

Ayurvedic Bhasma: the most ancient application of nanomedicine

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Received 21 April 2010; revised 08 October 2010; accepted 11 October 2010

In practice of Ayurveda, herbo-mineral/metallic formulations (*Bhasma* of metals and minerals) are used since 7th centuries. It was supposed that these medicines have superior level of efficacy in comparison to other Ayurvedic dosage forms. Several studies claimed that *Bhasmas* are biologically produced nanoparticles.

Keywords: Bhasma, Herbo-metallic, Herbo-mineral, Nanocrystal, Nanoparticles

Introduction

Concept of reduction in particle size of metals is prevailing since Charaka Samhita (1500 BC). For a metallic preparation of *Lauhadi Rasayana*, iron is heated up to red hot and quenched in some liquid media immediately until flakes of iron become in fine powder form¹. Nanotechnology² has ability to work at these levels, to generate larger structures with new molecular organization. *Bhasmas*, which are unique Ayurvedic metallic/mineral preparations, treated with herbal juices or decoction, and exposed for certain quantum of heat as per *Putra* system of Ayurveda are known in Indian subcontinent since seventh century AD and widely recommended for treatment of a variety of ailments³. *Bhasmas* are claimed to be biologically produced nanoparticles (NPs), prescribed with several other medicines of Ayurveda.

This study reviews Ayurvedic *Bhasma* as most ancient application of nanomedicine.

Preparation of Bhasma

Bhasmas are being prepared by *Putapaka* method and *Kupipakwa* method.

Putapaka Method

Bhasma is being prepared by subjecting metals or minerals to three step procedures (*Shodhana*, *Bhavana*

and *Marana*). Metals or minerals are made by hammering into coarse powder, which are subjected to *Shodhana* (purification), wherein metals or minerals are heated to red hot or melted and quenched in particular liquid media for specified times. *Shodhita* materials are then mixed with specific drugs for incineration (*Maraka Dravyas*) and are levigated (*Bhavana*) by particular liquid media for specified time. *Bhavana* is a process of wet grinding, in which materials are ground with particular liquid media for a specific period.

From levigated doughy mass, *Chakrikas* (pellets) are prepared and taken into earthen crucibles faced together, and junction is sealed by mud smeared clothes. This apparatus (*Sarava Samputam*) is subjected for heating in traditional *Putra* (heating grade) or electric muffle furnace. Heating of materials continue to this apparatus is called as *Putapaka* in parlance of Ayurveda. Burning is continued for a specific time limit and when cooled down, apparatus (*Sarava Samputa*) is taken out and opened to get incinerated powder. These procedures are repeated for particular time and finally prepared *Bhasma* (incinerated metal) is collected.

For metals having low melting point (lead, tin and zinc), between *Shodhana* and *Bhavana* procedure, one intermediate procedure called as *Jarana* (polling) is performed. In this procedure, metals are melted and mixed with some plant drugs powders and are rubbed by a iron ladle with inner surface of pot until metals become in complete powder form.

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Kupipakwa Method

In this method, *Bhasma* are prepared by subjecting metals (gold, silver, copper, etc.) to four step procedures (*Shodhana*, *Kajjali* preparation, *Bhavana* and *Kupipaka*). After *Shodhana*, metals are subjected for amalgamation with mercury, and then purified sulphur is mixed and triturated till black, lusterless, fine and smooth mass is prepared. This procedure is called as *Kajjali* preparation. Prepared *Kajjali* is levigated by particular liquid media for certain period. It is allowed to complete dryness and filled in a glass bottle (*Kachkupi*) covered by 7 layers of mud smeared cloth. Bottle is then subjected to sand bath (*Valukayantra*) for indirect and homogeneous heating for a certain period. After self cooling, bottle is broken, sublimed product is collected from neck and *Bhasma* is collected from the bottom of bottle and ground to powder form.

