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CONCEPT OF NANOTECHNOLOGY IN MERCURIAL PREPARATIONS

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ABSTRACT

Nanotechnology is the study of manipulating matter on an atomic and molecular scale. Generally nanotechnology deals with developing materials, devices, or other structure possessing at least one dimension from 1 to 100 nanometers. The drug is encapsulated in nanoparticles which helps it pass through the stomach to deliver the drug in to the blood stream. There are efforts underway to develop oral administration of several different drugs using a variety of nanoparticles. Here comes the relevance of mercurial and other metallic preparations which authentically prescribed in Ayurveda rasashastra classics like rasaratnasamuchaya, rasatarangini etc. Different studies using advanced instrumental techniques have characterized nanoparticles in mercurial preparations such as rasa sindoor etc used in Rasashastra. Present paper throws light on such evidences. *Manufacturing methods of Bhasma are in tune of nanotechnology of contemporary era and proved advancement of Rasashastra.*

KEYWORDS: *Nanoparticles, engineered particles, mercurial preparation, instrumental techniques.*

INTRODUCTION

Nanotechnology is the production and use of materials at the smallest possible scale. Nanotechnology can be useful in diagnostic techniques, drug delivery etc.

There are two types of nanoparticles mainly herbal as well as mineral origin are used in ayurveda for curative as well as rasayana purposes.

1. Herbal nanoparticles
2. Mineral nanoparticles

Mineral nanoparticles

It mainly consist of bhasmas prepared out of different minerals mentioned in classics as rasa varga, uparsa varga, sadharana rasa varga loha varga etc. The process is called satvapatana. According to form of satvas are classified in to

1. Dhatu rupa

Abhraka, svarna makshika etc.

2. Adhatu rupa

Haratala etc

Mercury, the liquid metal, which combines with sulphur, other mineral as well as herbal dravyas produces specialsed nanoparticle structures in the mercurial preparations after the procedures like shodhana marana etc. Bhasmas, which are unique ayurvedic metallic 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 7th century AD and widely recommended for treatment of a variety of ailments. The difference between the ayurveda and modern methods of preparing nanomaterials are given below:[1]

Traditional	**Modern (Bio-Synthetic)**
Top – Down approach	Bottom-up approach
Bulk metal is converted in to smaller particles	Ions/ atoms are grown from smaller to bigger particles
Heat – Beat-Treat chemistry	Better size control
Very elaborate and time consuming	Main use in electronic and biotechnological applications
Used in Medicine	Medicinal use as diagnostic/therapeutics
Efficacy is proven	----------

MATERIALS AND METHODS

In the classics of ayurveda rasashasthra classics we can infer this type of engineering is well explained for each type of mercurial preparations, in order to fulfill all those desired treatment effects. Mainly by kupipakwa method as well as putapaka method, the mercurial preparations are prepared in ayurveda traditional system.

Different studies using advanced instrumental techniques have characterized nanoparticles in mercurial preparations such as rasa sindoor etc used in Rasashastra. Present paper throws light on such evidences.

DESCRIPTION

This study reviews mercurial and other ayurvedic bhasmas as most ancient application of nanomedicine.

Preparation of Bhasma

1. Putapaka method
2. Kupi pakwa 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 a specific period.

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

For metals having low melting point (lead, tin and zinc), between Shodhana and Bhavana procedures, 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.

Kupi pakwa 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 (kachakupi) covered by seven layers of mud smeared cloth. Bottle is then subjected to sand bath (Valuka yantra) for indirect and homogeneous heating for a certain period. After self cooling, bottle is broken, sublimed product is collected from the bottom of bottle and ground to powder form.

Changes in each stage of 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 reacts with atmospheric oxygen or steam and form chemical compound. Iron, when heated to red hot, reacts with atmospheric oxygen or steam to form ferro-ferric oxide(Fe_3O_4)[2]. Copper in moist air is converted to basic copper sulphate, which on red hot state is completely decomposed to cupric oxide.[2]

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 titration 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.[3] 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.[4] After Marana, metals generally convert to their compound forms, which are biologically favourable to the body.

Attributes of Bhasmas

All Bhasmas have some common properties like Rasayana, Yogavahi etc. Yogavahi indicates ability of drug carry and targeted drug delivery by Bhasmas. These are prescribed in very minute dose(15-250mg/day). Shigravyapti[5] indicates that after Marana, Bhasma becomes easily absorbable and assimiliable in the body and spreads quickly in the body. Under agnideepana[5], Bhasma increases metabolism at cellular level and acts as catalyst.

These attributes of Bhasmas are comparable with the action of Nanoparticles in the body. These are biodegradable, biocompatible and non – antigenic in nature. Nanoparticles, 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 body.

Ayurvedic Bhasma and Nanotechnology

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 - 10-500

Immune modulation (Rasayana) – 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 100nm in at least one dimension. Formation of nanocrystalline material during mechanical alloying and milling was first suggested by Koch and was validated by Fecht. 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) reduce particle size is an ultimate result of these processes.

Detection of Nanoparticles in Bhasma

Methodologies used to test Nanoparticles are environmental electron microscopy, scanning electron microscopy(SEM), transmission electron microscopy(TEM), cryoTEM, 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 nano particles testing in Bhasmas involves 5 steps

a. To establish presence of nanoparticles in test sample
b. To ascertain whether chemical composition is homogeneous
c. Whether nanoparticles are crystalline or amorphous
d. Nature of defects in the sample
e. 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

Bhasma 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 percentage level, several other essential elements (Na,K,Ca,Mg,Fe,Cu and Zn) have also been found in µ/g amounts and ultra trace(ng/g) amount of Au and Co. These seem to remain chelated with organic legends derived from medicinal herbs.

Bhasmas as Nanoparticles

Gold in traditional Indian ayurvedic medicine as Svarna Bhasma (gold ash) has been characterized as globular particle s gold (average size, 56-57nm). Swarna Bhasma and gold nanoparticles prepared by modern method are quite comparable with respect to TEM and SAED analysis. Nanosized gold particles (27 ±3nm) have been proven to be effective in ameliorating symptoms of mycobacterial, collagen and pristine-induced arthritis in rat models. Anti oxidant/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 56-57nm. 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

Rasasindoor (sublimed mercury compound) is contains mercury sulphide(crystalline, size 25-50nm) associated with several organic macromolecules derived from plant extract used during processing of a drug. Several macro/trace elements are also be present in different

amounts, which were bio-available and responsible for adding to medicinal value of rasa sindoor.

Nanoparticle size of Ayurvedic Bhasmas has been confirmed in another study, where it is proposed that Nanoparticles are responsible for its fast and targeted action. Subsequent actions upon DNA/MRNA 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 the effect of Yashada Bhasma (Zinc) on intracellular DNA and proteins of treated human lung adenocarcinoma cell line (A549). Another study found gold nanoparticles(4nm 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.

CONCLUSION

Herbo-mineral formulations of ayurveda constituting mercurial products, Bhasmas etc as 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, which may cover scientific validation today.

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