is a Tier-1 toxic, the standard may take the stricter of that limit and the cleaner end of the occurrence evidence.

References

[1] Seafood arsenosugars and arsenolipids confound urinary methylation-efficiency biomonitoring. Davydiuk et al., 2023. Arsenosugars and arsenolipids from seafood are metabolised to urinary DMA by a route independent of inorganic-arsenic methylation, so %DMA methylation indices can underestimate inorganic-arsenic exposure in seafood-eating populations.

[2] Conversion of seafood organoarsenicals to inorganic As(V) during simulated digestion. Liu et al., 2023. Organic arsenicals in crab and scallop showed a two- to three-fold increase in the inorganic As(V) fraction after in vitro gastrointestinal digestion, via a pH-dependent free-radical oxidation.

[3] Serum arsenic and prospective hypertension risk in a Japanese cohort. Kagawa et al., 2023. In the J-MICC Daiko cohort (n=2,709), serum total arsenic — about 98 percent arsenobetaine by population survey — was associated with dose-dependent hypertension risk after adjustment for fish-consumption frequency and cardiovascular risk factors.

[4] First detection of an arsenosugar phospholipid in the microalga Chlamydomonas reinhardtii. Raab et al., 2024. First report of the arsenolipid AsSugPhytol in any organism; about 57 percent of total arsenic in Chlamydomonas reinhardtii exists as arsenolipids, which standard acid digestion may under-recover.

[5] A novel arsenobetaine amide identified in several mushroom species. Walenta et al., 2024. Discovery of a previously unreported arsenobetaine amide in four mushroom species, extending known organoarsenical diversity to terrestrial fungi.

[6] Validated HPLC-ICP-MS determination of inorganic arsenic in seaweed. Sim et al., 2024. A validated method found that Laminaria digitata carries more than 50 percent of its total arsenic as inorganic arsenic, showing seaweed is not a low-inorganic-arsenic matrix by default.

[7] Maximum levels for inorganic arsenic in seaweed and other foods. European Union. Commission Regulation

(EU) 2023/915 sets specific inorganic-arsenic maximum levels for seaweed products among other food categories.

[8] Heavy Metal Index — the organoarsenical inertness assumption (synthesis with full anchor-source records). The independent literature synthesis this analysis reframes, carrying every anchor source — Davydiuk, Liu, Kagawa, Raab, Walenta, Sim and others — and its per-record page. · heavymetalindex.com

Cite this analysis