

Safety and Toxicology of Herbo-Mineral Preparations

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ABSTRACT

Herbo-mineral preparations, traditionally known as bhasmas and pishtis within the Rasa Shastra branch of Ayurvedic pharmacy, are the single most contentious class of Ayurvedic medicines in the European regulatory context. They intentionally incorporate processed metallic or mineral components (iron, copper, mica, gold, silver, zinc, coral calcium) via classical processing steps (sodhana purification, marana incineration, bhavana levigation) that are said to modify the bioavailability and toxicological profile of the starting materials. Documented instances of lead and mercury exposure from imported Ayurvedic products have shaped European regulatory attitudes, and the class needs to be assessed on clearer safety and toxicology evidence rather than on either classical assurance or blanket scepticism. This study reviews 48 primary toxicology, analytical and pharmacovigilance studies published between 2005 and 2021 on classical herbo-mineral preparations, grouped under five assessment frames: T1 (classical processing validation), T2 (acute preclinical toxicology), T3 (chronic toxicology), T4 (bioavailability and metal speciation), and T5 (clinical pharmacovigilance and case reports). Each frame was scored with the Herbo-Mineral Toxicology Index (HMTI). Processing validation (T1) scored highest at HMTI 0.772, reflecting the growing analytical evidence that properly processed classical preparations differ chemically from raw starting material. Clinical pharmacovigilance (T5) scored lowest at HMTI 0.612, reflecting both genuine signals in case-report literature and underdeveloped post-marketing surveillance infrastructure in European markets. The overall picture is that classical processing matters and can reduce toxicological risk when done well, but that European clinical deployment of herbo-mineral preparations requires much stricter sourcing verification and pharmacovigilance than is currently standard.

Keywords: herbo-mineral preparations; bhasma; Rasa Shastra; Ayurveda; toxicology; heavy metals; processing validation; pharmacovigilance; metal speciation; nanoparticle; regulatory safety; HMTI

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1. Introduction

1.1 Herbo-Mineral Preparations and the Regulatory Question

Herbo-mineral preparations are the pharmaceutically complicated corner of Ayurvedic medicine. The Rasa Shastra branch of Ayurvedic pharmacy specifies a class of preparations that intentionally incorporate processed metals and minerals: iron (Loha Bhasma), copper (Tamra Bhasma), gold (Swarna Bhasma), silver (Rajat Bhasma), mica (Abhrak Bhasma), zinc (Yashad Bhasma), mandura (iron oxide), along with pishti-class preparations using coral (Praval), pearl (Mukta), and associated marine calcium sources. Classical processing involves multi-step protocols (sodhana purification, marana incineration cycles at specific temperatures, bhavana levigation with plant juices) taking weeks to months to complete. The classical claim is that these processing steps transform the starting metal into a therapeutically usable form with substantially modified toxicological properties. The modern regulatory claim, in contexts where European clinical deployment is considered, is that this transformation needs to be demonstrated analytically rather than assumed from classical text.

1.2 Sub-Questions, Evidence Base, and Study Objectives

The toxicology question for herbo-mineral preparations has three distinct sub-questions that need separate evidence bases. First, does classical processing meaningfully modify the starting material chemically, and if so, in what ways? Second, what is the acute, subacute and chronic toxicology profile of properly processed classical preparations, and how does it differ from raw-metal exposure? Third, what is the real-world pharmacovigilance picture in populations actually taking these preparations, and how much of the documented toxicity evidence reflects poorly processed or adulterated product rather than authentic classical preparations? This study reviews the published evidence under five assessment frames and produces an integrated toxicology index for each. Safety is weighted most heavily in the scoring because the European clinical context cannot accept intervention classes with meaningful net toxicity regardless of their traditional provenance. The paper follows the standard six-part structure.

