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Parallels between Nanoscience and Rasashastra, the Ancient Indian Science of Iatrochemistry W.S.R. to Lohabhasma – A Critical Review

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ABSTRACT

Nanoscience is an emerging field of study in the modern world. However, the ancient Indian science of Indian iatrochemistry, i.e., *Rasashastra*, has already employed several techniques to produce minuscule particles whose size is often found to be in the nanoscale. While the safety of nanoparticles synthesized through modern techniques is yet to be proven, *Rasashastra* has long been successfully using its nanoparticles through several routes of drug administration besides oral. Therefore, viewing current nanoscience from the light of *Rasashastra* may provide clues on how to make nanoparticles safer to use and may lead to aspects of their applicability that are different from the currently acknowledged uses of nanoparticles. The present work presents a critical analysis of nano synthesis through both sciences and concludes that an approach that unites both would benefit the scientific world by potentially filling various knowledge gaps that exist today.

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INTRODUCTION

Nanomedicine is one of the hot topics in the medical world today, owing to the manifold benefits provided by nanoparticles therapeutically. While this subject is often considered the brainchild of several scientists of the modern world, it must be noted that the ancient Indian science of *Rasashastra* (Indian iatrochemistry) has explored the activity of nanoparticles of various metals and minerals, known as *Bhasma* (calyx). In *Rasashastra,* crude earth materials have been subjected to specific serial processes and converted into nanoparticles *(Bhasmas)* that are safe for consumption, compatible with the body and beneficial therapeutically when prescribed in minimal doses with specific adjuvants. Despite the long journey made by *Rasashastra* through several centuries, serving the society by dexterously processing metals and minerals into potent medicines, over recent times, the modern world has developed certain apprehensions against the use of these classical herbomineral formulations. Understanding the already-established science of *Rasashastra* would not only reveal the depth of the scientific knowledge present in these texts but also open new doorways in modern nanomedicine. With this background, the present article attempts to present an overview of both sciences in a crux so as to trigger ideas of collateral thinking in terms of application of *Rasashastra* and nanomedicine for the benefit of mankind.

Main text

The concept of *Bhasma*

The Sanskrit term *Bhasma* literally refers to something that can frighten, censure, blame, shine or insult.[1] At the outset, it might just appear that the word *Bhasma* refers to “ash.” But looking at its etymology, one might wonder what could be so frightening about it. Well, the *Bhasmas* of *Rasaśāstra* can frighten diseases when used appropriately and the *Kuvaidyas* (physicians with inadequate knowledge) do not know how to use them. The raw drugs involved in the formation of *Bhasmas* are subjected to so many procedures that by the time they attain the *Bhasma* form, they are so potent that they can exhibit tremendous action with minimal dose. One of the important factors that contribute to this potency of *Bhasmas* is the minuteness of particle size. Recent studies have confirmed that *Bhasmas* prepared using the classically mentioned procedures are made up of particles with sizes that range in nanometres. This suggests that our ancient seers were indeed doyens of nanotechnology, for they have described how crude metals, minerals and ores can be brought to the nanosize and

provide therapeutic benefits. Traditionally prepared nanoparticles *(Bhasmas)* can be effectively used for the prevention and management of a wide range of diseases, thus essentially improving Quality of Life and life expectancy.

The concept of nano synthesis and its correlation with *Rasashastra*

Nanoparticles are prepared by two methods:

- Bottom-up
- Top-down

The "top-down" method is the mechanical grinding of bulk metals with subsequent stabilisation using colloidal protecting agents, i.e., reducing bulk matter into nanoform The "bottom-up" methods include chemical reduction, electrochemical methods, and sono-decomposition, i.e., building up of material from the bottom, from the atomic level.[2] Among these, we may observe that the *Bhasma* preparation method in *Rasaśāstra* usually involves the top-down method. *Bhasma* preparation is a long process with several Standard Operating Procedures, which begins right at the level of identification of the appropriate *(grāhya)* raw drug, followed by its elaborate procedures of *śōdhana, māraṇa* and any intermediate procedures such as *jāraṇa* based on the Dravya.

