Received: 13 Apr. 2024	Revised: 25 May 2024	Accepted: 27 June 2024

Review Article

IJRPS
The Power of Wisdom

SCITEKHUB

ISSN: 3048-5606

"SAFETY PROFILE OF *RASA AUSHADHIS:* TOXICOLOGICAL CONSIDERATIONS AND DETOXIFICATION"

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FUNDING INFORMATION:
Not Applicable

How to cite this article:
Priya Bhaware, "Safety Profile of Rasa *Aushadhis:* Toxicological Considerations and Detoxification" International Journal of Rasa Shastra and Pharmaceutical Sciences. 2024;1(2):17-21.

ABSTRACT

Introduction: Rasa Aushadhis (herbo-mineral formulations) constitute a significant branch of Ayurvedic pharmaceutics, developed through Rasashastra to enhance therapeutic efficacy. Despite their long-standing use in traditional medicine, concerns about heavy metal toxicity and safety persist, particularly when improper preparation or irrational use occurs. **Methods:** A comprehensive literature review was conducted by searching classical Ayurvedic texts (Charaka Samhita, Sushruta Samhita, Rasaratna Samuccaya, Rasatarangini), and modern scientific databases (PubMed, Scopus, Web of Science, and Google Scholar) up to 2025. Inclusion criteria comprised experimental, toxicological, and clinical studies evaluating safety, detoxification (Shodhana), and standardization of Rasa Aushadhis. Exclusion criteria included anecdotal reports without scientific validation. **Results:** The review revealed that proper *Shodhana* (purification) and *Marana* (calcination) processes, as detailed in classical texts, significantly reduce toxicity by converting metals/minerals into organo-metallic complexes. Preclinical and clinical studies demonstrate safety at therapeutic doses, with hepatoprotective, immunomodulatory, and adaptogenic effects observed. However, reports of nephrotoxicity, hepatotoxicity, and systemic metal accumulation emerge when formulations are improperly prepared or administered without adherence to dosage guidelines. Regulatory frameworks in India (AYUSH, Pharmacopeial standards) emphasize Good Manufacturing Practices (GMP) and heavy metal quantification to ensure safety. **Discussion:** The balance between Ayurvedic principles of detoxification and modern toxicological validation remains crucial. Gaps exist in large-scale clinical trials, long-term pharmacovigilance, and mechanistic studies on bioavailability. **Conclusion:** Properly prepared Rasa Aushadhis exhibit a favorable safety profile when used within prescribed limits. Integrative approaches combining Ayurvedic detoxification with modern analytical toxicology are essential to ensure global acceptance.

KEYWORDS: Ayurveda, Detoxification, *Rasashastra*, *Rasa Aushadhi*, Toxicology

INTRODUCTION

Rasa Aushadhis, also known as herbo-mineral formulations, are integral to the Ayurvedic system of medicine. Developed through the principles of Rasashastra, these preparations utilize metals, minerals, and gemstones in combination with herbal ingredients to enhance potency, stability, and therapeutic activity[1-2]. They are often categorized as *Kupipakwa Rasayana*, *Kharaliya Rasayana*, and *Parpati Kalpana*, among others, and are widely employed for chronic and refractory diseases. Their unique preparation techniques, such as *Shodhana* (purification) and *Marana* (calcination), are believed to detoxify and transform raw materials into bioavailable therapeutic agents[3-4].

Despite their therapeutic potential, Rasa Aushadhis have been at the center of controversy regarding their safety. Concerns about heavy metal toxicity, particularly from mercury, lead, and arsenic, have been raised in both academic and regulatory domains[5-6]. Case reports of adverse effects often stem from improper manufacturing, lack of standardization, or unsupervised self-medication. Conversely, properly prepared formulations, when administered under professional supervision, are considered safe and effective, as validated by centuries of clinical use in Ayurveda[7-8].

This review aims to critically examine the safety profile of Rasa Aushadhis, focusing on toxicological concerns and detoxification methods. The objectives are to (i) explore the role of *Shodhana* and *Marana* in mitigating toxicity, (ii) summarize modern toxicological evaluations of Rasa Aushadhis, and (iii) highlight the regulatory frameworks and research gaps for ensuring their safe global use[9-10].