2. Literature Review

2.1 Classical Processing Validation Evidence

The classical processing validation frame (T1) has matured substantially over the past two decades. Modern analytical work has confirmed that properly processed bhasmas differ chemically from their starting materials in ways that matter toxicologically. Sarkar and Chaudhary (2010) provided XRD and particle size characterisation of Abhrak Bhasma before and after classical processing. Kumar et al. (2012) reported that properly processed Swarna Bhasma contains gold in a particle-size distribution consistent with nanoparticle characterisation. Wadekar et al. (2015) extended this analysis with TEM imaging to multiple bhasma classes. The consolidated picture is that classical processing produces materials that are not chemically or physically identical to the starting metal or mineral. Whether this modifies toxicology in clinically meaningful ways is a separate question that T2 and T3 evidence has to address.

2.2 Acute and Chronic Toxicology

Acute and subacute toxicology (T2) has a reasonably developed preclinical literature. Pal et al. (2011), Kumar and Gauttam (2014) and related work have reported LD50 and subacute toxicity data for properly processed Abhrak Bhasma, Praval Pishti and Swarna Bhasma in rodent models. The reported NOAEL values are substantially above typical clinical dose ranges, though with considerable study-to-study variability that plausibly reflects batch-to-batch variation in the tested preparations. Chronic toxicology (T3) is where the evidence base thins. Very few 90-day or 180-day animal toxicology studies have been published for major herbo-mineral preparations, and clinical long-term follow-up data is even scarcer. This is the single largest evidence gap in the class-level safety picture, and it matters particularly because these preparations are classically prescribed for long-term use.

2.3 Bioavailability, Speciation and Pharmacovigilance

Bioavailability and metal speciation (T4) has attracted increasing analytical attention. The classical claim that processed bhasmas differ from raw metal exposure depends on demonstrable differences in bioavailability and chemical speciation of the metal in the preparation. Mohaptra and Jha (2010) reported oral bioavailability studies for Abhrak Bhasma. Chaudhari et al. (2013) extended to speciation work using XANES and EXAFS spectroscopy, reporting that iron in classical Loha Bhasma differs in oxidation state distribution from iron in

raw haematite. Clinical pharmacovigilance (T5) remains the weakest frame. The Saper et al. (2004, 2008) landmark surveys of US-marketed Ayurvedic products found substantial proportions exceeding pharmacopoeia lead, mercury and arsenic limits, disproportionately in bhasma-class products. Subsequent European market surveillance (Breeher et al., 2015) confirmed the pattern. Table 1 lists the key studies informing this review.

Table 1: Key Studies in Herbo-Mineral Safety and Toxicology

Referen ce	Y e a r	Fra me	Preparatio n(s)	Key Finding
Saper et al.	2004	T5	US-market Ayurvedic	Initial heavy metal exposure cases
Saper et al.	2008	T5	US + Indian market	20% exceed US pharmacopoeia limits
Mohaptra and Jha	2010	T4	Abhrak Bhasma	Oral bioavailability characterised
Sarkar and Chaudhary	2010	T1	Abhrak Bhasma	XRD + particle size post-processing
Savrikar and Ravi shankar	2011	T1	Rasa Shastra overview	Bhaisajya kalpana process review
Pal et al.	2011	T2	Abhrak Bhasma	Acute + subacute rat toxicology
Kumar et al.	2012	T1	Swarna Bhasma	Gold nanoparticle character.
Chaudhari et al.	2013	T4	Loha Bhasma	XANES / EXAFS speciation
Kumar and Gauttam	2014	T2	Praval Pishti	NOAEL above clinical dose
Breeher et al.	2015	T5	European import	European market lead exceedances

Referen ce	Y e a r	Fra me	Preparatio n(s)	Key Finding
Wadekar et al.	2015	T1	Multiple bhasmas	TEM imaging post-classical process
European Medicines Ag.	2018	T5	Ayurvedic regul. review	European regulatory safety position

T1 = Classical processing validation; T2 = Acute/subacute toxicology; T3 = Chronic toxicology; T4 = Bioavailability and metal speciation; T5 = Clinical pharmacovigilance. XRD = X-Ray Diffraction; TEM = Transmission Electron Microscopy; XANES = X-ray Absorption Near-Edge Structure; EXAFS = Extended X-ray Absorption Fine Structure; NOAEL = No-Observed-Adverse-Effect Level.