The resultant *Bhasma* obtained is considered fit for use only if it passes through a series of Quality Assessment parameters known as *Bhasmasiddhilakṣaṇas.* This assessment is known as *Bhasmaparīkṣā.* The various assessment criteria mentioned here prove that one of the intentions behind these tests is to check for the presence of particles in the nanoscale. For instance, there are criteria such as *Rēkhāpūrṇatva,* wherein the *Bhasma* must satisfy the condition of being so minute that it can penetrate the fissures of the fingerprint. To quote yet another example, it is mentioned that *Svarṇabhasma* should be red like *kuṅkuma.* However, insufficient reduction of particle size does not result in this red colour. Modern studies have explained that during the formation of nanoparticles of gold, there comes an intermediate stage of the formation of gold "nanowires."[3] These nanowires tend to absorb most of the visible light. During this stage, their colour is blue. Then, they transform into spherical nanoparticles which only absorb light in the blue-green region, leading to the formation of red colour. Thus, red colour is obtained only when nanoparticles of gold are formed. This

means that in the process of reducing the particle size of gold, our *Ācāryas* have not settled for any stage less than the nano stage. As we can see, our seers have left no stone unturned.

Bhasma preparation in *Rasashastra* follows the top-down approach and involves various procedures and can be broadly brought under the following heads:

1. Collection of *Grahyadravya* – Collection of minerals or ores of optimum quality, i.e., possessing appropriate geological features as stated by the classical texts

2. *Shodhana* – Subjecting the mineral or ore to purificatory procedures

3. *Jarana/Marana* – The final stage of particle size reduction

Sometimes, the prepared *Bhasma* is further subjected to trituration or levigation to fortify the *Bhasma*, and these process further aids in particle size reduction.

The science behind the pharmaceutics of *Bhasma* may be understood along the following lines.

1. Collection of *Grahyadravya*: The first step of *Bhasma* pharmaceutics lies in the selection of the appropriate ore or mineral. The collection of authentic sample influences the quality of finished products, which is directly related to the therapeutic effect of a drug.[4]The chemical and structural makeup of minerals directly affects their physical properties. The physical characteristics of colour, lustre, streak, hardness, cleavage, fracture, crystal shape, and specific gravity are the most helpful for identifying minerals. Other characteristics including magnetism, tenacity, taste, and odour, as well as heating in open and closed tubes, can be used to identify specific minerals.[5] Thus, looking at the *Grahyalakshana* ensures that the base material used for pharmaceutics is of nothing but optimum quality.

2. *Shodhana:* *Shodhana* involves various procedures that are intended for purifying the raw drug. However, its role is much wider than mere purification. In some drugs, *Shodhana* aids to reduce particle size, fortifies the drug in some, and removes toxicity in some others. A few *Shodhana* procedures are shown here.

Table 1: Probable mechanisms of various pharmaceutical procedures of Shodhana

Name of the process	Description	Probable mechanisms involved
Bhavana	Levigation of solid drugs with specified liquid media such as plant juices, extracts, water or milk	The mechanical force exerted during levigation and the metabolites of the liquid used for levigation may account for the reduction of particle size. Furthermore, the phytoconstituents from the liquid medium get imparted into the material being levigated and thereby add therapeutic value to it, detoxifying it or fortifies it.
Dhalana	Liquefaction of metal and pouring the molten metal into a liquid medium (such as the pouring of molten lead into lime water)	The process of pouring a molten metal into a liquid at room temperature causes the separation of adulterants and heterogenous substances from the desired material. Further, the rapid change in temperature experienced by the metal can cause the breakage of some chemical bonds thereby altering the chemical and physical structure.
Mardana	Trituration	Trituration too, may act in a fashion similar to that of levigation, with the main roles being reduction of particle size and chemical alteration.
Nimajjana	Soaking in water or other	Soaking the material in water aids

	liquid media	in the removal of any chemical impurities that are water soluble and also washes the substance to remove physical impurities. It may also aid in softening and disintegration of the particles.
Nirjalikarana	Removal of water	This process involves the evaporation of water molecules which makes the material free from moisture.
Nirvapa	Quenching of red hot metal, mineral or ore into a liquid medium at room temperature	The rapid quenching of a red hot material essentially lowers the temperature all of a sudden. This contrast of temperature breaks the bonds and creates spaces in the crystal lattice that paves the way for phytoconstituents of the liquid medium to enter. Further, the temperature change induces brittleness and softness.