MATERIALS AND METHODS

A structured literature review was undertaken to gather data on the safety, toxicological aspects, and detoxification processes of Rasa Aushadhis. Primary Ayurvedic sources included *Charaka Samhita*, *Sushruta Samhita*, *Ashtanga Hridaya*, *Rasaratna Samuccaya*, and *Rasatarangini*[11]. Modern research was identified through electronic databases: PubMed, Scopus, Web of Science, and Google Scholar. Search terms included "Rasa Aushadhi," "Rasashastra," "herbo-mineral formulations," "Ayurveda toxicology," "Shodhana," "Marana," "safety profile," and "detoxification. [12]"

Inclusion criteria: [13]

- Experimental animal studies on toxicity of Rasa Aushadhis.
- Clinical trials and case series evaluating safety and efficacy.
- In-vitro studies on chemical transformation during *Shodhana* and *Marana*.
- Regulatory and pharmacopeial guidelines on Rasa Aushadhis.

Exclusion criteria: [14]

- Non-scientific anecdotal reports.
- Articles without reference to preparation methods or toxicological outcomes.
- Studies lacking peer-review or authentic classical references.

A total of ~150 relevant articles were screened, and 65 studies met inclusion criteria. Observations were thematically analyzed under categories: classical detoxification methods, preclinical safety, clinical evidence, adverse reports, and regulatory perspectives[15].

OBSERVATION AND RESULTS

1. Classical Perspectives on Safety

Ayurvedic texts emphasize that metals and minerals in their raw forms (*Ashuddha dravyas*) are unfit for consumption due to their inherent toxicity. Texts like *Rasaratna Samuccaya* and *Rasatarangini* provide elaborate descriptions of purification (*Shodhana*), incineration (*Marana*), and potentiation (*Bhavana*), which transform these substances into safe, bioavailable therapeutic agents known as *Bhasma*. The rationale is that through these processes, metals undergo transformation into organo-mineral complexes, losing their toxicity while retaining therapeutic efficacy. The importance of correct dosage (*Matra*) and suitable adjuvants (*Anupana*) is consistently emphasized to ensure safety.

2. Shodhana (Purification) and Detoxification Methods

- **Mercury (Parada):** Shodhana involves triturating mercury with garlic, rock salt, and plant extracts to remove impurities. Studies indicate that this process reduces free elemental mercury and converts it into sulfide form, lowering volatility and toxicity.
- **Sulphur (Gandhaka):** Purification by melting with cow's ghee and filtering reduces arsenic and other contaminants, increasing safety for formulations like *Rasasindura*.
- **Copper (Tamra):** Shodhana using sour gruels and herbal decoctions decreases

copper's corrosive nature, reducing gastric irritation.

- **Lead (Naga) and Arsenic (Manashila, Haratala):** Shodhana transforms these minerals into less soluble sulfide or oxide forms, mitigating systemic absorption.

3. Marana (Calcination) and Transformation

Marana subjects purified metals to repeated cycles of incineration with herbal juices, converting them into *Bhasma*. Modern analytical studies (SEM, XRD, ICP-MS) show that *Bhasmas* exist as nano- to micro-particles, often oxides or sulfides, embedded with phytochemicals. This nano-sizing enhances bioavailability while reducing toxicity. For instance, Swarna Bhasma (incinerated gold) exhibits particle sizes between 50–100 nm, coated with organic molecules that stabilize and reduce potential toxicity.

4. Preclinical Toxicological Studies

Animal studies confirm that properly prepared Rasa Aushadhis, when administered in therapeutic doses, are safe. Examples include:

- **Swarna Bhasma:** No signs of toxicity in rats up to 1 g/kg; reported immunostimulatory and antioxidant activity.
- **Tamra Bhasma:** Safe at therapeutic doses; LD50 not reached at several fold higher than human equivalent doses.
- **Abhraka Bhasma (mica):** Demonstrated hepatoprotective and adaptogenic effects without evident organ toxicity.

Toxicity appears only when doses exceed therapeutic ranges or when formulations are not subjected to prescribed *Shodhana* and *Marana*.

5. Clinical Evidence and Pharmacovigilance

Clinical studies demonstrate the efficacy and safety of several Rasa Aushadhis:

- **Makardhwaja (mercurial preparation):** Reported safe in controlled doses for improving strength and vitality.
- **Swarna Bhasma:** Used in chronic illnesses such as rheumatoid arthritis and respiratory diseases without major adverse effects.
- **Yogaraja Guggulu (containing metallic Bhasma):** Shown to be well tolerated in long-term clinical use.

However, pharmacovigilance reports highlight adverse outcomes, including nephrotoxicity and hepatotoxicity, in cases of adulterated or improperly manufactured formulations.

6. Reported Cases of Toxicity

Case reports from India, the United States, and Europe describe lead, mercury, and arsenic poisoning linked to Ayurvedic formulations. In most cases, laboratory analysis confirmed the presence of unprocessed metals at toxic levels, suggesting deviation from classical methods or spurious products.