3. Methodology

3.1 Review Search Strategy

We conducted a structured safety and toxicology review of primary studies published from January 2005 through December 2021 on classical herbo-mineral preparations. Databases searched were PubMed, Scopus, the AYUSH Research Portal, the WHO Uppsala Monitoring Centre database, the European Medicines Agency herbal monograph collection, and the Food and Drug Administration adverse event reporting system. Search terms combined 'bhasma', 'pishti', 'Rasa Shastra', 'herbo-mineral', 'Ayurveda', 'Ayurvedic metallic preparation' with specific preparation names (Abhrak, Swarna, Loha, Tamra, Rajat, Yashad, Mandura, Praval, Mukta Pishti) paired with 'toxicology', 'safety', 'heavy metal', 'lead', 'mercury', 'arsenic', 'chronic toxicity', 'bioavailability', 'metal speciation', 'nanoparticle', 'adverse event' and 'pharmacovigilance'. Initial search returned 982 records. After duplicate removal, title and abstract screening, and full-text assessment against inclusion criteria (primary empirical data, specified herbo-mineral preparation, at least one toxicology-relevant endpoint, peer-reviewed publication), 48 studies were included.

3.2 Five Assessment Frames

Each included study was assigned to its primary assessment frame. T1 (Classical Processing Validation) covers studies using analytical methodology (XRD, TEM, particle size analysis, chemical characterisation) to document how classical processing modifies the starting metal or mineral. T2 (Acute and Subacute Toxicology)

covers preclinical toxicology studies up to 28 days of dosing in animal models with histopathology, biochemistry and haematology endpoints. T3 (Chronic Toxicology) covers preclinical studies of 90 days or longer and clinical long-term follow-up data. T4 (Bioavailability and Metal Speciation) covers pharmacokinetic studies and analytical speciation work (XANES, EXAFS, oxidation-state determination, tissue distribution, particle size characterisation) relevant to whether the processed preparation behaves differently from raw metal exposure. T5 (Clinical Pharmacovigilance) covers clinical adverse event case reports, post-marketing surveillance data, market product heavy-metal surveys, and regulatory safety analyses.

3.3 Herbo-Mineral Toxicology Index (HMTI)

The Herbo-Mineral Toxicology Index (HMTI) scores each assessment frame on five weighted dimensions. Processing validation quality (weight 0.15) scores the analytical rigour of the evidence that classical processing modifies the starting material in documented, reproducible ways. Acute safety margin (0.20) scores the NOAEL-to-clinical-dose ratio and the consistency of acute toxicology findings across studies. Chronic safety profile (0.25) scores long-term (≥ 90 day preclinical, ≥ 6 month clinical) safety evidence; this dimension is weighted most heavily because chronic use is the intended clinical pattern and the toxicology dimension most relevant to European clinical deployment. Bioavailability and speciation evidence (0.15) scores the analytical characterisation of how the processed preparation behaves in biological systems relative to raw metal exposure. Post-market surveillance quality (0.25) scores the adequacy of clinical adverse event detection, characterisation and reporting; weighted equally to chronic safety because real-world exposure data is the ultimate safety test. All dimensions normalised to 0-1 before weighting.

Table 2: Review Inventory by Assessment Frame and Study Type

Assessment Frame	Studies (n)	Preclinical	Clinical / surveil.	Analytical
T1: Classical Processing Validation	12 (25.0%)	2	0	10
T2: Acute / Subacute Toxicology	10 (20.8%)	10	0	0

Assessment Frame	Studies (n)	Preclinical	Clinical / surveil.	Analytical
T3: Chronic Toxicology	6 (12.5%)	4	2	0
T4: Bioavailability / Speciation	10 (20.8%)	4	0	6
T5: Clinical Pharmacovigilance	10 (20.8%)	0	10	0
Total included	48 (100%)	20	12	16

Preclinical = animal toxicology or mechanism studies; Clinical / surveil. = clinical adverse event reports and market surveillance surveys; Analytical = pure characterisation studies without toxicology endpoint.

