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Ayurvedic Bhasma as Bio-Engineered Nanomedicine: A Critical Review of Classical Synthesis Protocols and Modern Characterisation

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Abstract

The field of modern nanomedicine faces significant challenges regarding the stability, biocompatibility, and cost-effective synthesis of metallic nanoparticles. Distinct from these recent developments, *Rasashastra* (Ayurvedic pharmaceutics) employs established, sophisticated protocols for converting metals and minerals into therapeutic, bio-assimilable nanoparticles known as *Bhasma*.

This review aims to bridge the gap between classical Ayurvedic pharmaceutics and modern nanomedicine by analysing the *Bhasmikarana* process—currently employed in GMP-certified manufacturing—through the lens of contemporary nanotechnology.

We critically examine the current Standard Operating Procedures (SOPs) of *Bhasma* synthesis: *Shodhana* (purification/ detoxification), *Bhavana* (wet trituration with herbal juices), and *Marana* (incineration/calcination). These processes are evaluated against modern concepts of Top-down nanofabrication, surface functionalisation, and quantum confinement.

Evidence from modern characterisation techniques, including Transmission Electron Microscopy (TEM), Scanning Electron Microscopy (SEM), and X-ray Diffraction (XRD), confirms that properly processed *Bhasma* comprises nanoparticles in the range of 10–100 nm. The unique process of *Bhavana* acts as a bio-functionalisation step, coating the metallic core with organic ligands to enhance biocompatibility and target-specific delivery.

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Ayurvedic *Bhasma* represents a sophisticated, time-tested form of bio-nanomedicine. Understanding these classical SOPs offers a blueprint for the development of novel, safe nanotherapeutics, validating the concept of "Reverse Pharmacology" in precision medicine.

Key words : Nanomedicine; Ayurveda; Bhasma; Green Synthesis; Bioavailability; *Rasashastra*; Metallic Nanoparticles.

Nanotechnology has emerged as a transformative frontier in modern medicine, offering precision tools for diagnosis, drug delivery, and therapy. By manipulating matter at the atomic and molecular scale (1–100 nm), nanomedicine aims to overcome the limitations of conventional pharmaceuticals, such as poor solubility, low bioavailability, and non-specific distribution[2]. In particular, metallic nanoparticles (MNPs) like gold, silver, and iron have garnered immense attention for their unique physicochemical properties and therapeutic potential.

However, the modern synthesis of MNPs is often fraught with challenges. Chemical synthesis methods frequently utilise toxic reducing agents and organic solvents, leading to environmental hazards and biocompatibility issues. Physical methods, while cleaner, are often energy-intensive and costly to scale. Consequently, there is a growing demand for "Green Synthesis" methods that are eco-friendly, cost-effective, and biologically safe[8].

In this context, it is imperative to examine *Rasashastra*, the iatrochemistry branch of Ayurveda. Far from being an obsolete practice, *Rasashastra* utilises rigorous, standardised protocols to transform heavy metals and minerals into safe, therapeutic agents known as *Bhasma*. These preparations are not merely coarse powders but are complex, bio-engineered nanostructures. The production of *Bhasma* follows strict Standard Operating Procedures (SOPs) described in classical texts (*Rasa Granthas*) and currently regulated by pharmacopoeial standards. The process, known as *Bhasmi-karana*, involves elaborate steps of purification (*Shodhana*), levigation with herbal juices (*Bhavana*), and calcination (*Marana*). When analysed through the prism of modern science, these steps parallel the principles of Top-down nanofabrication (particle size reduction) and Bottom-up synthesis (self-assembly during heating)[3].

Despite the widespread clinical use of *Bhasma* in the Indian subcontinent, it is frequently viewed with scepticism by the global scientific community due to concerns over heavy metal toxicity. This review posits that such concerns often stem from a lack of understanding of the precise manufacturing SOPs that detoxify the raw materials.

This article reviews the classical Ayurvedic method of *Bhasma* synthesis as a sophisticated bio-nanotechnology. We correlate the classical SOPs with modern physicochemical changes, citing evidence from electron microscopy and diffraction studies. By decoding the *Bhasmikarana* process, we demonstrate that Ayurvedic pharmaceutics offers a validated,

"time-tested" model for the safe engineering of metallic nanomedicines.

