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"HEAVY METAL SAFETY OF *RASAUSHADHI*: A CRITICAL REVIEW OF PRECLINICAL TOXICITY AND CLINICAL SAFETY EVIDENCE"

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ABSTRACT

Background: *Rasaushadhi*, the herbo-mineral and herbo-metallic formulations of Ayurveda, intentionally contain metals such as mercury, lead, arsenic, copper and gold. Their safety is contested: case reports of poisoning sit alongside a long classical tradition and a growing body of animal studies reporting no toxicity at therapeutic doses. **Objective:** To review what the preclinical and clinical evidence shows about the heavy metal safety of *Rasaushadhi*, and to identify what is needed to settle the question. **Methods:** A critical narrative review of market surveys, case reports and case clusters, animal and zebrafish toxicity studies, and clinical safety studies, with attention to chemical speciation, dose and study design. **Results:** Market surveys consistently detect lead, mercury or arsenic in a substantial share of Ayurvedic products, more often in *Rasa Shastra* products, and some at levels far above herbal medicine limits. Case reports and clusters of lead poisoning are well documented. Animal and zebrafish studies of processed mercurials, *bhasmas* and compound formulations generally report low toxicity at therapeutic doses and differences from simple mercury salts, but most are short-term, use single products and rarely measure tissue metal accumulation. Clinical safety studies are few, small and seldom report blood or urine metal levels. **Conclusion:** The evidence does not support either blanket claims of safety or blanket bans. Safety depends on chemical form, dose, duration and product quality. Long-term studies with biomonitoring, product-level quality control and active pharmacovigilance are required.

KEYWORDS: *Rasaushadhi*; Herbo-mineral formulations; Heavy metals; Mercury; Lead; Arsenic; Toxicity; Pharmacovigilance

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INTRODUCTION

Rasa Shastra deliberately uses metals and minerals as medicines. Mercury (*parada*), sulphur (*gandhaka*), arsenic compounds (*haratala*, *manahshila*), lead (*naga*), tin (*vanga*), copper (*tamra*), iron (*lauha*), zinc (*yashada*), silver (*rajata*) and gold (*swarna*) are converted into *bhasmas*, *kupipakva rasayanas* and compound formulations through purification (*shodhana*), incineration (*marana*) and trituration with herbal media. Classical authorities hold that properly processed metals are free from toxicity and that toxicity arises from improper processing, inappropriate dose or unsuitable use.

Outside the tradition, these products are viewed with suspicion. Lead, mercury and arsenic are among the most studied toxic elements, with no known physiological role, and their presence in medicines conflicts with modern pharmaceutical norms. Reports of lead poisoning linked to Ayurvedic products, and surveys detecting heavy metals in products sold internationally, have shaped regulatory and public opinion[1-3].

Within Ayurveda, a growing body of animal and analytical research argues the opposite: that processing transforms metals into stable, poorly soluble compounds of low toxicity. Both positions are often stated with more confidence than the evidence allows. This review sets out what the published evidence actually shows, distinguishes problems that are often conflated, and identifies the studies needed to resolve the question.

METHODS OF THE REVIEW

This is a critical narrative review. Literature was identified through PubMed, PubMed Central, Crossref-indexed records and publisher databases, using combinations of the terms Ayurveda, *Rasaushadhi*, herbo-mineral, herbo-metallic, *bhasma*, *Rasasindura*, *kajjali*, mercury, lead, arsenic, toxicity, safety, case report and blood lead. Reference lists of retrieved reviews were screened. Four types of evidence were considered: market surveys of metal content, clinical case reports and case clusters, preclinical toxicity studies (rodent, zebrafish and cell models), and clinical studies that reported safety outcomes. Each study was assessed for chemical speciation, dose relative to human therapeutic dose, duration of exposure, and whether metal levels were measured in blood, urine or tissue. Because study designs were heterogeneous, no quantitative synthesis was attempted.

THREE DIFFERENT PROBLEMS THAT ARE OFTEN CONFLATED

Discussions of heavy metals in Ayurveda frequently merge three distinct problems. Separating them is the first step towards a useful answer.

Contamination. Herbal products can contain unintended metals from soil, water, processing equipment or adulteration. This applies to all herbal medicine traditions and is addressed by limits for contaminants[4]. A large survey of 1,773 Chinese herbal medicine samples, for example, found that 30.5% exceeded pharmacopoeial limits for at least one heavy metal[5].

Intentional metal content. In *Rasaushadhi*, the metal is the active ingredient. Contaminant limits designed for herbs are not appropriate measures of quality for these products, and their safety has to be judged by toxicology of the specific compound, at the specific dose, for the specific duration.