3. *Marana*

Table 2: Probable mechanisms involved in the pharmaceutical procedures of Marana

Name of the process	Description	Probable mechanisms involved
Chakrikanirmana	Making small even pellets of triturated material prior to incineration	The process of making thin pellets makes the transmission of heat even throughout the set-up. Since the pellets are placed in such a manner that there is no overlapping, heat is distributed efficiently and in an even fashion, ensuring appropriate incineration throughout the material.
Samputikarana	Arranging the pellets on an earthen plate such that the pellets do not touch each other and closing it with another earthen plate inverted and sealing the joint of the two plates through layers of mud-smeared cloth	The role of mud may be due to its heat resistance. It is also chemically inert, organic and safe to use.
Putapaka	Incineration of the above set-up using appropriate fuel (classically cow dung cakes)	Cow dung cake is known to be able to absorb fumes generated while burning and also serve as a fuel that provides sustained heat. It also provides controlled temperature for incineration which can be tailored as per the substance in question. Due to the various properties of cow dung, it may be stated that the biofuel renders the bi-products of combustion safe into the environment.

The above concepts are being discussed herewith using the example of *Lohabhasma* (iron calyx). *Lohabhasma* is prepared through the steps shown in *Figure 1*.

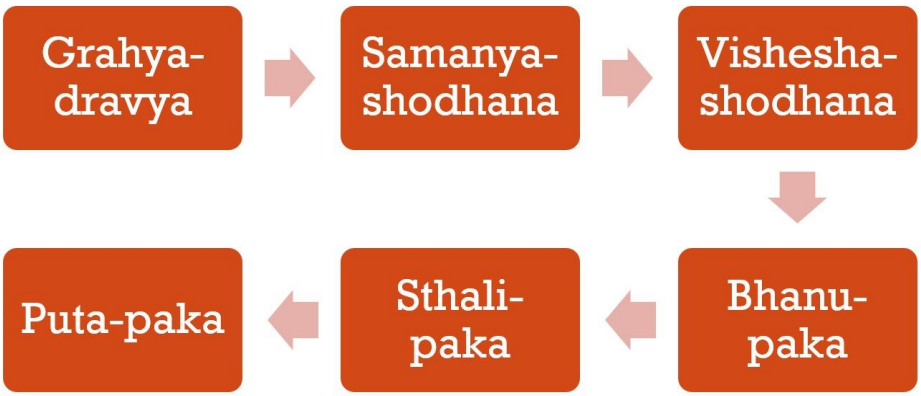

Figure 1 - Pharmaceutical processes involved in the preparation of Lohabhasma

Figure 2: The concept of Nirvapa

Step 1: *Shodhana of Loha*

Lohashodhana is classically to be done by *Nirvapa* method (as described in Table 2). When red hot iron is quenched into *Triphalakwatha* (a polyherbal decoction) at room temperature, there is the formation of microcracks which may be helpful in incorporating nanostructure and in improving reactivity with herbal constituents. There is also the removal of oxides of Fe^{+3} by forming complexation with herbal and animal products. Further, iron forms complexes with corilagin, chebulagic acid and ellagic acid from Triphala which effectively results in the preservation of iron molecules in biocompatible form. These complexes are said to be then converted into gallic acid which is hepatoprotective.[6]

Step 2: *Trividhapaka*

Following *Shodhana*, *Loha* is subjected to three stages of *Paka* (processing) – *Bhanupaka* (exposure to direct sun rays), *Sthalipaka* (placing the contents over the direct fire) and *Putapaka* (incineration).

Name of the process	**Description**	**Probable mechanisms involved**
Bhanupaka	*Loha* is immersed in *Triphalakwatha* (a polyherbal decoction) and placed under direct sun rays.	The contents are exposed to physical and chemical changes in the open atmosphere which leads to the oxidation of iron. Further, UV radiation from the sun in the presence of ascorbic acid reduces the oxidation state of Fe.
Sthalipaka	The mixture of *Loha* and *Triphalakwatha* is placed over a direct fire and cooked.	This may hasten the process of oxidation, soften the particles and fortify the *Bhasma.*
Putapaka	Pellets are prepared and incinerated.	Incineration leads to the carbonisation of the herbal material in the liquid media.[7] Carbon helps in reducing the metal. Cow dung cakes used as biofuel hastens the process by the quantum of heat applied.[8] Some studies also demonstrate the corrosive potential of cow dung ash[9] which may also contribute to particle size reduction. Furthermore, bacteriocin producing lactic acid bacteria were isolated from cow dung cakes and were found to control the growth of post-harvest spoilage microorganisms of fruits, which means the cow dung ash that results out of the

