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"ARE *BHASMAS* NANOMEDICINES? A CRITICAL REVIEW OF THE PHYSICOCHEMICAL CHARACTERISATION EVIDENCE"

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ABSTRACT

Background: *Bhasmas*, the calcined metal and mineral preparations of *Rasa Shastra*, are now widely described as "ancient nanomedicines". The claim is attractive, but it rests on characterisation data of uneven quality and on terms that are often used loosely. **Objective:** To examine what the published physicochemical evidence actually shows about particle size in *bhasmas*, and whether it supports the nanomedicine label. **Methods:** A critical narrative review of characterisation studies on metal, mineral and marine *bhasmas* and herbo-mineral formulations, interpreted against current nanomaterial definitions and the known limits of each analytical technique. **Results:** Most studies report nanometre-scale crystallite domains, usually from Scherrer analysis of X-ray diffraction peaks, while electron microscopy, laser diffraction and dynamic light scattering show that these domains are held in sub-micron to micron-sized aggregates. Representative examples include Swarna *bhasma* with 28 nm crystallites but hydrodynamic diameters of about 670–720 nm, Naga *bhasma* with 60 nm lead sulphide crystallites in sub-micron agglomerates, and Swarna Makshika *bhasma* with particles of 1–2 µm. Number-based size distributions, which current regulatory definitions require, are almost never reported. Commercial Suvarna *bhasma* samples differ widely in gold content (32–98 wt%), surface area and in vivo bioaccumulation. **Conclusion:** Crystallite size is not particle size. The evidence supports describing many *bhasmas* as nanostructured, micron-scale materials rather than as nanoparticle suspensions. A minimum reporting standard combining several orthogonal techniques is proposed.

KEYWORDS: *Bhasma*; *Rasa Shastra*; Nanomedicine; Particle size; X-ray diffraction; Characterisation

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INTRODUCTION

Rasa Shastra, the pharmaceutical science of metals and minerals in Ayurveda, converts metals such as gold, silver, copper, iron, zinc and lead, minerals such as mica and chalcopyrite, and marine materials such as pearl and conch into fine, non-lustrous powders called *bhasmas*. The conversion runs through *shodhana* (purification), *bhavana* (trituration with herbal juices or decoctions) and repeated *puta* (calcination cycles). Classical texts describe the end-point through organoleptic and physical tests: *rekhapurnatva* (the powder fills the lines of the fingers), *varitaratva* (it floats on water), *nishchandratva* (it has no metallic lustre) and *apunarbhava* (it does not revert to the metal)[1].

Over the last two decades these traditional quality tests have been read in the language of nanotechnology. Several reviews describe *bhasmas* as "the ancient Indian nanomedicine" and attribute their low doses, rapid action and claimed safety to nanoscale particle size[1-3]. The same framing now appears in proposals for new indications, including antiviral and anticancer uses[4-6].

The nanomedicine framing matters for three reasons. Scientifically, a claim about size has to be backed by the right measurement, because different techniques measure different things. Clinically, nanoscale size changes how a material is absorbed and distributed, so the claim has safety consequences as well as efficacy ones. Regulators increasingly treat nanomaterials as a separate category with their own data requirements[7]. A loose "nano" label can therefore expose *Rasaushadhi* to scrutiny that the underlying data cannot withstand.

This review asks a narrow question: what does the published physicochemical evidence actually show about the size of *bhasma* particles, and does it support the nanomedicine label? It then proposes a minimum characterisation standard for future studies.

METHODS OF THE REVIEW

This is a critical narrative review. Literature was identified through PubMed, PubMed Central, Crossref-indexed journal records and the Directory of Open Access Journals, using combinations of the terms *bhasma*, *Rasaushadhi*, herbo-mineral, nanoparticle, nanocrystalline, X-ray diffraction, scanning electron microscopy, transmission electron microscopy, dynamic light scattering and particle size. Reference lists of retrieved reviews were screened for further primary studies. Studies were included when they reported at least one instrumental measurement of particle or crystallite size on a *bhasma* or a *bhasma*-based formulation. Each study was then read against two benchmarks: the measurand of each technique (what it actually measures) and the current regulatory definition of a nanomaterial[7,8]. No quantitative pooling was attempted, because the studies used different materials, methods and reporting formats.

WHAT COUNTS AS A NANOMATERIAL?

The European Commission's 2022 recommendation, the most widely cited regulatory definition, defines a nanomaterial as a natural, incidental or manufactured material consisting of solid particles, present on their own or as identifiable constituent particles in aggregates or agglomerates, where 50% or more of the particles in the number-based size distribution have at least one external dimension between 1 and 100 nm[7]. Three features of this definition are important for *bhasmas*.