Poor manufacturing quality. Products of the same name can differ widely in composition between manufacturers and batches, and incompletely processed products may contain more soluble, more toxic forms of a metal. This problem cuts across both of the others[6,7].

CHEMICAL FORM DETERMINES TOXICITY

The toxicity of a metal depends on its chemical form. Mercury illustrates this most clearly. Methylmercury is rapidly absorbed and highly neurotoxic; inorganic mercuric chloride is soluble and nephrotoxic; mercuric sulphide (HgS), the main form in cinnabar, *kajjali* and *Rasasindura*, is very poorly soluble and far less bioavailable. Studies of cinnabar-containing traditional medicines have shown that HgS differs markedly from common mercurials in absorption, distribution and toxicity, although it is not inert, and long-term or high-dose use can still lead to mercury accumulation[8]. A toxicological review of mercury-based herbo-metallic preparations reached a similar conclusion: total mercury content is a poor guide to risk, and speciation, solubility and bioavailability must be considered[9].

The same principle applies to other metals. Naga *bhasma*, for example, has been characterised as lead sulphide rather than lead oxide[10], and Swarna *bhasma* as metallic gold[11]. These findings do not establish safety on their own, but they explain why results for one metal salt cannot be transferred to a processed

bhasma, and why results for one product cannot be transferred to another of the same name.

EVIDENCE FROM MARKET SURVEYS

Table 1 summarises representative surveys of metal content in Ayurvedic products.

Table 1. Representative market surveys of heavy metal content in Ayurvedic products

Study	Products and setting	Main findings
Saper et al. 2004	70 Ayurvedic products from South Asian stores in the Boston area, USA	About one in five products contained lead, mercury and/or arsenic at potentially harmful levels
Saper et al. 2008	193 US- and Indian-manufactured products purchased via the Internet	About one in five products contained detectable lead, mercury or arsenic; *Rasa Shastra* products were positive more often than non-*Rasa Shastra* products
Bhalla and Pannu 2022	42 over-the-counter products from licensed shops in Chandigarh, India	Heavy metals detected in every product; median mercury 13.52 µg/g, maximum about 61,096 µg/g; zinc, mercury, arsenic and lead above FAO/WHO limits in 35, 29, 6 and 2 products respectively
Biswas et al. 2021	Five commercial Suvarna *bhasma* products	Gold content 32–98 wt%; one product contained 5.4 wt% arsenic; mercury not detected
Mikulski et al. 2017	Products linked to a lead poisoning cluster in the USA	Toxic metals identified in preparations consumed by affected individuals

Two points stand out. First, metal detection is common and is not limited to *Rasaushadhi*; it is also reported in products that are not supposed to contain metals, which points to contamination or undeclared ingredients[3,14]. Second, when *Rasaushadhi* are measured against herbal contaminant limits, they will almost always fail, because the metal is intended. This is a category error, but it is also a warning: the label rarely tells the user that the product contains a metal, or how much.

EVIDENCE FROM CASE REPORTS AND CLUSTERS

Clinical lead poisoning associated with Ayurvedic products is well documented. In 2004 the United States Centers for Disease Control and Prevention reported a series of lead poisoning cases associated with Ayurvedic medications across five states[15]. Later, a cluster of lead poisoning among consumers of Ayurvedic medicine was investigated by a public health team[16], and analysis of the preparations involved identified toxic metals[13]. Similar reports have been published from several countries.

Case reports cannot estimate how common toxicity is, and in many reports the product was not analysed, the formulation was unknown or proprietary, or the patient was taking several products at once for long periods. Nonetheless, they establish beyond reasonable doubt that some Ayurvedic products, as used in practice, have caused clinically significant metal poisoning.

Any defence of *Rasaushadhi* safety has to start from this fact.

EVIDENCE FROM PRECLINICAL STUDIES

1. Mercurial formulations

Mercury-containing formulations have received the most experimental attention. In zebrafish, *Rasasindura* and *kajjali* were compared with other mercury compounds for neurotoxicity[17]. A later study showed that Ayurvedic processing of α-HgS produced distinct physicochemical features and toxicokinetics compared with unprocessed mercuric sulphide[18], and *Rasasindura* was further examined in NIH3T3 fibroblasts and zebrafish larvae[19]. A 2024 scoping review identified only five peer-reviewed in vitro and in vivo studies on *Rasasindura* safety, four from a single institution. These studies suggested safety at therapeutic doses in zebrafish and rat models, but the authors concluded that acute, subacute and chronic toxicity studies in higher mammals were still needed[20].

