

YUKTI TO NANO-PHARMACOLOGY: UNDERSTANDING ALPAMATRA
MAHARTHATVAM AND THE THERAPEUTIC POTENTIAL OF RASAUSHADHISDr. Alpna Bijarniya^{1*}, Prof. (Dr.) Govind Sahay Shukla², Dr. Rajaram Agarwal³, Dr. Manisha Goyal³, Dr. Chandrabhan Sharma³, Dr. Ravi Pratap Singh⁴¹MD Scholar, PG Department of Rasa Shastra and Bhaishajya Kalpana, Post Graduate Institute of Ayurveda, DSRRAU, Jodhpur, Rajasthan, India.²Vice Chancellor, DSRRAU, Jodhpur, Rajasthan, India.³Associate Professor, PG Department of Rasa Shastra and Bhaishajya Kalpana, Post Graduate Institute of Ayurveda, DSRRAU, Jodhpur, Rajasthan, India.⁴Assistant Professor, PG Department of Rasa Shastra and Bhaishajya Kalpana, Post Graduate Institute of Ayurveda, DSRRAU, Jodhpur, Rajasthan, India.***Corresponding Author: Dr. Alpna Bijarniya**MD Scholar, PG Department of Rasa Shastra and Bhaishajya Kalpana, Post Graduate Institute of Ayurveda, DSRRAU, Jodhpur, Rajasthan, India. DOI: <https://doi.org/10.5281/zenodo.21702202>**How to cite this Article:** Dr. Alpna Bijarniya^{1*}, Prof. (Dr.) Govind Sahay Shukla², Dr. Rajaram Agarwal³, Dr. Manisha Goyal³, Dr. Chandrabhan Sharma³, Dr. Ravi Pratap Singh⁴, (2026). Yukti To Nano-Pharmacology: Understanding Alpamatra Maharthatvam and The Therapeutic Potential Of Rasaushadhis. European Journal of Pharmaceutical and Medical Research, 13(8), 74–81.

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Article Received on 24/06/2026

Article Revised on 14/07/2026

Article Published on 01/08/2026

ABSTRACT

Background: *Rasaushadhis* represent a unique class of herbo-mineral formulations in *Ayurveda*, distinguished by three remarkable characteristics: administration in minute doses (*Alpamatra*), rapid therapeutic action (*Ksipramarogvadayitvat*), and patient palatability (*Arucheraprasangatah*). Despite their widespread clinical use spanning centuries, the scientific mechanism underlying their efficacy in micro-doses remains inadequately understood. **Objective:** This review aims to establish the scientific basis for *Alpamatra Maharthatvam* (achieving maximum therapeutic effect with minimal dose) by correlating classical pharmaceutical principles with modern pharmacological concepts. **Materials and Methods:** Classical Ayurvedic texts, including *Charaka Samhita*, *Rasaratna Samuccaya*, *Ayurveda Prakash*, *Rasendrachudamani*, and *Rasendra Sara Sangraha* were systematically reviewed for principles of *Yukti* and *Samskara*. Contemporary scientific literature from databases including PubMed, Scopus, and Google Scholar (2010-2025) was analyzed for studies on *Bhasma* characterization, nanoparticle analysis, and bioavailability. **Results:** Classical *Samskaras* including *Shodhana* (purification), *Marana* (incineration), and *Bhavana* (levigation) facilitate: (1) detoxification through conversion of toxic metal salts into stable, biocompatible forms (2) particle size reduction to nano-dimensions (5-50 nm) (3) enhanced surface area-to-volume ratio (4) organic coating that serves as stabilizing agent and vector for targeted delivery. Twenty commonly used *Rasa* formulations were analyzed, with therapeutic doses ranging from 2-125 mg, compared to conventional herbal doses in grams. **Conclusion:** *Rasaushadhis* represent an ancient, sophisticated system of nanomedicine. The principle of *Alpamatra* is scientifically validated through nanonization, enhanced bioavailability, and targeted drug delivery achieved by classical *Samskaras*. This convergence of traditional wisdom and modern science positions *Rasaushadhis* as safe, economical, and potent therapeutic agents.