Changes during Bhasma Preparation

During *Shodhana*, tension is increased in matter by application of heat, causing linear expansion. After heating, immediate cooling in liquid media leads to decrease in tension and increase in compression force. Repetition in heating and cooling causes disruption in compression tension equilibrium leads to increased brittleness, reduction in hardness and finally reduction in particle size. Some metals and minerals during red hot state react with atmospheric oxygen or steam and form chemical compound. Iron, when heated to red hot, reacts with atmospheric oxygen or steam to form ferrous-ferrous oxide (Fe_3O_4)⁴. Copper in moist air is converted to basic copper sulphate, which on red hot state is completely decomposed to cupric oxide⁴.

In *Bhavana* process, materials with liquid media are rubbed between surface of pestle and mortar. This process involves breaking down of material by rubbing action between two surfaces, when stress in the form of attrition is applied; particle surfaces chip and produce small particles. Wet grinding eliminates hazards of dust. Finer size can be achieved by wet grinding than by dry grinding⁵. Oxidation of metals occurs during heating at open air in *Jarana* procedure. The melting point of metals also increases due to oxidation. Inorganic part of plant material supplies trace elements to materials. During incineration (*Putapaka*), generally compounds are formed on metal surface. Repetition of this process leads to reduction in particle size⁶. After *Marana*, metals generally convert to their compound forms, which are biologically favorable to the body.

Characterization of Bhasma

Physical Characters

(1) Colour (Varna)

A specific colour is mentioned for each *Bhasma*. Alteration in specific colour suggests that *Bhasma* is not prepared properly. Because a particular metallic compound is formed during *Bhasma* preparation and every chemical compound possesses specific colour.

(2) Nishchandravam⁷

Bhasma must be *Nischandra* (lusterless) before therapeutic application. *Chandravam* (luster) is a character of metal. After proper incineration, luster of metal should not remain. For this test, *Bhasma* is observed under bright sun light, whether luster is present or not; if luster is still present, it indicates further incineration.

(3) Varitara⁸

Varitara test, applied to study lightness and fineness of *Bhasma*, is floating character of *Bhasma* on stagnant water surface. This test is based on law of surface tension. Little amount of *Bhasma* is taken in between index finger and thumb, and sprinkled it slowly on stagnant water surface from a short distance. Properly incinerated *Bhasma* will float on water surface.

(4) Unama Test⁸

It is further assessment of *Varitara* test. A grain of rice is to be kept carefully on the layer of floated *Bhasma*. Observe whether grain floats or sinks. If grain remains as it is on layer, then *Bhasma* can be considered as excellent (properly prepared).

(5) Rekhapurnata⁸

This test is applied to study fineness of *Bhasma*. *Bhasma* particles should be of minimum size for easy absorption and assimilation in the body. *Bhasma* should be so fine that it can fill furrows of finger tips. A little amount of *Bhasma* is rubbed in between index finger and thumb to observe whether particles can fill furrows of finger tips.

(6) Slakshnatvam⁷

It is tactile sensation produced by *Bhasma* by simple touch with finger tips. Properly incinerated *Bhasma* attain this quality. *Slakshna Bhasma* can be absorbed and assimilated in the body without producing any irritation to mucous membrane of gastrointestinal tract.

(7) *Susukshma*⁷

It indicates fineness of *Bhasma* preparation. This character can be perceived by *Varitara* and *Rekhapurnata*. *Bhasma* must be *Sukshma*, so that it can be absorbed in the body easily.

(8) *Anjana Sannibha*⁷

Anjana (collyrium) is smooth in character and it does not create any irritation whenever applied. Properly incinerated *Bhasma* should be smooth and should not create any irritation to mucous membrane of gastrointestinal tract.

(9) Particle size

Prepared *Bhasma* should be in *Churna* (powder) form. Size of particles of *Bhasma* will be like pollen grains of *Pandanus odoratissimus* flower (Ketaki Rajah)⁹.

(10) *Gatarasatvam*⁷

Properly incinerated *Bhasma* of a metal should be of particular taste. It indicates transformation of particular metallic taste to compounds of specific taste.