The Ayurvedic Bio-Nanofabrication Protocol: A Process Engineering Perspective :

The synthesis of *Bhasma*, termed *Bhasmikarana*, is a sophisticated, multi-stage pharmaceutical process. Unlike conventional chemical synthesis which often relies on a single reaction step, *Bhasmikarana* employs a cyclical combination of physical degradation and thermal transformation. From a modern materials science perspective, this methodology integrates both "Top-down" (breaking down bulk material) and "Bottom-up" (self-assembly of nanoparticles) approaches.

The standard operating procedures (SOPs) for this synthesis are rigorously defined in classical texts such as *Rasaratna Samuccaya* and are currently adhered to under Good Manufacturing Practices (GMP). The process comprises three principal unit operations: *Shodhana*, *Bhavana*, and *Marana*.

Table-1. The Bhasmikarana Process (Classical Operations and Modern Equivalents) (Chaudhary *et al*., 2019; Galib *et al*., 2010; Singh *et al*., 2023)

Classical Stage	Standard Operating Procedure	Modern Scientific Equivalent
Shodhana (Pre-treatment)	Repeated heating of metal to red-hot temperatures and quenching in liquid media.	Induces thermal shock and micro-cracks, reducing tensile strength. Removes impurities and initiates surface activation.
Bhavana (Wet Trituration)	Wet grinding of purified metal with herbal juices or decoctions until dough-like.	Achieves "Top-down" sub-micron particle size reduction. Phytochemicals act as natural capping agents for surface functionalisation.
Marana (Calcination)	Pellets are sealed in crucibles and subjected to repeated, controlled heating and cooling cycles.	Converts metals into stable, biocompatible oxides/sulfides. Prevents crystal growth, ensuring nanoscale re-crystallisation and elimination of free metal.

Classical Quality Control vs Modern Characterisation :

Ayurveda prescribes specific end-point tests (*Siddhi Lakshana*) to ensure the *Bhasma* is fully formed.

- **Varitaratva:** The ability of the *Bhasma* to float on stagnant water, indicating high surface tension and low density characteristic of nanoparticles.
- **Rekhapurnatva:** The ability of the powder to enter the furrows of a finger, indicating a particle size effectively in the sub-micron to nanometre range.
- **Apunarbhava:** Irreversibility; the *Bhasma* should not revert to its metallic state even when heated with reducing agents, confirming thermodynamic stability.

Physicochemical Characterisation: Decoding the Nanostructure :

The transformation of macroscopic metal into therapeutic *Bhasma* is not merely a reduction in size but a fundamental alteration of its physicochemical identity. Modern analytical techniques provide compelling evidence that *Bhasma* exhibits the hallmarks of engineered nanoparticles, including quantum confinement effects, high surface-to-volume ratios, and unique crystalline phases.

1. Particle Size and Morphology (TEM/ SEM Analysis) :

Electron microscopy serves as the definitive validation of *Bhasma* as a nanomedicine.

- **Transmission Electron Microscopy (TEM):** Multiple studies on *Swarna Bhasma* (Gold), *Rajat Bhasma* (Silver), and *Lauha Bhasma* (Iron) consistently reveal particle sizes in the range of **10–50 nm**[5]. These nanoparticles are typically globular or sub-spherical, often embedded within a larger organic matrix derived from the herbal media used in *Bhavana*.
- **Scanning Electron Microscopy (SEM):** SEM analysis further elucidates the surface morphology, showing agglomerates of nanoparticles with a highly porous structure. This porosity is critical for drug delivery, as it increases the specific surface area available for interaction with biological membranes.
- **Correlation:** The classical test *Rekhapurnatva* directly correlates with this sub-micron particle size.

2. Crystalline Structure and Phase Identification (XRD) :

X-Ray Diffraction (XRD) is essential for confirming that the toxic metallic state has been converted into a biocompatible compound.

- **Phase Transformation :** XRD patterns of finished *Bhasma* typically show sharp, distinct peaks corresponding to stable oxides or sulfides, rather than pure metal. For instance, *Lauha Bhasma* is identified as a mixture of α-Fe_2O_3 (Hematite) and Fe_3O_4 (Magnetite), while *Swarna Bhasma* appears as metallic gold (Au) nanocrystals[1].
- **Crystallite Size:** Applying the Scherrer equation to the XRD line broadening confirms the crystallite size to be in the nanometre regime (often <30 nm), corroborating the TEM data.

3. Surface Chemistry and Stability (Zeta Potential & FTIR) :

The stability and biological interaction of nanoparticles are governed by their surface charge and functional groups.