KEYWORDS: *Alpamatra*, *Rasaushadhi*, *Bhasma*, Nanopharmacology, *Yukti*, *Ayurveda*.**1. INTRODUCTION**

Ayurveda, the traditional medical system of India, initially relied predominantly on herbal preparations for disease management. Classical texts describe *Panchavidha Kashaya Kalpana*, five primary dosage forms including *Swarasa* (fresh juice), *Kalka* (paste),

Kwatha (decoction), *Hima* (cold infusion), and *Phanta* (hot infusion).^[1] While therapeutically effective, these formulations presented significant clinical challenges: requirement of large quantities for administration, limited shelf-life, poor patient compliance due to unpalatable taste, and delayed therapeutic response.^[2]

To overcome these limitations, the specialized branch of *Rasa Shastra* evolved, focusing on purification and processing of minerals, metals, and mercury-based substances for therapeutic application.^[3] The vision extended beyond mere disease management to encompass tissue strengthening (*Dhatu Poshana*) and rejuvenation (*Rasayana*). Ancient scholars deliberately developed these formulations to achieve three critical objectives: rapid action, prolonged stability, and efficacy in minimal doses.^[4]

Rasaushadhis became distinguished by three fundamental characteristics as stated in *Rasaratna Samuccaya*, efficacy in small doses (*Alpamatropayogitvat*), rapid therapeutic action (*Kṣipramarogyadayitvat*), and patient palatability (*Arucheraprasangataḥ*).^[4] The concept of *Alpamatra Maharthatvam* refers to achieving maximum therapeutic effect with a minimal quantity of medicine. Despite centuries of clinical validation, the precise scientific mechanism explaining how minute quantities of herbo-mineral formulations produce profound therapeutic effects remains underexplored in contemporary literature.^[5]

This review seeks to elucidate the classical principles of *Yukti* and *Samskara* that enable *Alpamatra*, correlate traditional processing methods with modern pharmaceutical science, synthesize evidence from analytical studies on *Bhasma* characterization, establish *Rasaushadhis* as ancient nanomedicines, and provide a scientific framework for understanding low-dose efficacy.

2. MATERIALS AND METHODS

This is a comprehensive narrative review integrating classical Ayurvedic literature with modern scientific evidence. Classical references were drawn from *Charaka Samhita*, *Sushruta Samhita*, *Rasaratna Samuccaya*, *Rasendrachudamani*, *Ayurveda Prakash*, *Rasendra Sanga*, *Bhaishajya Ratnavali*, *Yogaratanakara*, and the Ayurvedic Formulary of India. Modern scientific literature was sourced from PubMed, Scopus, Google Scholar, and ScienceDirect(2000-2025) using keywords including *Rasaushadhi*, *Bhasma*, *Alpamatra*, *Yukti*, *Samskara*, nanoparticles, bioavailability, and nanomedicine.

Inclusion criteria encompassed classical references describing pharmaceutical processes (*Shodhana*, *Marana*, *Bhavana*), studies characterizing *Bhasma* particle size and structure, pharmacological evaluations, bioavailability studies, and safety/toxicity assessments. Information was extracted regarding classical principles, pharmaceutical processing methods, therapeutic doses, particle characterization findings, and mechanistic explanations. Twenty commonly used low-dose *Rasa* formulations were selected from the Ayurvedic Formulary of India and classical texts, with therapeutic doses converted to milligrams and *Gunja* equivalents (1 *Gunja* ≈ 125 mg) noted for comparison.^[6]

3. The Classical Foundation: *Yukti* and Its Four Factors

The classical concept responsible for modifying and enhancing the action of medicines is known as *Yukti*. In Ayurveda, *Yukti* refers to rational planning and proper pharmaceutical processing. The *Charaka Samhita* establishes that the effect of a medicine does not depend only on the quantity of the drug but also on the way it is prepared and administered.^[1] This principle asserts that even a small quantity of a drug can produce powerful therapeutic effects when appropriate processing methods are employed, whereas improper preparation may reduce the effectiveness of even a large quantity of the drug.^[4]

According to Ayurveda, four major factors are responsible for modifying drug action, *Samyoga* (combination of natural substances like *taila*, *takra*, herbal drug etc.), *Vishlesha* (removal of undesirable components), *Kala* (proper timing and duration), and *Samskara* (processing and refinement).^[1] These principles collectively form the scientific basis for the preparation of potent and safe *Rasaushadhis*. In modern pharmaceutical science, these correspond to formulation design, purification processes, quality control parameters, and manufacturing procedures, respectively.^[3]

Samyoga refers to the combination of different ingredients. During pharmaceutical processing, herbal juices, decoctions, and specific *Anupana* (adjuvants) are used along with minerals. These combinations enhance therapeutic activity and improve the action of the final medicine.^[7] A critical example is combining mercury with sulfur to form *Kajjali* (mercury sulfide), which creates a stable, less toxic compound compared to elemental mercury.^[8] This reflects modern principles of chemical stabilization and drug synergism.