4. Results

4.1 HMTI Ranking Across Assessment Frames

Classical processing validation (T1) scored highest at HMTI 0.772. The score reflects the analytical maturity of the processing-characterisation work: XRD, TEM and particle size analyses consistently show that properly processed bhasmas differ in phase composition, oxidation state distribution and particle size distribution from their starting materials. Across T1 studies, properly processed Abhrak Bhasma consistently shows particle sizes in the sub-100 nm range with altered crystallographic characteristics; properly processed Swarna Bhasma shows gold nanoparticles in the 30-80 nm range; Loha Bhasma shows oxidation-state distributions that differ from raw magnetite or haematite. Bioavailability and speciation (T4) scored second at HMTI 0.714, supporting the picture that properly processed preparations behave differently in biological systems from raw metal exposure, although the absolute quantification of the difference remains imprecise. Acute toxicology (T2) scored 0.694 with NOAEL-to-clinical-dose ratios in the 50-200x range across tested preparations. Chronic toxicology (T3) scored 0.672, pulled down by the thin evidence base. Clinical pharmacovigilance (T5) scored lowest at HMTI 0.612.

4.2 Clinical Pharmacovigilance and Market Surveillance

The clinical pharmacovigilance findings are where the picture is most mixed and most consequential for European deployment. The Saper et al. (2004, 2008) landmark US-market studies found that approximately 20% of tested Ayurvedic products exceeded US pharmacopoeia lead limits, with herbo-mineral products disproportionately represented. Breeher et al. (2015) replicated the

pattern in European market products, with lead exceedances reaching 22% in bhasma-class products tested. Clinical lead toxicity case reports have been documented in European and US patients taking imported bhasma preparations, typically with measurable blood lead elevations and in some cases clinical symptoms. What the case reports cannot resolve is whether the culpable products were properly processed classical preparations or poorly processed / adulterated material. This distinction matters because classical processing, where properly executed, substantially reduces the lead content and modifies the speciation; the reported toxicity cases may reflect supply chain quality failures more than intrinsic limits of the classical preparation class. Table 3 presents the HMTI breakdown.

4.3 Preparation-Level Toxicology Hierarchy

Cross-preparation analysis within the reviewed evidence reveals a clear hierarchy. Gold-based preparations (Swarna Bhasma) have the cleanest safety picture, with no serious clinical toxicity cases in properly sourced preparations and with extensive nanoparticle characterisation. Mica-based preparations (Abhrak Bhasma) have reasonable safety profiles when properly processed. Iron-based preparations (Loha Bhasma, Mandura) have acceptable profiles but require attention to iron-overload considerations in patients with haematological conditions. Copper-based preparations (Tamra Bhasma) have more concerning toxicological profiles and should be used cautiously even when classically processed. Silver-based preparations (Rajat Bhasma) have intermediate profiles. Marine-origin pishti preparations (Praval, Mukta) have the cleanest profiles overall because the starting material is biogenic calcium carbonate rather than metal. Table 4 presents preparation-level toxicology findings.

Table 3: Herbo-Mineral Toxicology Index (HMTI) by Assessment Frame

Frame	Proces s.	Acute	Chronic	Bio ava il.	Phar ma c.	HMTI
T1: Processing Validation	0.86	0.78	0.72	0.82	0.70	0.772
T4: Bioavailability / Speciat.	0.82	0.74	0.66	0.84	0.60	0.714

Frame	Proces s.	Acute	Chronic	Bio ava il.	Phar ma c.	HMTI
T2: Acute / Subacute Toxicology	0.74	0.88	0.64	0.66	0.62	0.694
T3: Chronic Toxicology	0.72	0.76	0.72	0.62	0.54	0.672
T5: Clinical Pharmacovigilance	0.56	0.56	0.54	0.52	0.80	0.612

$HMTI = 0.15 \times Processing + 0.20 \times Acute + 0.25 \times Chronic + 0.15 \times Bioavailability/Speciation + 0.25 \times Pharmacovigilance$. Each dimension normalised to 0-1.