- The criterion is **number-based**. A size distribution weighted by intensity (as in dynamic light scattering) or by volume (as in laser diffraction) cannot by itself show that the threshold is met.
- The criterion concerns **external dimensions of particles**, including identifiable constituent particles inside aggregates. It does not concern internal crystal domains.
- The definition is **descriptive, not evaluative**. Meeting it does not make a material safe or effective. It simply identifies materials for which nanospecific data may be needed.

WHAT EACH TECHNIQUE MEASURES

Most of the disagreement about *bhasma* size comes from treating results from different techniques as if they measured the same quantity. Table 1 summarises the measurand and main limitation of each technique in common use.

DLS, dynamic light scattering; EDX, energy-dispersive X-ray spectroscopy; ICP-OES/MS, inductively coupled plasma optical emission/mass spectrometry; AAS, atomic absorption spectroscopy.

The distinction between crystallite size and particle size is the single most important point. The Scherrer equation relates the broadening of a diffraction peak to the size of the crystal domains that diffract coherently. A one-micron particle made of many 30 nm

crystallites will give a Scherrer value of about 30 nm. XRD therefore shows that a material is nanocrystalline, which is a statement about its internal structure, not that it consists of nanoparticles.

Dynamic light scattering has the opposite bias. It reports the hydrodynamic diameter of particles diffusing in a liquid, and because scattered intensity rises steeply with particle size, a small number of large aggregates can dominate the result. For broad or multimodal samples, the polydispersity index becomes high and the mean diameter is hard to interpret[8]. Zeta potential, often reported alongside DLS, describes the electrokinetic potential at the slipping plane and does not by itself predict colloidal stability[8]. Electron microscopy can resolve individual primary particles, but unless several hundred particles are counted from representative fields, it gives an impression rather than a distribution.

WHAT THE PUBLISHED STUDIES SHOW

Table 2 brings together representative characterisation studies across the main groups of bhasmas. The pattern is consistent: nanometre-scale crystallites, organised into sub-micron or micron-sized particles and aggregates.

Table 1. Analytical techniques used to characterise *bhasmas*.

Technique	What it measures	Common misreading in *bhasma* studies
X-ray diffraction (XRD) with Scherrer analysis	Mean size of coherently diffracting crystal domains (crystallite size), plus phase identity	Crystallite size is reported as "particle size"; one particle can contain many crystallites
Scanning electron microscopy (SEM)	Surface morphology and apparent size of particles and aggregates in a small field of view	Size of a few selected particles generalised to the whole sample; no number-based distribution
Transmission electron microscopy (TEM)	Projected size and shape of primary particles at high resolution	Small, non-representative fields; sample preparation can break or create aggregates
Dynamic light scattering (DLS)	Intensity-weighted hydrodynamic diameter of particles moving in liquid	Intensity weighting favours large particles; unreliable for broad, polydisperse powders
Laser diffraction	Volume-weighted size distribution, typically from about 0.1 µm upwards	Insensitive to the nanoscale fraction; often not reported at all
Energy-dispersive X-ray analysis (EDAX/EDX)	Semi-quantitative surface elemental composition	Treated as bulk composition; light elements and organic carbon poorly quantified
ICP-OES, ICP-MS, AAS	Bulk elemental content after digestion	Rarely linked to the size fraction that is absorbed

Table 2. Representative characterisation findings for *bhasmas* and *bhasma*-based formulations

Material	Techniques	Key size findings	Main phase or composition
Swarna *bhasma* (gold), two batches	DLS, XRD, SEM-EDAX	Crystallite size 28 nm (Scherrer); mean hydrodynamic diameter 669 and 717 nm; zeta potential about −17 mV	Metallic gold, about 90% Au by EDAX
Swarna *bhasma*, commercial	SEM, DLS, XRD, ICP-MS	Crystallites about 60 nm; aggregates with mean DLS diameter about 4.7 µm	Metallic gold
Suvarna *bhasma*, five manufacturers	XRD, TEM/SEM, BET, ICP-AES	Marked differences in surface area and morphology between products	Gold 32–98 wt%; one product with 5.4 wt% arsenic