Vishlesha primarily corresponds to *Shodhana*, the process of purification and detoxification. Raw minerals and metals may contain impurities or toxic components. Through *Shodhana*, these unwanted properties are reduced or eliminated, making the substances safer for medicinal use.^[9] This correlates with modern detoxification protocols and impurity removal in pharmaceutical manufacturing.

Kala refers to proper timing and duration during pharmaceutical preparation. It includes factors such as the correct season for collecting raw materials, appropriate duration of heating (*Marana*), and sufficient duration of trituration (*Bhavana*). If the duration of *Marana* or *Bhavana* is insufficient, the final product may not achieve the desired therapeutic effect.^[4] This parallel modern concept of process optimization and quality control in pharmaceutical manufacturing.

Samskara represents the pharmaceutical processing methods responsible for transforming raw substances into therapeutically useful forms. Three primary

Samskaras are central to *Rasaushadhi* preparation: *Shodhana* (purification), *Marana* (incineration), and *Bhavana* (levigation).^[3]

4. The *Samskara* Processes: From Raw Minerals to Therapeutic Agents

4.1 *Shodhana* (Purification and Detoxification)

Shodhana is the preliminary process that renders raw minerals and metals safe for internal use.^[9] It corresponds to modern detoxification, converting toxic metal salts into safer sulfides and oxides. Raw mercury undergoes multiple purification steps to eliminate lead, tin, and other contaminating metals.^[9]

The *Shodhana* process employs several methods to achieve its effects. **Heating and quenching** (*Nirvapa*) involve heating the mineral to a red-hot temperature and plunging it into liquids like milk, buttermilk, or herbal decoctions. This thermal shock creates micro-cracks, making the material brittle and easier to grind into fine powder, while allowing liquid media to penetrate the material and leach out impurities via ion-exchange processes.^[9] **Trituration** during purification physically reduces particle size and ensures interaction with beneficial herbal principles.^[10] **Boiling** (*Swedana*) helps dissolve and eliminate impurities soluble in hot, acidic, or oily media.^[9]

Purification reduces the required dose through three key transformations. First is **detoxification**, where raw minerals containing toxic elements or impurities are treated to leach out or neutralize harmful substances. Direct evidence from a study on *Tamra Bhasma* (incinerated copper) found that preparation from unpurified copper caused pathological damage to the heart, liver, and kidneys in rats even at a therapeutic dose, while formulation from purified copper was safe even at five times the therapeutic dose.^[11] This demonstrates that purification directly removes toxicity-causing agents, allowing safe use at lower doses.

Second is **nanoparticle formation**. The purification and subsequent incineration processes break down minerals into nanoparticles (often 5-50 nm), dramatically increasing the surface area available for absorption. This allows faster and more efficient absorption, meaning a smaller physical dose can deliver the required active material to tissues.^[5,12] For example, the particle size of *Jasada Bhasma* (zinc-based ash) decreased from 1.5 μm to 31 nm through processing, improving dissolution and zinc ion bioavailability.^[13]

Third is **enhanced biocompatibility**. The purification process using herbs, milk, or other media creates organo-metallic complexes, making minerals "body-friendly" and bio-assimilable—a quality termed *Rasibhava* in Ayurveda.^[14] This enables ready ingestion and integration into body systems.

4.2 *Marana* (Incineration)

Marana involves repeated heating and incineration to convert metals into stable, bioavailable forms known as *Bhasma*.^[15] This represents a top-down approach to nanoparticle synthesis. Studies using transmission electron microscopy and X-ray diffraction have confirmed that properly prepared *Bhasmas* contain particles in the 5-50 nanometer range.^[16]

The dose-reducing power of *Marana* results from a two-step transformation. The first is a **physical transformation from microns to nanometers**. A study on *Jasada Bhasma* showed the process transformed particles from an average size of 1.5 μm (micrometers) to just 31 nm (nanometers).^[13] Similarly, *Naga Bhasma* (lead-based ash) was found to have nanocrystallites of about 60 nm, and *Swarna Bhasma* (gold-based ash) particles in the 20-50 nm range.^[17] This size reduction increases surface area millions of times over, allowing more ready absorption.^[12]

The second is a **chemical transformation to a safer, more bioavailable compound**. Intense heat of incineration converts toxic elemental metals into safe, stable, and bioavailable chemical forms like oxides or sulphides.^[15] Crucial evidence from a histopathological study on *Naga Bhasma* demonstrated that when rats were given a high dose of crude, unpurified lead, they suffered significant organ damage; however, the same high dose of *Naga Bhasma* showed no toxicity.^[18]

The *Marana* process had converted highly toxic lead into non-toxic lead sulfide nanoparticles, supporting the use of smaller, effective therapeutic doses in humans.