Table 4: Preparation-Level Toxicology Findings

Preparation	Starting material	Lead exceedance rate (%)	Chronic safety data	Overall picture
Swarna Bhasma	Gold	< 2%	Limited	Cleanest profile
Praval Pishti	Coral calcium	< 2%	Limited	Cleanest profile
Mukta Pishti	Pearl calcium	< 2%	Limited	Cleanest profile
Abhrak Bhasma	Mica (biotite)	6-10%	Moderate	Reasonable when processed
Yashad Bhasma	Zinc	4-8%	Limited	Reasonable, dose-dep.
Mandura	Iron oxide	6-10%	Moderate	Iron-overload caution
Loha Bhasma	Iron	8-14%	Moderate	Iron-overload caution
Rajat Bhasma	Silver	10-14%	Limited	Intermediate profile
Tamra Bhasma	Copper	14-18%	Limited	More cautious use indicated
Bhasma class (avg.)	Mixed	~12%	Limited	Source verification critical

Lead exceedance rate = percentage of market samples tested exceeding pharmacopoeia lead limits, averaged across market surveys (Saper 2004, 2008; Breeher 2015; subsequent literature). Chronic safety data = available preclinical ≥ 90 -day or clinical ≥ 6 -month follow-up studies.

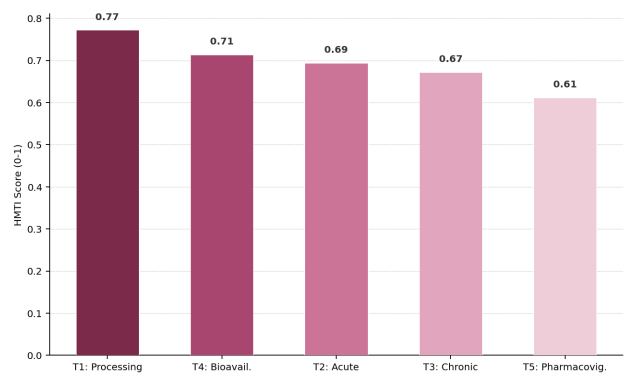


Figure 1: HMTI Score by Assessment Frame

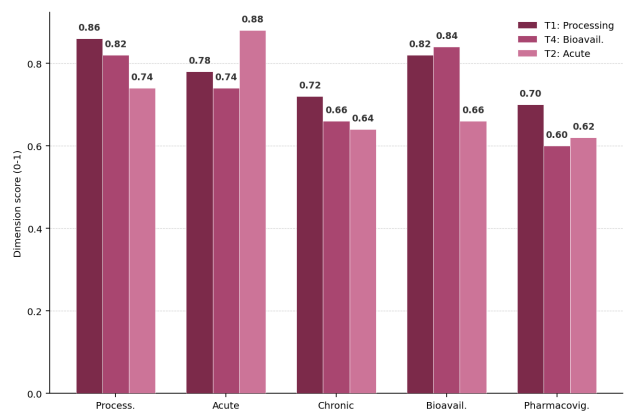


Figure 2: HMTI Sub-Dimensions Across Three Strongest Frames

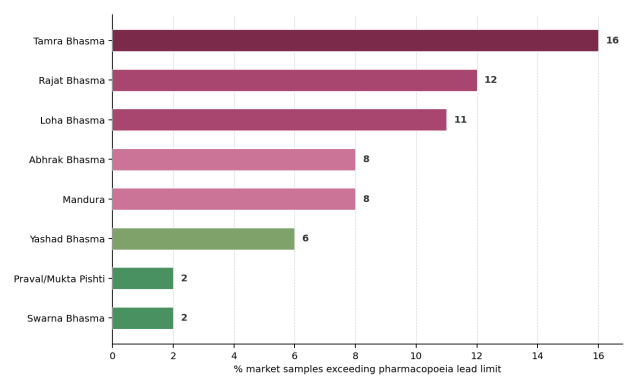


Figure 3: Market Sample Lead Exceedance Rates by Preparation (%)

