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 Puta 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 Sampatam) is subjected for heating in traditional Puta (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 Samputam) 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.
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 ferroso-ferric oxide (Fe$_3$O$_4$). Copper in moist air is converted to basic copper sulphate, which on red hot state is completely decomposed to cupric oxide.

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 grinding. 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 size. 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) Nischandratvam

Bhasma must be Nischandra (lusterless) before therapeutic application. Chandratva (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) Varitara

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 figure and thumb, and sprinkled it slowly on stagnant water surface from a short distance. Properly incinerated Bhasma will float on water surface.

(4) Unama Test

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) Rekhapurnata

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) Slakshnatvam

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) Susuksha
It indicates fineness of Bhasma preparation. This character can be perceived by Varitara and Rekapurnata. Bhasma must be Suksha, so that it can be absorbed in the body easily.

(8) Anjana Sannihtha
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).

(10) Gatarasatvam
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
Apunarbhava means incapability to regain original metallic form. For this test, Bhasma is mixed with equal quantity of Mitra Panchaka (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
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, properly prepared Bhasma must be readily absorbable, adaptable and assimilable in the body, and will be non-toxic. Shighravyapti indicates that after Marana, Bhasma becomes easily absorbable and assimilable in the body and spreads quickly in the body. Under Agnideepana, 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/control 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 body.

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 follows: 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 dimension. Formation of nanocrystalline material during mechanical alloying and milling was first suggested by Koch et al. and was validated by Fecht et al. 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 milling. 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 phases. 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 μg/g amounts and ultratrace (ng/g) amounts of Au and Co. These seem to remain chelated with organic legends derived from medicinal herbs.

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 reported. Typical features of Ayurvedic Swarna Bhasma have been demonstrated through TEM and atomic force microscopy. A further study has shown Swarna Bhasma principally constituted of globular gold particle of 56-57 nm. Same study 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 abroad.

Ras-Sindoors (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-Sindoors.

NP size of Ayurvedic Bhasmas has been confirmed in another study, 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.

Pyrgiotakis, 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 study 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 Puta (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.

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 medicine.

Ayurvedic pharmaceutics 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 applications.

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.

References

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