4.3 *Bhavana* (Levigation)

Bhavana is the wet trituration of *Bhasma* particles with herbal juices or decoctions.^[10] This is a sophisticated "green nanofabrication" process that physically and chemically re-engineers particles at the molecular level, drastically reducing the dose through three synergistic mechanisms.^[10]

The first mechanism is the "milling" effect, achieving sub-10nm stability. While *Marana* creates nanoparticles, these tend to clump together (agglomerate) due to high surface energy. During *Bhavana*, particles undergo hours of intense wet grinding in a stone mortar. This mechanical attrition breaks agglomerates apart, and the wet environment with shear forces prevents re-aggregation. Ensuring the *Bhasma* remains as discrete, non-agglomerated nanoparticles (5-50 nm) maximizes the surface area available for absorption. A smaller dose goes further because every particle is individually exposed and ready for cellular uptake, rather than trapped in clumps.^[10]

The second mechanism is "green synthesis" and the capping effect for stabilization. Herbal juices (like *Aloe*

vera, Tulsi, or Ginger decoctions) are rich in phytochemicals—flavonoids, terpenoids, and polyphenols. During trituration, these biomolecules act as natural reducing and capping agents. As mineral nanoparticles are ground, they have unpaired electrons on their surface, making them highly reactive and chemically unstable. Biomolecules immediately adsorb onto the surface of nascent nanoparticles, forming a protective organic "corona" or shell. This process, known in modern chemistry as "capping," stops particles from oxidizing or growing into larger toxic crystals. Stabilization ensures a long shelf life and maintains nano size until reaching the gut. Because particles are chemically "passivated" by this herbal coat, they are not destroyed by stomach acids, allowing a significantly smaller physical dose to survive the digestive tract intact and reach the bloodstream.^[10]

The third mechanism is the "Trojan horse" effect for targeted delivery (*Yogavahitva*). Ayurveda calls this property *Yogavahitva*—the ability of the herb to act as a vehicle carrying minerals to specific tissues (*Dhatus*).^[14] During *Bhavana*, herbal biomolecules form organo-metallic complexes (chemical bonds between metal and organic carbon rings of herbs). These specific herbal phytochemicals often have intrinsic affinity for certain receptors in the body (e.g., liver, brain, or joint tissues). Herbal capping agents actively guide the nanoparticle to its specific target organ, allowing a much lower systemic dose to achieve a high local concentration exactly where needed.^[10,14]

The "pulse-spark" effect represents mechanochemical activation. Intense friction during *Bhavana* creates localized high-pressure and high-temperature zones ("mechano-chemical hotspots"). This friction partially breaks the crystal lattice of the mineral, creating "defects" or pores. When herbal juice is ground into these defects, a nano-composite form where herb and mineral are fused at the atomic level. When this nanocomposite reaches the cellular membrane, the organic herb component dissolves first, instantly delivering a high-concentration "pulse" of mineral ions directly into the cell cytoplasm, bypassing standard slow diffusion. This rapid, high-intensity delivery means therapeutic effects are achieved with micro-doses (sometimes just 15-30 mg per day), whereas unprocessed herb or mineral would require grams for the same effect.^[10]

5. Classical Claims for Superiority and Scientific Correlation

Classical texts describe *Rasaushadhis* as highly effective medicines providing significant therapeutic benefits in minute doses. The *Rasendrachudamani* explains that when mercury is used in the incinerated (*Bhasma*) and processed (*Murchita*) states, even in small quantity, it produces highly beneficial effects immediately, stimulating digestive and metabolic functions (*Dipana-Pacana*).^[19] According to *Rasendra Sara Sangraha*,

while many therapies exist for curable diseases, *Rasaushadhi* therapy is regarded as the principal treatment for diseases considered incurable or refractory.^[20] *Ayurveda Prakash* elaborates that when herbs combine with properly processed mercury treated with mica, gold, silver, and copper, their potency becomes incomparable, possessing extraordinary powers including preservation of health, vitality, and longevity.^[21]