Naga *bhasma* (lead)	XRD, TEM, EDAX, FTIR, AAS	Crystallite size 60 ± 4 nm; spongy sub-micron agglomerates on TEM	Lead sulphide (PbS), no lead oxide detected
Swarna Makshika *bhasma* (chalcopyrite)	XRD, SEM	Particle size reduced from 6–8 µm (raw) to 1–2 µm (*bhasma*)	Fe_2O_3, FeS_2, CuS, SiO_2
Mukta *bhasma* (pearl), three batches	XRD, SEM, EDAX	Particles 79.9–279.2 nm on SEM (raw pearl 214.7–718.7 nm)	Aragonite converted to calcite, minor portlandite
Shankha *bhasma* (conch)	Particle size, XRD, SEM, TGA, FTIR	Particle size reported as a measured parameter; nacre organic matrix absent	Aragonite converted to calcite
Hridayarnava Rasa (*kajjali* + Tamra *bhasma*)	XRD, FEG-SEM, EDAX, ICP-AES, laser diffraction, TGA/DSC	Crystallite aggregates 100–1000 nm on SEM; 50% of material below 16.4 µm	CuS, HgS, free sulphur

1. Gold (*Swarna*) *bhasma*

Gold *bhasma* is the best-studied example and illustrates the gap between crystallite and particle size most clearly. Paul and Sharma characterised two batches of Swarna *bhasma*: Scherrer analysis gave a gold crystallite size of 28 nm for both, while DLS gave mean diameters of 717 and 669 nm, and EDAX indicated about 90% gold[9]. Beaudet and colleagues compared commercial Swarna *bhasma* with citrate-capped gold nanoparticles of about 32 nm. The *bhasma* contained crystallites of about 60 nm, but these formed aggregates with a mean DLS diameter of about 4.7 µm. Only after mechanical and ultrasonic breakdown did a 100–200 nm fraction behave like synthetic nanoparticles inside cells[10]. Patil-Bhole and colleagues described the gold in Swarna *bhasma* as nanostructured[17], and characterisation of a Suvarna *bhasma* prepared with mercury (*Parada marit*) has also been reported[18]. Earlier work focused on chemical constituents and antioxidant activity[19], and on the broader place of gold in pharmacy[20,21].

Taken together, these studies show that gold *bhasma* contains nanoscale gold crystallites, but that in the form administered most of the material is in sub-micron or micron-sized aggregates. Whether these aggregates break down in the gut, and to what extent, has not been measured.

2. Lead and copper-containing *bhasmas*

In Naga *bhasma*, prepared through 60 heating cycles, XRD showed a single lead sulphide phase with a crystallite size of about 60 nm, while TEM showed spongy, irregular particles in the sub-micron range that the authors attributed to agglomeration bound by herbal organic residues[12]. Swarna Makshika *bhasma* showed a reduction from 6–8 µm in the raw mineral to 1–2 µm after nine *puta*, with conversion of chalcopyrite into oxide and sulphide phases[13]. In the herbo-mineral compound Hridayarnava Rasa, which combines *kajjali* and Tamra *bhasma*, field-emission SEM showed crystallite aggregates of about 100–1000 nm, while laser diffraction placed half of the material below 16.4 µm[16]. This last study is useful because it reports both an image-based and a distribution-based measurement on the same sample, and the two clearly describe different scales.

3. Calcium-based marine *bhasmas*

The marine *bhasmas* show a well-defined chemical transformation. In Mukta *bhasma*, repeated calcination converted the aragonite of raw pearl into calcite with minor portlandite, and SEM sizes fell from 214.7–718.7 nm in raw and purified pearl to 79.9–279.2 nm in the finished product[14]. Shankha *bhasma* showed a similar aragonite-to-calcite conversion and loss of the organic nacre matrix[15]. These are among the few studies in which SEM sizes approach the nanoscale, but they are still based on image fields rather than number-based distributions.

4. Silver, iron, zinc and mica *bhasmas*

Rajata *bhasma* has been characterised alongside synthetic silver nanoparticles[22], Abhraka *bhasma* has been prepared and characterised by two different methods[23], and a mica-based Krishna Vajra Abhraka *bhasma* has been discussed as a nanomedicine for breast cancer[6]. For Mandura *bhasma*, a deliberately

size-reduced "nano" preparation has been developed and tested with ascorbic acid to improve iron bioavailability[24]. Jasada *bhasma* has served as the starting point for a zinc-based nanomedicine programme[25]. These studies are valuable, but several of them engineer a nanoscale product from the classical *bhasma* rather than show that the classical product is itself nanoscale. The distinction should be stated explicitly in the title and abstract of such work.

INTERPRETING THE EVIDENCE

1. Nanocrystalline is not the same as nanoparticulate

Across materials, the evidence supports a consistent description: *bhasmas* are nanostructured or nanocrystalline materials, in which crystal domains of tens of nanometres are organised into particles and aggregates of hundreds of nanometres to a few micrometres. The classical tests are compatible with this picture. *Rekhapurnatva* and *varitaratva* need very fine, light particles with large surface area, but particles of about 1 µm already meet these tests. None of the classical tests can distinguish 50 nm from 500 nm definition requires[7]. Most reports rely on Scherrer analysis, a few SEM or TEM fields, or intensity-weighted DLS. On the current evidence, it is not possible to say whether any classical *bhasma* meets the nanomaterial definition, either way.