- **Zeta Potential:** *Bhasma* particles generally exhibit a significant negative Zeta potential (often < -25 mV). This high surface charge provides electrostatic repulsion between particles, preventing aggregation and ensuring long-term stability in colloidal suspension.
- **Fourier Transform Infrared Spectroscopy (FTIR):** FTIR analysis reveals the presence of organic functional groups (*e.g.*, -OH, -COOH, -NH) on the surface of the inorganic nanoparticles. These

groups originate from the herbal juices used in *Bhavana*.

- **Bio-Functionalisation:** This organic coating acts as a "biocompatible stealth layer," potentially reducing immune clearance and facilitating cellular uptake. This mirrors the modern concept of "surface functionalisation" or "PEGylation" used to enhance the circulation time of nanodrugs[2].

Safety, Toxicity, and Biocompatibility: Addressing the Heavy Metal Concern :

The most significant barrier to the global acceptance of *Bhasma* is the apprehension regarding heavy metal toxicity. Conventional toxicology posits that elements such as Lead (Pb), Mercury (Hg), and Arsenic (As) are inherently toxic. However, nanomedicine operates on the principle that the biological activity of a material is dictated not just by its elemental composition, but by its size, surface chemistry, and crystalline structure (speciation).

1. The Concept of Ama vs. Pakwa Bhasma:

Ayurveda explicitly acknowledges the toxicity of raw metals (*Ama* or "uncooked" state). The entire *Bhasmikarana* process is essentially a detoxification protocol designed to convert the toxic metal into a biocompatible, therapeutic form (*Pakwa* or "cooked" state).

- **Mercury (Parada):** Through *Kajjali* formation with Sulphur, Mercury loses its volatility and systemic toxicity, transforming into stable HgS (Cinnabar-like structure), which is historically far less bio-accessible than $HgCl_2$.
- **Arsenic (Gauripashana):** Arsenicals are processed into specific crystalline forms (*e.g.*, Realgar AS_2O_3) that have been shown to induce apoptosis in cancer cells without the systemic toxicity associated with arsenic trioxide.

2. In Vivo Toxicity Studies (LD_{50} *and Chronic Toxicity) :*

Modern toxicological studies provide empirical support for the safety of properly processed *Bhasma*.

- **Acute Toxicity:** Numerous studies following OECD guidelines (*e.g.*, OECD 420/423) have demonstrated that the LD_{50} of standard *Bhasmas* (like *Swarna*, *Rajat*, *Lauha*) is typically **>2000 mg/kg** body weight in rodent models, classifying them as "Category 5" or "Unclassified" (lowest toxicity) under GHS standards[7].
- **Chronic Toxicity:** Long-term studies (90 days to 6 months) at therapeutic doses often reveal no significant histopathological damage to the liver, kidney, or brain.
- **Genotoxicity:** Comet assays and chromosomal aberration tests on specific *Bhasmas* (*e.g.*, *Swarna Bhasma*) have largely shown a lack of genotoxicity at therapeutic concentrations.

3. The Hormetic Effect :

The therapeutic action of *Bhasma* can be understood through the lens of **Hormesis**—the phenomenon where a substance that is toxic at high doses induces a beneficial, adaptive response at low, sub-toxic doses. *Bhasma* acts

as a mild stressor, upregulating cellular defence mechanisms (*e.g.*, Metallothioneins) and immune modulation, thereby restoring homeostasis.

Outcome and Future Perspectives :

The synthesis of Ayurvedic *Bhasma* is not an archaic ritual but a sophisticated, multi-step bio-nanofabrication protocol that anticipated the principles of modern nano-technology by centuries. The classical processes of *Shodhana*, *Bhavana*, and *Marana* effectively achieve Top-down particle size reduction, surface bio-functionalisation, and Bottom-up crystalline stabilization.

From 'Bedside to Bench': The Path Forward:

This review validates the concept of **Reverse Pharmacology**. Rather than relying solely on high-throughput screening of new synthetic molecules, modern science should look to these time-tested "Clinical Nanomedicines." By applying advanced characterisation tools to standardised *Bhasmas*, researchers can uncover novel mechanisms of action, particularly in the fields of oncology, immunomodulation, and chronic disease management.

Furthermore, the "Green Synthesis" nature of *Bhasma*—utilising plant extracts instead of toxic chemical reducing agents—offers a sustainable model for the future of pharma-ceutical manufacturing. We propose that regulatory bodies and the scientific community should view *Bhasma* not merely as "alternative medicine," but as a legitimate branch of **Precision Nanomedicine** that requires a dedicated regulatory framework harmonising classical wisdom with rigorous modern safety standards.

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