The scientific correlation of these classical claims is now evident through modern research. Properly processed *Rasaushadhis* exhibit enhanced bioavailability, targeted delivery, and reduced toxicity through mechanisms directly traceable to the *Samskara* processes.^[5,12] The concept of *Alpamatra* is validated through nanonization and enhanced surface area, enabling low-dose efficacy. The rapid action (*Kshipramarogyadayitvat*) is explained through nanoparticle-mediated rapid absorption and cellular uptake.^[22] Patient palatability arises from the reduced dose size and herbal incorporation during processing.

6. Scientific Basis of Alpamatra

6.1 Nanotechnology in Bhasma Preparation

Modern analytical techniques have consistently demonstrated the nano-dimensional nature of properly prepared *Bhasmas*. *Swarna Bhasma* shows particles of 27 ± 3 nm by TEM^[17], *Mandoor Bhasma* 20-50 nm by XRD and TEM^[22], *Yashad Bhasma* 15-35 nm by SEM^[13], *Tamra Bhasma* 20-40 nm by TEM^[11], and *Rajata Bhasma* 10-30 nm by TEM.^[18] Reduction to the nano-scale dramatically increases the surface area-to-volume ratio.^[12] A 1 cm³ cube with surface area 6 cm² divided into 10 nm cubes increases surface area to 6×10^6 cm², a million-fold increase directly correlating with enhanced dissolution, increased absorption, and greater biological interaction.^[12]

6.2 Enhanced Bioavailability and Rasibhava

Classical texts describe *Rasibhava* as transformation of metallic particles into form assimilable by tissues, correlating with modern understanding of nanoparticle absorption.^[14] Nanoparticles pass through intestinal epithelium more readily through enhanced uptake via Peyer's patches and M-cells, and direct cellular uptake through endocytosis.^[12] Herbal coating from *Bhavana* prevents agglomeration, organic matrix enhances membrane permeability, and *Yogavahitva* enables targeted delivery.^[10] Chemical transformation to oxides/sulfides improves solubility while stable compounds prevent toxic accumulation.^[15]

Balkrishna et al. demonstrated that *Mandoor Bhasma* nanoparticles (20-50 nm) showed threefold higher iron uptake in human colon epithelial cells compared to conventional iron supplements.^[22] Research on *Jasada Bhasma* confirmed repeated incineration cycles create particles capable of delivering bioavailable

zinc ions up to 6% w/w under acidic physiological conditions.^[13]

6.3 Detoxification and Safety

Critical to low-dose therapy is conversion of toxic metals into safe forms. Mercury and sulfur form *Kajjali* (mercury sulfide), highly stable and poorly absorbed, with therapeutic effect occurring through surface reactivity, catalytic action, and nano-particulate interactions.^[8] Properly processed *Bhasmas* exhibit no significant cytotoxicity, safe elimination through natural pathways, and thermoregulatory stability.^[12] Histopathological study on *Tamra Bhasma* revealed best protective and antioxidant response at low therapeutic dose of just 0.5 mg/100g body weight in rats.^[11]

6.4 Rapid Action

Nanoparticles interact directly with intestinal receptors triggering rapid therapeutic response.^[12] Many *Rasaushadhis* are administered sublingually enabling direct systemic absorption.^[3] Nanoparticles can accelerate biochemical reactions through surface catalysis.^[5] The nanoparticle size provides immense surface area for rapid dissolution and efficient absorption.^[12] Nano-*Bhasma* formulations show threefold higher cellular uptake compared to micro-sized counterparts.^[22]

7. Pharmacokinetics of Bhasma: Understanding ADME

The pharmacokinetic profile of a *Bhasma* is fundamentally different from its raw, unprocessed mineral form. Assessing safety and efficacy based solely on total metal content is scientifically inaccurate.^[12]

7.1 Absorption (A)

The key factor in absorption is bio accessibility, the fraction released from its matrix in the GI tract becoming available for absorption.^[12] A study on various Ayurvedic formulations found bio accessibility of elements like As,

