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"ABSORPTION, DISTRIBUTION AND EXCRETION OF *BHASMAS*: A SCOPING REVIEW OF THE PHARMACOKINETIC EVIDENCE"

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ABSTRACT

Background: The therapeutic and safety claims made for *bhasmas* rest on assumptions about how much of the metal is absorbed, where it goes and how it is eliminated. These assumptions are rarely tested. **Objective:** To map the available evidence on the absorption, distribution, metabolism and excretion of metal and mineral *bhasmas* and related herbo-mineral formulations, and to identify the main evidence gaps. **Methods:** A structured narrative review following scoping principles. Studies reporting dissolution or bioaccessibility in simulated gastrointestinal fluids, cellular uptake, animal blood or tissue metal levels, or human pharmacokinetic data were identified through bibliographic databases and reference lists and charted by study type and metal. **Results:** The evidence base is small and dominated by in vitro and animal studies. For gold, rat studies show measurable absorption with large differences between commercial products (peak blood gold 4.66–8.55 µg/L after 0.8 mg/kg), and cell studies show that intact aggregates and fine fractions enter cells by different routes. For iron and zinc *bhasmas*, simulated digestion and Caco-2 models show pH-dependent dissolution and uptake that can be raised by size reduction and ascorbic acid (about threefold for a modified Mandura *bhasma*). For mercurials, mercuric sulphide shows low solubility and absorption relative to other mercury compounds. Human pharmacokinetic data are almost absent. **Conclusion:** *Bhasmas* are absorbed, but the extent depends on composition, surface area and dissolution rather than on the classical label. Standardised dissolution testing and small human pharmacokinetic studies are the priorities.

KEYWORDS: *Bhasma*; Pharmacokinetics; Bioavailability; Bioaccessibility; Gold; Iron; Zinc; Mercury

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INTRODUCTION

Classical *Rasa Shastra* describes *bhasmas* as light, fine and quickly assimilated, and attributes their action at small doses to these qualities. Modern authors have restated these claims in pharmacokinetic terms, suggesting that small particle size and large surface area give high bioavailability and rapid action[1,2]. Paradoxically, safety arguments often rest on the opposite assumption, namely that metals in *bhasmas* are bound in insoluble forms that are poorly absorbed and therefore not toxic.

Both claims cannot be true for all *bhasmas* in the same way, and both can be tested. Pharmacokinetics, the study of absorption, distribution, metabolism and excretion (ADME), is the bridge between the composition of a product and its effect, wanted or unwanted. This scoping review maps what is known about the ADME of *bhasmas* and identifies where the evidence is missing.

METHODS OF THE REVIEW

This review follows scoping principles: its purpose is to map the extent and nature of the evidence, not to estimate an effect. Studies were identified through PubMed, PubMed Central, Crossref-indexed records and publisher databases, using combinations of *bhasma*, herbo-mineral, Ayurvedic metal, bioavailability, bioaccessibility, pharmacokinetics, absorption, tissue distribution, excretion and the names of individual metals. Reference lists of retrieved studies were screened. Studies were charted by level of evidence (in vitro dissolution or bioaccessibility, cell uptake, animal pharmacokinetics or tissue distribution, and human data) and by metal. Formal screening counts were not recorded, and readers wishing to update this work as a systematic scoping review should register a protocol and report a flow diagram.

WHAT THE ADME QUESTIONS ARE FOR A BHASMA

For a conventional drug, ADME describes a dissolved molecule. A *bhasma* is a solid, usually a metal oxide, sulphide, carbonate or the metal itself, administered as a powder, often with honey, ghee or another vehicle (*anupana*). Its fate in the body therefore has extra steps:

- **Dispersion and dissolution** in saliva, gastric acid and intestinal fluid, which depend on chemical form, surface area, crystallinity and the vehicle.
- **Uptake** of dissolved ions through physiological transporters (for iron, zinc and copper), or of particles through endocytosis or paracellular routes.
- **Distribution** to blood and tissues, where essential metals enter regulated pools while non-essential metals such as mercury, lead and gold may accumulate.
- **Excretion**, mainly in faeces for unabsorbed material and in urine or bile for absorbed metal.

Because most of a solid dose is never dissolved, measuring total metal content tells little about exposure. The useful measures are bioaccessibility (the fraction released in simulated digestion), bioavailability (the fraction reaching the circulation) and tissue accumulation.

MAPPING THE EVIDENCE

Table 1. Evidence on the absorption and distribution of *bhasmas* and related formulations.