		incineration is also useful as manure. Thus, no part in the entire pharmaceutical process stated herewith is harmful to the environment.[10] Cow dung is also recognized as an eco-friendly and indigenous material for biosorption (removal) of heavy metal ions,[11] adding to the safety of the final product. Cow dung ash ash is an eco-friendly and low-cost absorbent that contains 12.48% calcium oxide, 0.9% magnesium oxide, 0.312% calcium sulfate, 20% aluminium oxide, 20% ferric oxide and 61% silica. The presence of a maximum percentage of silica exhibits considerable affinity for metal ions. This also proves that the biofuel used aids in the removal of heavy metals.[12]

Other evidence of nanotechnology in *Rasashastra*

Nanoparticles have been detected in formulations such as follows.

- **Vishaghnadhuma:** Balkrishna A et.al., (2022); demonstrated that polyherbal fumigation was able to produce on combustion, particles of 354 ± 84 nm size, laden with anti-microbial metabolites.[13]

- **Anutaila:** Duraipandi S et.al., (2018); analysed "Anutaila," a classical Ayurvedic formulation for its microarchitecture and demonstrated that the formulation contains nanoparticles and interpreted that the formulation has the ability to cross the blood-brain barrier due to its small particle size.[14]

- **Guggulutiktaka-ghrita:** Duraipandi S et.al., (2018) studied the microarchitecture of Guggulutiktaka ghrita, a classical Ayurvedic formulation made out of herbs and ghee and detected particles of the size 49.31±11.3 d.nm with PDI of 0.156.[15]

- **Rasasindura:** Ramanan N et.al., (2015); investigated the structural aspects of *Rasasindura,* a unique classical formulation made out of mercury and sulphur following several inimitable pharmaceutical procedures and detected particles sized 24 nm.[16]

Based on the above studies, it may be stated that preparations where several *Sanskaras* (pharmaceutical procedures creating transformation of the qualities of the contents) are involved, may show the presence of nanoparticles owing to the various steps that lead to particle size reduction. These processes are those that often involve high temperature and high pressure or application of heat for a long period of time, as seen in the above preparations. Furthermore, the phytochemicals present in the herbs that constitute the above formulations may also be held responsible for this unique microarchitecture reported. It is now a question of interest to investigate other formulations of Ayurveda for their particle size.

CONCLUSION

There are several pieces of evidence from Rasashastra and Bhaishajyakalpana that pronounce the presence of modern scientific concepts in Ayurveda. In fact, the current knowledge seems primitive in comparison to what our seers were experts in.

There remains not the faintest of doubts that our *Ācāryas* were, unquestionably, masters in nanoscience. Crude earth materials were processed into nanoparticles, thereby not only making them available for assimilation but also enhancing their bioavailability and stability. Their thorough understanding of metals and minerals is evident in their recognition of the versatility of these substances, owing to which, the therapeutic applicability of these substances has been described in a detailed fashion with accurate instructions regarding their dose, adjuvants, cautions against hazards and antidotes in case of toxicity by improper use. While it is now the dawn of modern nanomedicine towards the administration of metallic nanoparticles, the traditional science of *Rasashastra* gives clear instructions regarding their pharmaceutical aspects and therapeutical applicability. Talking about the nonacceptance of *Ayurvedic* metallic preparations among many in society today, it may be noteworthy that ancient science has given us clear instructions on the conversion heavy metals and even

markedly toxic substances such as arsenic and mercury into safely consumable and therapeutically promising medicines. Understanding *Rasashastra* in its true sense along with the viewpoint of modern scientific knowledge would enable us to apply our traditional knowledge in newer ways and march dynamically towards better public health by preventing and treating various diseases through traditionally prepared nanoparticles *(Bhasmas),* ultimately opening new doorways to longevity.

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