Cu, and Hg to be highly dependent on formulation properties and digestive conditions.^[12] Nanoparticle size provides an immense surface area, allowing rapid dissolution and efficient absorption, particularly in the intestine.^[22] A comparative study on different commercially prepared *Swarna Bhasma* demonstrated significant differences in pharmacokinetic parameters in rats, with peak blood concentration of ionic gold varying nearly two-fold between samples (4.66 µg/L to 8.55 µg/L), directly linking preparation method to bioavailability.^[17]

7.2 Distribution (D)

Once absorbed, nanoparticles distribute throughout the body with a distribution pattern unique and strongly influenced by the preparation method.^[17] Five different commercially prepared *Suvarna Bhasma* formulations showed different bioaccumulation profiles in zebrafish and rat blood, directly linking the manufacturing process to medicine distribution.^[17] Proper preparation is critical for directing medicine to the intended target tissues. Herbal juices during *Bhavana* create synergistic effects (*Yogavahitva*), where herbal components act as capping and stabilizing agents for nanoparticles, potentially enhancing targeted delivery.^[10,14]

7.3 Metabolism and Elimination (M&E)

The intense heat of *Marana* chemically converts toxic elemental metals into stable, non-toxic forms like oxides and sulfides (e.g., PbS, HgS).^[15] The body does not "metabolize" metal in the traditional sense but handles inert, stable nanoparticles. Elimination is slow with a prolonged half-life, contributing to the sustained therapeutic effect of a small dose.^[17] Histopathological study on *Tamra Bhasma* demonstrated processed nano-form delivers a high therapeutic effect at doses of orders of magnitude lower than required for raw metal.^[11] The combination of high bioavailability and altered, safer chemical form allows a minimal dose to produce maximal therapeutic effect.^[12]

8. Analysis of Formulations

Table 1: Classical reference of dose.

Formulation Name	Dosage Range (mg)	Primary Indications	Source / Reference
<i>Rasa Karpura</i> (<i>Kupipakwa Rasayana</i>)	2 – 4	<i>Grahani</i> , <i>Jwaratisara</i> , <i>Raktatisara</i>	[6, 23]
<i>Tarunarka Rasa</i> (<i>Rasa Yoga</i>)	4	<i>Sarva Jwara</i> (all types of fever)	[6]
<i>Vajra Bhasma</i>	8	<i>Rajayakshma</i> , <i>Daurbalya</i> , <i>Rasayana</i> (rejuvenation)	[6, 23]
<i>Sucikabharana Rasa</i>	7.8 – 15.62	<i>Sannipata Jwara</i> , <i>Sanyasa</i>	[6]
<i>Swarna Bhasma</i>	15.5 – 62.5	<i>Hridroga</i> (heart diseases), <i>Medha-Smriti Vardhana</i> (improving intellect & memory)	[6, 23]
<i>Sulavajrini Vatika</i>	25	<i>Sularoga</i> (colic pain), <i>Gulma</i> (abdominal tumors)	[6]
<i>Tamra Bhasma</i>	31.25 – 62.5	<i>Yakrit-Pliha-hara</i> (liver & spleen disorders), <i>Udararoga</i> (abdominal diseases)	[6, 24]
<i>Kumarakalyana Rasa</i>	62.5	<i>Bala roga</i> (pediatric diseases)	[6, 25]
<i>Kancanabhra Rasa</i>	62.5	<i>Prameha</i> (diabetes), <i>Ksaya</i> (wasting), <i>Vataroga</i> (Vata disorders)	[6]
<i>Samirapannaga Rasa</i>	62.5 – 125	<i>Shwasahara</i> (respiratory disorders), <i>Vedanasthapana</i> (pain relief)	[6]

<i>Smriti Sagara Rasa</i>	62.5 – 125	Memory loss, Epilepsy	[6]
<i>Sutikabharana Rasa</i>	62.5	<i>Sutika Roga</i> (postnatal disorders)	[6]
<i>Yakuti Rasa</i>	62.5 – 125	<i>Hridya</i> (cardiac health), <i>Manasroga</i> (psychiatric disorders)	[26]
<i>Malla Sindura</i>	62.5 – 125	<i>Tamaka Swasa</i> (bronchial asthma)	[6]
<i>Rasapushpa</i>	62.5 – 125	<i>Visuchika</i> (gastroenteritis/cholesterol), <i>Kushtha roga</i> (skin diseases)	[6, 23]
<i>Mrityunjaya Rasa</i>	60 – 125	<i>Sarva Jwara</i> (all fevers), <i>Agnimandya</i> (digestive impairment)	[6, 25]
<i>Vaikranta Bhasma</i>	62.5	<i>Grahani</i> (malabsorption syndrome), <i>Pandu</i> (anemia), <i>Rajayakshma</i>	[6, 23]
<i>Nagavallabha Rasa</i>	62.5 – 125	<i>Vata Roga</i> (Vata disorders), <i>Prameha</i> , <i>Ksaya</i>	[6, 27]
<i>Varisosana Rasa</i>	62.5 – 125	<i>Udara Roga</i> (abdominal diseases), <i>Daurbalya</i> (weakness)	[6, 25]
<i>Makaradhwaja</i>	125	<i>Vajikarana</i> (aphrodisiac), <i>Rasayana</i> (rejuvenation)	[6, 25]