Metal and product	Study type	Main findings
Gold: five commercial Suvarna *bhasma* products	Rat pharmacokinetics (20 rats, 0.8 mg/kg); zebrafish accumulation	Significant differences in pharmacokinetics; peak blood gold 8.55 µg/L for the highest and 4.66 µg/L for the lowest product; ionic gold accumulation in zebrafish varied about 5.5-fold and correlated with surface area × gold fraction ($R^2 = 0.974$)
Gold: commercial Swarna *bhasma* vs synthetic gold nanoparticles	Cell uptake (HeLa, HFF-1)	Intact aggregates and 100–200 nm fractions entered cells by different routes; actin and clathrin inhibitors roughly halved the share of cells containing *bhasma* particles
Gold: Swarna *bhasma*	Blood compatibility; Caco-2 monolayer	Very low haemolysis; weaker staining of the tight-junction protein ZO-1 in Caco-2 cells
Gold: nano Swarna *bhasma* formulation	Oral dosing in tumour-bearing mice; pilot clinical use	Dose-dependent anti-tumour effects after oral dosing, indicating systemic exposure

Iron: Mandura *bhasma*, size-reduced and ascorbic acid-modified	Simulated digestion; Caco-2 uptake and ferritin	Iron dissolution higher in the intestinal phase; about threefold higher iron uptake for the modified form; dose-related rise in ferritin
Zinc: Jasada *bhasma*	Synthesis and Zn^{2+} bioavailability	Effect of classical incineration on zinc oxide nanoparticle formation and Zn^{2+} availability examined
Mercury: selected Ayurvedic medicines	Bioaccessibility in simulated gastrointestinal fluids	Mercury bioaccessibility measured in a range of products
Mercury: processed α-HgS	Zebrafish toxicokinetics	Ayurvedic processing gave distinct physicochemistry and toxicokinetics compared with unprocessed HgS
Mercury and copper: Arogyavardhini Vati	Rat safety study; clinical cohort	Safety evaluated in brain, liver and kidney of rats; urinary mercury mentioned but not reported in a 7-week clinical cohort

1. Gold

Gold *bhasma* has the most informative data. In a comparison of five commercial Suvarna *bhasma* products, rats given 0.8 mg/kg showed significantly different blood gold profiles, with peak concentrations ranging from 4.66 to 8.55 µg/L. In zebrafish, accumulation of ionic gold varied about 5.5-fold between products and was almost perfectly predicted by the product of specific surface area and gold content[3]. This result is important because it links a measurable physical property to exposure, and because it shows that products sold under the same name are not pharmacokinetically equivalent.

At the cellular level, Swarna *bhasma* aggregates of several micrometres and fine 100–200 nm fractions behaved differently from each other and from synthetic gold nanoparticles. Inhibitors of actin-dependent uptake and of clathrin-mediated endocytosis roughly halved the proportion of cells containing *bhasma* particles, whereas an inhibitor of caveolae-mediated uptake had no effect[4]. In Caco-2 cells, which model the intestinal epithelium, Swarna *bhasma* weakened staining of the tight-junction protein ZO-1[5], raising the possibility of a paracellular route that deserves direct study. Oral nano-gold formulations derived from Swarna *bhasma* have shown dose-dependent effects in tumour-bearing mice, which implies systemic exposure, although blood or tissue gold levels were not the focus of that work[6].

2. Iron

Iron is an essential metal with tightly regulated absorption. Non-haem iron is taken up mainly as ferrous iron through the divalent metal transporter in the duodenum, after reduction of ferric iron, and its bioavailability is strongly influenced by dietary enhancers such as ascorbic acid and inhibitors such as phytate[14,15]. Iron *bhasmas* consist mainly of iron oxides, which dissolve slowly at intestinal pH. A modified Mandura *bhasma*, reduced in size and coated with ascorbic acid, showed greater iron dissolution in the intestinal phase of a simulated digestion, about threefold higher iron uptake in Caco-2 cells than the unmodified microparticles, and a dose-related increase in cellular ferritin[7]. These data support the classical practice of combining iron preparations with acidic or reducing *anupana*, but they also show that the unmodified *bhasma* is less available than is often assumed.

3. Zinc and copper

For zinc, the effect of classical incineration on the formation of zinc oxide nanoparticles in Jasada *bhasma* and on Zn^{2+} availability has been investigated[8], and Jasada *bhasma* has served as the starting point for a zinc nanomedicine programme[9]. As with iron, zinc oxide dissolves readily in gastric acid, so the particle size of the original powder is likely to matter less for zinc than for poorly soluble metals. Direct animal pharmacokinetic data for copper *bhasmas* were not identified in this review.