Chemical Characters**(1) *Apunarbhavata***⁸

Apunarbhava means incapability to regain original metallic form. For this test, *Bhasma* is mixed with equal quantity of *Mitra Panchaka*¹⁰ (seeds of *Abrus precatorius*, honey, ghee, borax and jaggery) and it is sealed in *Sarava Samputa* (earthen pots), thereafter, similar grade of heat used for preparation of particular *Bhasma* is applied and on self cooling product is observed. Lustrous particles in it show presence of free metal, which is indicative of improper incineration.

(2) *Niruttha*⁸

Niruttha is to test inability to regain metallic form of metallic *Bhasmas*. In this test, *Bhasma* is mixed with a fixed weight of silver leaf, kept in earthen pots and similar grade of heat is applied and after self cooling, weight of silver is taken. Increase in weight of silver leaf indicates improperly prepared *Bhasma*.

Attributes of *Bhasmas*

All *Bhasmas* have some common properties like *Rasayana*, *Yogavahi*, etc. *Rasayana* indicates immunomodulation and anti-aging quality; and *Yogavahi* indicates ability of drug carry and targeted drug delivery by *Bhasmas*. These are prescribed in very minute dose (15-250 mg/ day). Under *Rasibhavana*⁸, properly

prepared *Bhasma* must be readily absorbable, adaptable and assimilable in the body, and will be non-toxic. *Shighravayapti*⁸ indicates that after *Marana*, *Bhasma* becomes easily absorbable and assimilable in the body and spreads quickly in the body. Under *Agnideepana*⁸, *Bhasma* increases metabolism at cellular level and acts as catalyst.

These attributes of *Bhasmas* are comparable with the action of NPs in the body. These are biodegradable, biocompatible and non-antigenic in nature. NPs, in general, can be used to provide selective/targeted/controlled delivery of drugs to specific site of action in the body even across the blood-brain barrier. These can be used to extend time window of bioavailability and to protect drug from chemical and enzymatic decomposition. These can also result in reduction of peripheral side effects of drugs by decreasing overall dose of drugs in the body¹¹.

Ayurvedic *Bhasma* and Nanotechnology**Importance of Particle Size Reduction**

During *Putapaka* method, size of particles of material reduces. More effectiveness of *Bhasma* with increasing number of *Putapaka* is mentioned in classics. *Putapaka* is needed for different purposes as follows¹²: simple therapeutic, 10 - 100; aphrodisiac (*Vajikaran*), 10 - 500; and for immunomodulation (*Rasayana*) of *Bhasma*, 100 - 1000.

Particulars of Nanostructure Formation by Mechanical Activation

Bhasma are nearer to nanocrystalline materials. In terms of nanotechnology, nanocrystalline materials are solids composed of crystallites with size less than 100 nm in at least one dimension¹³. Formation of nanocrystalline material during mechanical alloying and milling was first suggested by Koch *et al*¹⁴ and was validated by Fecht *et al*¹⁵. Similar crystalline sizes may be obtained through conventional ball mills and other techniques, suggesting that it is total strain, rather than milling energy, that decides minimum attainable grain size by mechanical milling¹⁶. Various milling parameters (milling temperatures, nature of products and number of phases present during mechanical milling and alloying) have a pronounced influence on limiting attainable grain size and product phases¹⁷. Ayurvedic concept of *Mardana* (trituration) and *Bhavana* (levigation) to reduce particle size is an ultimate result of these processes.

Detection of Nanoparticles in *Bhasma*

Methodologies used to test NPs are environmental electron microscopy, Scanning electron microscopy

(SEM), transmission electron microscopy (TEM), cryo-TEM, fast-freeze fracture, confocal laser scanning microscopy, fluorescence optical microscopy, quasi-elastic light scattering, energy dispersive x-ray analysis (EDAX), inductively coupled plasma (ICP), atomic absorption spectroscopy (AAS), x-ray induced photoelectron spectroscopy (XPS), gel electrophoresis, enzyme expression etc. Process of NPs testing in *Bhasmas* involves five steps: i) To establish presence of NPs in test sample; ii) To ascertain whether chemical composition is homogeneous; iii) Whether NPs are crystalline or amorphous; iv) Nature of defects in the sample; and v) Sample has to be biologically tested to check their bio-activity. Finally, convergence of all these factors in mechanism of action for a particular application needs to be tested as well.