2. Biological relevance depends on surface and composition, not on the label

The most informative studies link structure to biological behaviour. In cells, intact aggregates of gold *bhasma* and synthetic gold nanoparticles followed different uptake routes, whereas the 100–200 nm fraction behaved like the synthetic particles[10]. In rats and zebrafish, gold bioaccumulation from five commercial Suvarna *bhasmas* differed significantly, and in zebrafish ionic gold accumulation varied about 5.5-fold and correlated with the product of surface area and gold fraction ($R^2 = 0.974$)[11]. In other words, what drives exposure is measurable surface area and composition. These properties can be measured directly, and the nano label adds nothing to them.

3. Variability between manufacturers is a larger problem than size

The same study found gold content ranging from 32 to 98 wt% across five marketed Suvarna *bhasmas*, with 5.4 wt% arsenic in one product and differing pharmacokinetics between brands[11]. This variability is consistent with the earlier finding of heavy metals in

4. Safety framing

Calling *bhasmas* nanomedicines can cut both ways. The nanoscale is often invoked to explain why small doses are effective and why toxicity is low. Nanotoxicology, however, generally treats increased surface area and cellular uptake as reasons for caution, not reassurance. Blood-compatibility data for gold *bhasma* were reassuring, with very low haemolysis[9], a 40-day rat study of Naga *bhasma* reported no notable organ changes at the dose tested, in contrast with crude lead[12], and the toxicity of Abhraka *bhasma* has been examined in rats[27], although concerns about possible dose-dependent hepatotoxicity and aluminium content have been raised for mica-based preparations[6]. These findings are encouraging but limited in duration and design, and they cannot be generalised to all products or to long-term human use.

PROPOSED MINIMUM CHARACTERISATION AND REPORTING STANDARD

Based on the gaps identified above, Table 3 proposes a minimum standard for any study that makes a size-related claim about a *bhasma*.

Table 3. Proposed minimum characterisation standard for size-related claims about *bhasmas*

Domain	Minimum requirement	Rationale
Sample description	Classical reference, batch number, raw material source, number of *puta*, temperature profile, number of batches	Allows replication and comparison across studies
Phase identity	Powder XRD with phase identification against reference patterns	Confirms the chemical form (for example metal, oxide, sulphide or carbonate)
Crystallite size	Scherrer or Williamson–Hall analysis, explicitly labelled "crystallite size"	Prevents confusion with particle size
Particle size distribution	Number-based distribution from electron microscopy (at least several hundred particles	Needed to test against nanomaterial definitions

	from representative fields), plus laser diffraction for the micron range	
Dispersion state	DLS in a stated medium with polydispersity index, ideally in simulated gastric and intestinal fluids	Shows how the material behaves after administration
Surface area	BET specific surface area	Linked to dissolution and bioaccumulation
Composition	Bulk elemental analysis (ICP-OES/MS or AAS) including Pb, Hg, As and Cd, plus free metal where relevant	Detects contamination and batch variation
Terminology	Use "nanocrystalline" or "nanostructured" unless the number-based criterion is shown	Keeps claims aligned with the evidence

RESEARCH GAPS AND FUTURE DIRECTIONS

Four gaps stand out. First, almost no study follows *bhasma* particles through simulated digestion to show what size and chemical form actually reach the intestinal epithelium. Second, there are very few human pharmacokinetic studies that relate measured particle characteristics to blood or tissue levels. Third, inter-laboratory comparison of the same *bhasma* batch using the same protocol has not been done, so method-dependent differences cannot yet be separated from product differences. Fourth, the influence of individual pharmaceutical steps, such as the number of *puta* or the herbal media used in *bhavana*, on final particle size distribution has been studied only for a few materials.

Addressing these gaps would allow *Rasa Shastra* to make size-related claims on firm ground. It would also make it possible to show where a classical *bhasma* differs from a synthetic nanoparticle, which may turn out to be its most useful scientific feature.

CONCLUSION

The published evidence shows that most *bhasmas* are nanocrystalline, with crystallite domains of roughly 20–60 nm, but that these domains are held in particles and aggregates ranging from about 100 nm to a few micrometres. The widespread description of *bhasmas* as nanoparticles rests mainly on crystallite size from XRD, and no study reviewed here has reported the number-based particle size distribution needed to meet current nanomaterial definitions. Composition, surface area and variability between manufacturers have a larger demonstrated effect on biological exposure than the nano label. Future work should use several orthogonal techniques, report number-based distributions, and describe classical products as nanostructured unless the stricter criterion is shown.

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