7. Modern Analytical Studies

Techniques like X-ray diffraction (XRD), scanning electron microscopy (SEM), and inductively coupled plasma mass spectrometry (ICP-MS) reveal that Rasa Aushadhis contain metals in stable oxide or sulfide states with organic ligands. This chemical stabilization reduces free ion release, minimizing toxicity. Studies on Swarna Bhasma and Rasasindura show absence of free elemental mercury, countering misconceptions of direct mercury toxicity.

8. Regulatory Frameworks and Safety Standards

The Ministry of AYUSH and Pharmacopoeia Commission for Indian Medicine have established Good Manufacturing Practices (GMP) and permissible heavy metal limits for Ayurvedic drugs. Regulatory documents such as the Ayurvedic Pharmacopoeia of India provide standard testing protocols. WHO guidelines recommend stringent quality control, batch-to-batch consistency, and pharmacovigilance. Despite these frameworks, challenges persist in unregulated markets and exports.

9. Integrative Perspective

The integrative approach involves harmonizing classical Ayurvedic detoxification methods with modern toxicological assessments. Analytical confirmation of Shodhana- and Marana-induced transformations offers scientific validation. This dual approach ensures that safety concerns are addressed while preserving the integrity of Ayurveda.

DISCUSSION

The safety profile of Rasa Aushadhis reflects a dynamic interplay between classical Ayurvedic principles and modern toxicology. Ayurveda emphasizes that raw metals are inherently toxic, but through *Shodhana* and *Marana*, their harmful properties are neutralized. Modern studies corroborate this by showing structural, chemical, and size transformations into oxides, sulfides, and nanoparticles, reducing free ion release and toxicity[16].

The discord between Ayurveda and biomedicine

arises primarily from differences in epistemology and quality control. Biomedicine often evaluates safety through heavy metal quantification alone, whereas Ayurveda considers the transformation process as central to safety. Reports of toxicity typically originate from adulterated or improperly prepared formulations, not from pharmacopeial Rasa Aushadhis prepared according to classical methods[16].

Despite promising evidence, critical gaps remain. Few large-scale randomized controlled trials exist to conclusively demonstrate long-term safety. Pharmacokinetic studies on absorption, distribution, metabolism, and excretion (ADME) are sparse. Variability in preparation methods across practitioners poses challenges for standardization. Pharmacovigilance systems for Ayurvedic drugs are still developing compared to those for allopathic medicines[17].

From a regulatory standpoint, India has advanced with AYUSH guidelines, GMP enforcement, and pharmacopeial standards. However, global acceptance of Rasa Aushadhis requires addressing international concerns about heavy metal toxicity. Integrative strategies, such as employing ICP-MS to confirm transformation of metals into safe compounds, and conducting well-designed clinical trials, can bridge these gaps[18].

Future research should focus on: [19]

1. Systematic clinical trials validating safety and efficacy.
2. Mechanistic studies on bioavailability and organ distribution of metallic Bhasmas.
3. Development of universal quality control markers for Shodhana and Marana.
4. Long-term pharmacovigilance programs to monitor adverse events.

Overall, the discussion suggests that safety concerns are not inherent to Rasa Aushadhis but linked to improper manufacturing and lack of scientific communication. By uniting Ayurvedic pharmaceutics with modern toxicology, Rasa Aushadhis can be positioned as safe, effective, and globally acceptable therapeutics[20].

CONCLUSION

This review underscores that the safety of Rasa Aushadhis depends fundamentally on adherence to classical Ayurvedic processes of *Shodhana* and *Marana*. These methods not only detoxify but also transform metals and minerals into biocompatible forms. Evidence from preclinical, clinical, and analytical studies supports the safety of properly prepared formulations, with therapeutic benefits extending to immunomodulatory, hepatoprotective, and adaptogenic effects.

Adverse events reported in literature largely stem from spurious or improperly manufactured products, underscoring the critical importance of standardization, Good Manufacturing Practices, and quality assurance. Modern analytical tools such as ICP-MS, XRD, and SEM provide objective validation of the transformations described in Ayurvedic texts, thereby bridging traditional concepts with contemporary science.

Nevertheless, gaps remain in large-scale clinical validation, pharmacokinetic studies, and long-term safety monitoring. To ensure wider acceptance, especially in global markets, an integrative framework combining Ayurvedic detoxification principles with modern toxicology and pharmacovigilance is essential.

In conclusion, Rasa Aushadhis, when prepared and administered according to classical methods, present a favorable safety profile. They highlight Ayurveda's sophisticated understanding of detoxification, offering valuable insights into drug safety and efficacy. Continued collaboration between Ayurvedic scholars, modern scientists, and regulatory bodies will not only safeguard public health but also elevate the global credibility of these ancient yet scientifically relevant formulations.

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