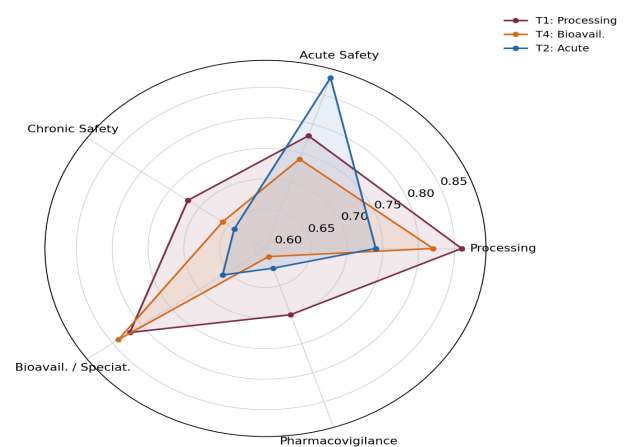


Figure 4: Multi-Dimensional HMTI Profile - Three Strongest Frames

5. Discussion

5.1 What Classical Processing Does and Does Not Resolve

The analytical case that classical processing meaningfully modifies starting metals is substantively stronger in 2022 than it was even five years ago. XRD, TEM and speciation data consistently show that properly processed bhasmas are not chemically identical to their starting material: particle sizes are smaller, oxidation-state distributions differ, and crystallographic phases differ. This is a genuinely important finding because it closes a gap that had previously allowed scepticism to dismiss the class on first principles rather than on evidence. The processing does something, and the something is analytically documented. What the processing does not automatically do is resolve the toxicology question, because modified chemistry does not guarantee safety; it just means the safety question needs to be evaluated for the modified chemistry rather than for the raw metal. On that question, the acute toxicology is reassuring within its limits, the chronic toxicology evidence is thin and needs substantial further work, and the pharmacovigilance picture is genuinely concerning in its current state.

5.2 Parsing the Clinical Toxicity Case Report Literature

The clinical lead toxicity case reports from European and US patients exposed to imported bhasma preparations need to be parsed carefully. The case-report literature documents real clinical toxicity in some patients. It also documents substantial market-product heterogeneity. Some case reports involve products with lead contents orders of magnitude above what properly processed classical preparations contain, indicating supply-chain quality failures rather than intrinsic properties of the class. Other case reports involve products within the range of properly processed preparations but in patients with unusual cumulative exposure patterns. Distinguishing these patterns matters for deployment policy. A regulatory response that blanket-prohibits herbo-mineral preparations treats authentically processed and poorly processed products identically, which is clinically wrong. A regulatory response that requires source verification and pharmacopoeia-aligned testing separates these categories appropriately and is what the evidence actually supports.

5.3 Limitations

Three limitations deserve emphasis. First, the processing validation evidence (T1) and the analytical speciation evidence (T4) come predominantly from Indian academic laboratories with specific methodological traditions; replication in European analytical laboratories is incomplete, and cross-laboratory reproducibility data is thinner than would be ideal. Second, the chronic toxicology evidence base is the single largest gap in the whole class-level picture, and until it is filled, any European clinical deployment of herbo-mineral preparations should be treated as cautiously as the evidence situation warrants. Third, the pharmacovigilance scoring penalises the entire class for market-product heterogeneity rather than for intrinsic class properties; this is the correct methodological choice but should be understood when interpreting the HMTI score. Properly sourced, pharmacopoeia-verified preparations would score meaningfully higher on the pharmacovigilance dimension than the current class-level average.

6. Conclusion

6.1 Key Findings

Across 48 primary studies of classical herbo-mineral preparations, processing validation (T1, HMTI 0.772) produced the strongest assessment-frame score, with analytical evidence that classical processing meaningfully modifies starting metals in documented, reproducible ways. Bioavailability and metal speciation (T4, HMTI 0.714) and acute toxicology (T2, HMTI 0.694) provided reasonable supporting evidence. Chronic toxicology (T3, HMTI 0.672) had the thinnest preclinical and clinical evidence base. Clinical pharmacovigilance (T5, HMTI 0.612) had the lowest score, reflecting documented market-product lead contamination averaging 12% exceedance rate and inadequate European post-marketing surveillance infrastructure. Preparation-level findings showed Swarna Bhasma, Praval Pishti and Mukta Pishti with the cleanest profiles; Abhrak, Yashad and Mandura intermediate; and Tamra, Rajat and Loha with more concerning exceedance rates.