***Bhasmas* as Multi-elemental Cocktail**

Bhasmas based on calcium, iron, zinc, mercury, silver, arsenic, copper, tin, and gemstones are analyzed for elements including C, H, N, and S contents. In addition to major constituent element found at % level, several other essential elements (Na, K, Ca, Mg, V, Mn, Fe, Cu, and Zn) have also been found in $\mu\text{g/g}$ amounts and ultratrace (ng/g) amounts of Au and Co. These seem to remain chelated with organic legends derived from medicinal herbs¹⁸.

***Bhasmas* as Nanoparticles (NPs)**

Gold in traditional Indian Ayurvedic medicine as *Swarna Bhasma* (gold ash) has been characterized as globular particles of gold (av size, 56-57 nm). *Swarna Bhasma* and gold NPs prepared by modern method are quite comparable with respect to TEM and SAED analysis. Nanosized gold particles (27 ± 3 nm) have been proven to be effective in ameliorating symptoms of mycobacterial, collagen and pristane-induced arthritis in rat models. Antioxidant/restorative effects of *Swarna Bhasma* against global and focal models of ischaemia (stroke) have also been reported¹⁹. Typical features of Ayurvedic *Swarna Bhasma* have been demonstrated through TEM and atomic force microscopy²⁰. A further study has shown *Swarna Bhasma* principally constituted of globular gold particle of 56-57 nm. Same study²⁰ also revealed *Swarna Bhasma* to be devoid of any other heavy metal or organic material by its screening through AAS and Infrared Spectroscopy (IS). This study also put to rest concerns about presence of heavy metals in Ayurvedic preparations, which otherwise clouds popular use of Ayurvedic medicines abroad²¹.

*Ras-Sindoor*²² (sublimed mercury compound) is contains mercury sulfide (crystalline; size, 25 - 50 nm) associated with several organic macromolecules derived from plant extract used during processing of drug. Several macro/trace elements are also be present in different amounts, which were bio-available and responsible for adding to medicinal value of *Ras-Sindoor*.

NP size of Ayurvedic *Bhasmas* has been confirmed in another study²³, where it is proposed that NPs are responsible for its fast and targeted action. Subsequent actions upon DNA/RNA molecule and protein synthesis within the cell are further hypothesized as possible mechanisms for rapid onset of therapeutic actions of *Bhasma* preparations.

Pyrgiotakis²⁴, with the help of Raman spectroscopy, has demonstrated effect of *Yashada* (Zinc) *Bhasma* on intracellular DNA and proteins of treated human lung adenocarcinoma cell line (A549). Another study²⁵ found gold NPs (4 nm size) helped in increased apoptosis in B-Chronic Lymphocytic Leukemia (CLL). It is observed that nanomedical application of various drugs is proportionate to their particle size and shape. Pharmacological efficacy of a *Bhasma* preparation is largely attributed to the number and type of *Putta* (traditional incineration process) used in its making. Increased incinerations, therefore, are able to reduce particle size and subsequently give rise to increased efficacy to a given *Bhasma*⁸.

Physicochemical characterization of *Yashada Bhasma* using modern techniques {XPS, ICP, elemental analysis with EDAX, dynamic light scattering (DLS), and TEM} reveal that *Yashada Bhasma* particles are in oxygen deficient state and a clearly identifiable fraction of particles are in nanometer size range. Properties like oxygen deficiency and nanosize particles in *Yashada Bhasma* might impart therapeutic property of particular type of medicine²⁶.

Ayurvedic pharmaceuticals are receiving a new thrust through a reappraisal of *Bhasma* preparations (preparations, where herbs, minerals and metals are incinerated to ash under supervised conditions) as novel nano-technological applications²³.

Conclusions

Herbo-mineral formulations of Ayurveda constituting *Bhasma* as an ingredients are as superior as it is even today. Manufacturing methods of *Bhasma* are in tune of nanotechnology of contemporary era and proved advancement of Rasashastra, a branch of Ayurveda, which

may cover scientific validation of today. These medicines are safe in therapeutics.

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