2. Bhasmas and compound formulations

For Naga *bhasma*, a 40-day study in rats at 6 mg/100 g/day found no notable organ changes, whereas crude lead caused damage to lung, kidney, liver and other tissues[10]. Swarna *bhasma* showed very low haemolysis and minimal effects on complement and platelet activation in blood-compatibility tests[11]. In rats and zebrafish, five commercial Suvarna *bhasma* products produced significantly different blood and

tissue gold profiles[6]. Abhraka *bhasma* has been examined for toxicity in rats[21], although concerns about dose-dependent hepatotoxicity and aluminium content have been raised for mica-based preparations[22]. For the mercury- and copper-containing compound Arogyavardhini Vati, a safety evaluation in rats examined effects on brain, liver and kidney[23].

3. Limitations of the preclinical evidence

Taken together, the preclinical evidence is reassuring in direction but limited in depth. Common weaknesses include short duration relative to the months or years for which some formulations are used, single products from one manufacturer, doses not clearly related to human equivalent doses, small group sizes, and limited measurement of metal accumulation in target tissues such as kidney and brain. Studies are rarely conducted under good laboratory practice or according to OECD repeated-dose guidelines, and negative results from a well-made, characterised product do not establish the safety of commercial products of the same name.

EVIDENCE FROM CLINICAL STUDIES

Clinical evidence is the weakest part of the picture. In a pilot prospective cohort of patients with dyslipidaemia treated with Arjuna powder followed by Arogyavardhini Vati, 87 of 96 enrolled patients completed seven weeks of treatment, and liver and kidney function markers did not change significantly from baseline[24]. The study mentioned urinary mercury, but did not report its results, which illustrates a recurring gap: clinical studies of *Rasaushadhi* rarely publish blood or urine metal levels, even when they claim safety.

Without biomonitoring, normal liver and kidney tests over a few weeks cannot exclude metal accumulation, particularly for metals such as lead and mercury whose toxicity is chronic and often subclinical at first. Well-designed observational studies of long-term users, with blood lead, blood and urine mercury and urinary arsenic speciation, would add more to the debate than further short-term animal studies.

INTERPRETING THE EVIDENCE

The evidence supports four conclusions.

- **Risk is real but not uniform.** Clinical poisoning has occurred, but it is concentrated in poorly characterised, often contaminated or incompletely processed products, frequently taken for long periods or in combination.
- **Processing matters.** Experimental work supports the classical view that processing changes the chemical form and behaviour of metals. It does not support the stronger claim that processed metals are harmless at any dose or duration.
- **Product quality is the main modifiable risk factor.** Large differences between manufacturers in metal content, impurities and bioaccumulation[6], and very high mercury levels in some over-the-counter products[12], indicate that quality control is the most urgent issue.
- **Prescribing practice also matters.** Cumulative exposure from several formulations that share the same metal, prolonged use without monitoring, and self-medication with over-the-counter products increase risk[7,25].

RECOMMENDATIONS

Table 2 sets out practical recommendations for researchers, manufacturers, clinicians and regulators.

Table 2. Recommendations for improving the evidence on and safety of *Rasaushadhi*

Stakeholder	Recommendation
Researchers	Characterise the test product (phase, speciation, metal content) before toxicity testing; use OECD repeated-dose designs of adequate duration; relate doses to human equivalent doses; measure metal accumulation in blood and target tissues; test more than one commercial product
Clinical investigators	Include baseline and follow-up blood lead, blood and urine mercury and urinary arsenic where relevant; report results even when normal; follow up long-term users
Manufacturers	Declare the metal content on the label; adopt batch-level testing of total metals and of unintended metals; validate *shodhana* and *marana* end-points with instrumental methods
Clinicians	Avoid prolonged unmonitored use; check for overlapping metals across co-prescribed formulations; record and report adverse events

Regulators	Distinguish contaminant limits for herbal products from product-specific specifications for *Rasaushadhi*; strengthen post-marketing surveillance and testing of over-the-counter products

RESEARCH GAPS

The main gaps are: long-term (90-day or longer) repeated-dose studies in rodents with tissue metal measurement; human pharmacokinetic and biomonitoring studies in patients taking *Rasaushadhi* at therapeutic doses; studies comparing commercial products with well-characterised reference batches; and pharmacovigilance data that capture product identity and laboratory confirmation. The *Rasasindura* scoping review, which identified only five eligible studies[20], shows how narrow the current evidence base is for even the most widely used mercurial formulation.

CONCLUSION

The heavy metal safety of *Rasaushadhi* is neither proven nor disproven. Market surveys and case reports show that some products, as manufactured and used, cause harm. Experimental studies suggest that classical processing changes the chemical form and behaviour of metals and that well-made formulations may have low toxicity at therapeutic doses over short periods. The gap between these two bodies of evidence lies in product quality, chemical speciation, dose and duration, and in the near absence of clinical biomonitoring. Closing that gap requires product-level quality control, long-term studies with metal measurements, and active pharmacovigilance, rather than either blanket reassurance or blanket prohibition.

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