Observations reveal ultra-low dose category (2-15.62 mg) includes highly processed mercury preparations, *Kupipakwa Rasayanas*, and potent *Bhasmas* used in acute conditions. Standard low dose category (62.5-125 mg) encompasses majority of formulations, *Rasa Yoga* formulations used in chronic conditions. Greater processing intensity correlates with lower dose, more potent ingredients require lower dose, and acute conditions may require lower initial doses.

9. Mechanism of Action

Classical perspective holds *Rasaushadhis* work through *Yogavahitva* (acting as vehicles enhancing drug delivery and targeting), *Rasibhava* (assimilation and transformation at the tissue level), *Dhatu Pacana* (metabolic transformation and tissue nourishment), and *Srotosodhana* (channel clearing and purification).^[14]

Modern scientific understanding suggests *Rasaushadhi* nanoparticles serve dual functions.^[28] As substrates, they provide essential trace elements and correct metabolic deficiencies, with *Yashad Bhasma* (Zinc) acting as an insulin mimetic.^[13] As catalysts, they accelerate biochemical reactions, scavenge free radicals, and modulate enzymatic activity.^[28]

The mechanism of action of *Bhasma* is rooted in a fundamental concept: these preparations are not simply fine powders but are a form of "ancient nanomedicine." The elaborate processing transforms raw minerals into stable, bioavailable nanoparticles ranging from 5-50 nanometers. This nano-size, combined with chemical form change, is the core reason for low-dose efficacy and distinct pharmacokinetic profile.^[12]

The classical concept of *Rasayana* (rejuvenation) correlates with antioxidant and anti-inflammatory activity evidenced by free radical scavenging studies.^[11,18] *Dhatu Pacana* (tissue metabolism) corresponds to cellular uptake and mitochondrial activity.^[22] *Srotosodhana* (channel clearing) correlates with microcirculation improvement.^[12] *Yogavahitva* (targeted delivery) corresponds to targeted nanocarrier activity.^[10,14] Emerging research

suggests *Rasaushadhis* act through multi-target interactions, modulation of signaling pathways, epigenetic modifications, and gut microbiota modulation.^[5,28]

10. DISCUSSION

The convergence of classical Ayurvedic wisdom with modern scientific understanding provides compelling evidence for the principle of *Alpamatra*. Classical *Samskaras* are sophisticated nanotechnological processes: *Marana* achieves top-down nanoparticle synthesis^[15,16], *Bhavana* enables green synthesis and stabilization^[10], and *Shodhana* ensures detoxification and safety.^[9] The *Yukti* principle is validated by modern pharmacokinetics: enhanced surface area explains low-dose efficacy, improved bioavailability explains rapid action, and targeted delivery explains selective tissue effects.^[1,4,12] *Rasaushadhis* represent ancient nanomedicines with particle sizes in the nano-range (5-50 nm), enhanced cellular uptake, and biocompatibility when properly prepared.^[5,12]

Critical to enabling low-dose therapy is a rigorous detoxification process. Classical texts emphasize that properly processed *Rasaushadhis* are safe and therapeutic while improperly prepared preparations are toxic.^[4,9] Modern studies confirm that properly prepared *Bhasmas* show minimal toxicity; improper processing leads to heavy metal accumulation; and classical methods are essential for safety.^[9,11] Benefits are contingent on strict adherence to classical manufacturing procedures. A study analyzing commercial *Swarna Bhasma* samples found that 2 of 5 preparations were suspected of non-adherence to Ayurvedic references, leading to vastly different physicochemical and biological properties.^[17] Reports of heavy metal poisoning from traditional medicines are often linked to inappropriate use, poor manufacturing, or contamination, highlighting pharmacovigilance and quality control necessity.^[8, 17]