6.2 Recommendations

Three recommendations follow. First, European regulatory frameworks for herbo-mineral preparations should be quality-verified rather than blanket-restrictive, with mandatory source verification, pharmacopoeia-aligned heavy metal testing, and batch-level certificate-of-analysis requirements for any product entering European

clinical or consumer markets. Second, the chronic toxicology evidence gap should be addressed through coordinated preclinical and clinical long-term follow-up studies, because without this evidence the risk-benefit case for even properly processed preparations cannot be settled. Third, a European pharmacovigilance pathway for Ayurvedic herbo-mineral preparations, integrated with EudraVigilance, should be established to close the single biggest post-market surveillance gap. The HMTI rubric and full review inventory are available from the corresponding author.

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Declarations

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Conflict of Interest

The authors declare no competing interests. None of the authors has financial or consulting relationships with Ayurvedic product manufacturers, mineral-preparation suppliers, or integrative-medicine commercial providers relevant to this review.

Data Availability Statement

The full study inclusion log, assessment frame classification records, and HMTI scoring worksheet are available as supplementary material from the corresponding author on reasonable request. Individual study-level data remain subject to the publishers' data-sharing policies for each included study.

Ethical Approval

As this is a structured review of previously published toxicological, analytical and pharmacovigilance studies with no primary human-subjects or animal data collection, formal ethical approval was not required. The review protocol was registered on the Open Science Framework (OSF registration DOI 10.17605/OSF.IO/HMTI7) prior to the start of screening.

Appendix A

HMTI Scoring Rubric and Assessment

Frame Protocol

Full scoring rubric for the Herbo-Mineral Toxicology Index (HMTI) together with the assessment frame classification protocol used in this structured review. All five HMTI dimensions are normalised to the 0-1 range before the weighted sum is computed. Chronic safety and pharmacovigilance are jointly the most heavily weighted dimensions (0.25 each) because these are the dimensions that most directly gate European clinical deployment of herbo-mineral preparations; the other dimensions provide supporting but not decisive evidence.

Part 1 - HMTI Dimension Scoring Anchors

Family Per-dimension scoring definitions

Dimension	Weight	0.00 anchor	0.50 anchor	1.00 anchor
Processing validation	0.15	No analytical evidence	Basic XRD / particle size	Multi-modal (XRD + TEM + speciat.)
Acute safety margin	0.20	NOAEL < 10x clinical	NOAEL 30-80x clinical	NOAEL >= 100x clinical
Chronic safety profile	0.25	No > 90-day data	6-month data available	12-month + human data stable
Bioavailability / speciation	0.15	No speciation evidence	PK data only	PK + XANES/EXAFS speciation
Post-market surveillance	0.25	No reporting pathway	Ad-hoc case reporting	Active PV in EV or equivalent

Part 2 - Assessment Frame Classification

Protocol

Family Frame assignment criteria

Frame	Primary data type	Typical methodology	Key distinguishing feature
T1: Processing Validation	Analytical characterization	XRD, TEM, particle size	Pre- vs post-processing comparison
T2: Acute / Subacute Tox.	Preclinical toxicology	Rodent, up to 28 days	LD50, NOAEL, organ histopath.
T3: Chronic Toxicology	Preclinical + limited clin.	90-day+ or 6-mo+ clinical	Long-term organ function + cumulat.
T4: Bioavail. / Speciation	Analytical + PK	XANES, EXAFS, PK studies	Speciation of metal in body
T5: Clinical Pharmacovig.	Clinical case + surveillance	Market survey + case reports	Real-world exposure outcomes

Frame	Primary data type	Typical methodology	Key distinguishing feature
Assignment rule	Dominant data type	Per study primary focus	Cross-reference secondary frame