4. Mercury and lead

For mercurial formulations, the key determinant of absorption is speciation. Mercuric sulphide is very poorly soluble and far less absorbed than mercuric chloride or methylmercury[16,17]. Mercury bioaccessibility has been measured in selected Ayurvedic medicines using simulated gastrointestinal fluids[10], and Ayurvedic processing of α-HgS altered its toxicokinetics in zebrafish compared with

unprocessed HgS[11]. For lead, a rat study of Naga *bhasma* reported no organ damage at the dose tested, whereas crude lead caused damage[18], but blood and tissue lead levels were not the focus. For the compound formulation Arogyavardhini Vati, safety was evaluated in rat brain, liver and kidney[12], and a clinical cohort mentioned urinary mercury but did not report it[13].

5. Calcium-based *bhasmas*

For calcium carbonate-based marine *bhasmas* such as Shankha *bhasma*, processing converts aragonite to calcite and removes the organic matrix[19]. Calcium carbonate dissolves in gastric acid, and its absorption follows normal calcium physiology. Pharmacokinetic comparison of these *bhasmas* with conventional calcium salts has not been reported, and is addressed in another review in this series.

INTERPRETING THE EVIDENCE

1. Absorption is real, but product-dependent

The data refute the simple view that metals in *bhasmas* are not absorbed. Gold from Suvarna *bhasma* reaches the blood in rats, and iron and zinc *bhasmas* release absorbable ions in simulated digestion. At the same time, the gold study shows that absorption varies significantly between products of the same name[3]. Clinical and safety conclusions drawn from one product therefore cannot be transferred to another without comparative data.

2. Surface area and dissolution matter more than the nano label

The strongest predictor of gold accumulation identified so far is the product of surface area and gold content[3], and the main factor in iron uptake is dissolution in the intestinal phase, which can be modified by ascorbic acid[7]. Both observations point away from particle size as an isolated cause and towards measurable physicochemical properties: specific surface area, dissolution rate at relevant pH, and chemical form. These properties should be reported in every pharmacokinetic study, together with dispersion behaviour in the test medium[20].

3. Distinguishing essential from non-essential metals

For iron, zinc and copper, absorbed metal enters regulated physiological pools, and the main risk is overload with prolonged high-dose use. For mercury, lead and arsenic, there is no physiological requirement, and any absorbed fraction contributes to body burden. For gold and silver, the body has no specific handling pathway, and long-term distribution and retention are poorly understood. The pharmacokinetic questions, and the acceptable level of uncertainty, differ accordingly.

4. The role of *anupana* and co-administered herbs

Bhasmas are rarely given alone. They are taken with honey, ghee, milk or herbal juices, and are often part of compound formulations. These vehicles can change dispersion, pH and redox conditions, and so dissolution and uptake. The effect of ascorbic acid on iron uptake[7] is a clear example. Very few pharmacokinetic studies have tested the classical *anupana*, which is a significant gap, since it is the way the medicines are actually used.

A PROPOSED TIERED APPROACH

A practical, staged programme could fill the gaps efficiently:

- **Tier 1: dissolution and bioaccessibility.** Standardised dissolution in simulated gastric and intestinal fluids, with and without the classical *anupana*, reporting the fraction dissolved over time.
- **Tier 2: cellular uptake and transport.** Caco-2 or similar models to measure transport and to distinguish ionic from particulate uptake.
- **Tier 3: animal pharmacokinetics and tissue distribution.** Single and repeated dosing at human-equivalent doses, with blood, urine, faeces and target tissue analysis.
- **Tier 4: human pharmacokinetics and biomonitoring.** Small, well-controlled studies at therapeutic doses, followed by biomonitoring of long-term users.

Tier 1 and 2 data are inexpensive and could be generated for every marketed *bhasma*; they would also serve as release tests for batch-to-batch consistency.

RESEARCH GAPS

The main gaps are: human pharmacokinetic data for any *bhasma*; comparative studies of several commercial products under the same protocol; studies using the classical *anupana*; long-term tissue accumulation studies for non-essential metals; and methods to separate dissolved from particulate metal in blood and tissue. Without these data, both efficacy claims based on bioavailability and safety claims based on non-absorption remain assumptions.

CONCLUSION

The available evidence shows that metals from *bhasmas* are absorbed and distributed, but that the extent depends on chemical form, surface area and dissolution, and differs significantly between products of the same name. Iron and zinc *bhasmas* behave as slowly dissolving sources of essential ions, gold shows product-dependent absorption and accumulation, and mercuric sulphide is poorly absorbed. Human pharmacokinetic data are almost entirely missing. Standardised dissolution testing, comparative animal studies and small human pharmacokinetic studies, conducted with the classical *anupana*, should be the priorities for *Rasa Shastra* research.

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