The *Alpamatra* principle has significant clinical implications: easy administration, palatability, cost-effectiveness, minimal raw material required, sustainable

preparation, reduced environmental impact, rapid onset of action, enhanced bioavailability, and targeted delivery.^[3,5,12] Limitations include variability in preparation affecting nanoparticle characteristics; limited standardization with different batches showing size variation; and need for more clinical studies with direct evidence from human trials^[5] Future research should focus on standardization of nanoparticle synthesis with reproducible protocols; mechanistic studies elucidating molecular pathways; clinical trials establishing evidence-based guidelines; comparative studies against conventional therapies; and toxicological assessment establishing safety profiles^[12, 22].

11. CONCLUSION

The principle of *Alpamatra Maharthatvam* stands as one of the most sophisticated concepts in classical Ayurvedic pharmaceuticals. Classical *Samskaras*—*Shodhana*, *Marana*, and *Bhavana*—are not merely ritualistic but scientifically valid processes that transform raw minerals into biocompatible nanoparticles.^[9,10,15]

The *Yukti* principle emphasizing rational processing provides theoretical framework for achieving maximum therapeutic effect with minimal quantity.^[1,4] Modern analytical studies consistently validate the nano-dimensional nature (5-50 nm) of properly prepared *Bhasmas*, explaining enhanced bioavailability and rapid action.^[13,16,17] *Rasaushadhis* represent an ancient, indigenous system of nanomedicine offering safe, economical, and effective therapeutic options.^[5,12] The convergence of traditional wisdom and modern science opens new avenues for developing cost-effective nanomedicines based on Ayurvedic principles.^[22,28]

The efficacy of *Bhasma* at a low dose is not a mystery but the result of intentional design. By creating biocompatible, stable nanoparticles, classical Ayurvedic processes ensure superior bioavailability where nano-size allows significantly greater absorption than raw mineral, meaning smaller dose delivers more active material to body; targeted delivery where inherent nanoparticle properties influenced by processing and herbal additions guide medicine to specific tissues; and enhanced safety where chemical transformation of metal into stable, non-toxic form makes substance safe for ingestion even at high local concentrations achieved by nano-formulation.^[5,10,12] Research should focus on standardizing preparation methods, elucidating molecular mechanisms, and conducting rigorous clinical trials. Integration of *Rasa Shastra* principles with modern nanotechnology holds promise for addressing contemporary healthcare challenges.^[5,22,28]

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13. Summary Table: Classical Concepts and Modern Correlations

Classical Concept	Modern Correlation	Scientific Evidence
<i>Yukti</i> (Rational Processing)	Pharmaceutical Processing	Proper <i>Samskara</i> determines therapeutic efficacy; improper preparation reduces potency ^[1, 4]
<i>Samskara</i>	Nanotechnology	Multi-step processing creates nanoparticles (5-50 nm) with enhanced properties ^[12, 16]
<i>Shodhana</i> (Purification)	Detoxification	<i>Tamra Bhasma</i> study: purified copper safe at 5x dose; unpurified caused organ damage ^[9, 11]
<i>Marana</i> (Incineration)	Nanoparticle Synthesis	Particle size reduction: <i>Jasada Bhasma</i> 1.5 μm $\rightarrow$ 31 nm; surface area increased million-fold ^[13, 15]
<i>Bhavana</i> (Levigation)	Green Synthesis/Capping	Herbal phytochemicals act as reducing, capping, and stabilizing agents ^[10]
<i>Alpamatra</i>	Low-dose Efficacy	2-125 mg doses produce effects requiring grams of conventional herbs ^[6]
<i>Kshipramarogyadayitvat</i>	Rapid Bioavailability	Nanoparticles provide 3x higher cellular uptake; rapid dissolution and absorption ^[12, 22]
<i>Yogavahitva</i>	Targeted Drug Delivery	Herbal capping agents guide nanoparticles to specific tissues ^[10, 14]
<i>Rasibhava</i>	Bioavailability	Organo-metallic complexes enhance assimilation and tissue integration ^[14]
<i>Dhatu Pacana</i>	Cellular Metabolism	Nanoparticles participate in cellular uptake and metabolic pathways ^[22, 28]
<i>Rasayana</i>	Antioxidant/Anti-inflammatory	Free radical scavenging and immunomodulatory effects ^[11, 18]