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Nano – Bhasmas for Chronic Non-Communicable Diseases.

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ABSTRACT

Ancient medicines were proven to cure several types of diseases worldwide. Ayurveda is an ancient medicine system of Indo – Asian continent developed to medicate countless disorders; from common cold to chronic diseases. Ayurvedic Bhasma are nanomedicines used ingeniously by the ancestors of Indian subcontinent 2000 years ago. Ayurvedic Bhasma are the ashes obtained through incineration of metallic particles prepared in combination with minerals/herbal formulation eventually known to cure several disease ailments. The new concern on applying the concept of ayurvedic bhasma to today's nanomedicine system has been in emergence in these few years. The availability of abundant characterization facilities such as TEM, SEM-EDX, AFM, XRD, HPLC and GC-MS had increased the researcher's interest towards ayurvedic bhasmas. These bhasmas in nanosized formulation has various health benefits like immune-modulation, anti-aging, improving the strength of bones with no harmful side effects. Synchronization of ayurvedic bhasma with nanomedicine could ultimately leads to better treatment and prevention of various diseases. This review paper highlights the importance of Ayurvedic Bhasma and compares it with today's Nanomedicine with a specific example in the treatment of Non-Communicable Disease (NCD).

Keywords: Ayurvedic bhasma, nanomedicine, characterization, non-communicable diseases

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INTRODUCTION

Technological development over last decades has created tremendous interest in drug discovery and development in Pharma-biotech industries. Numerous drugs notably on diabetes and cancer are being processed through, in Phase II and III clinical trials. However, from discovery of a potential molecule to commercially available formulation takes approximately 10-15 years with billion dollars and thousands of failures. Moreover, issues like biocompatibility, toxicity, sub-optimal efficiency are still a great challenge. At current scenario, nearly 50% of the drugs being explored at pharmaceutical and biotech companies are from natural resources [1,2]. Exploration of new drugs focuses on rediscovering the existing one from traditional medical systems, reducing development and formulation cost to half to that of new molecules. Hence, the need for successful drug development resulted in emergence of new technologies like nanotechnology.

Ayurveda is a traditional medical system evolved for thousands of years in South East Asian continent. Ayurvedic bhasmas are nano sized particles used for the treatment all categories of diseases. This review will provide a crisp knowledge on prehistoric medical system, Ayurvedic Bhasmas and their importance in today's modern medicine system with specific example on chronic Non Communicable Diseases (NCDs).

AYURVEDIC MEDICINE

Ayurvedic medicines are native to Indian subcontinent. The drugs are polyherbal or mineral-herbal formulations prepared as churana (powder), Ghana (concentrated aqueous extracts) or tablets. Each formulation has various bioactive phytochemicals where, each phytochemical plays different role towards the target disease. This concept is the major asset of Ayurvedic medicines. Polyherbal formulation acts as a curative network with each phytochemical engaged in unique biological activities like self-healing and increasing the native immunity, apart from acting at the disease of interest.

EXISTING THERAPEUTIC SYSTEM

The current therapeutics deliberate "one-size-fits-all-approach" and face frequent failures, as some patients do not respond to the prescribed drugs. Initiative for personalized medicines approaches are at infancy. At present, combined drug regimens provide excellent remedies but has adverse side effects. Nanomedicine elucidates most of the glitches in current therapeutics.

NANOMEDICINE

Biopharmaceutical research and development of 21st century follows the technology of producing nanosized particles, "Nanotechnology". Nanoparticles are in the size range of 1 – 100 nm in each spatial dimension [3]. The particles possess novel properties such as, high surface to volume ratio, optical and magnetic properties, increased diffusivity, solubility, bioavailability, carries large payload etc.[4,5]. The unique properties and substantial advancement in characterizing techniques furnished nanomedicines to be more vital in biomedical science.

Numerous nano-drug candidates are in clinical trials and few drugs have already reached the market. Nanomedicines like Doxil[®], DaunoXome[®], Abraxane[®] are used in the treatment of cancer [6]. Nanomedicines can be prepared from synthetic drugs, phytochemicals or combination of drugs, polymers and metallic elements. Nevertheless, a precise form of nanomedicine existed in Ayurvedic medicine system as "Ayurvedic bhasma".

AYURVEDIC BHASMA –NANO DRUGS OF ANCIENT HERBAL MEDICINES

The custom of employing minerals/metals/gems to herbal formulations is known as *Rasa shastra* [7,8]. Bhasmas are the ashes obtained by calcination of heavy metal salts such as mercury, lead, arsenic, and iron and imparted with herbal formulation or with other ayurvedic constituents. They are designated based on the metals used such as Swarna bhasma (gold), Rajat bhasma (silver) as shown in Table 1. Bhasmas are used in the treatment of immunity disorders, rheumatoid arthritis, fevers, cough, diabetes, anemia, paralysis etc. [9] and are more effective for chronic Non Communicable Diseases [10]. Nano sized Bhasmas are prepared and

characterized by various techniques. A precise knowledge on ancient preparation methods of Bhasma will help us to convert the ancient methodologies into latest therapeutic productions.

Table 1: Different kinds of Ayurvedic Bhasma

<i>Bhasma</i>	<i>Common name</i>
Abhraka Bhasma	Mica
Kantalaucha Bhasma	Magnetic iron
Lauha Bhasma	Iron
Naga bhasma	Lead
Prawal Bhasma	Coral
Rajat bhasma	Silver
Sankha bhasma	Conch shell
Swarna bhasma	Gold
Swarnamakshika Bhasma	Ores of copper (Chalcopyrite)
Tamra Bhasma	Gypsum
Vaikranta Bhasma	Calcium fluoride
Vanga Bhasma	Tin
Yashada bhasma	Zinc

Bhasmikaran

Bhasmikaran is the process of converting pristine metals to biocompatible or pharmacologically active form. Bhasmikaran involves three major steps, Purva karma (pre operation), Pradahana Karma (main operation), Paschat Karma (post operation) as shown in Figure 1.

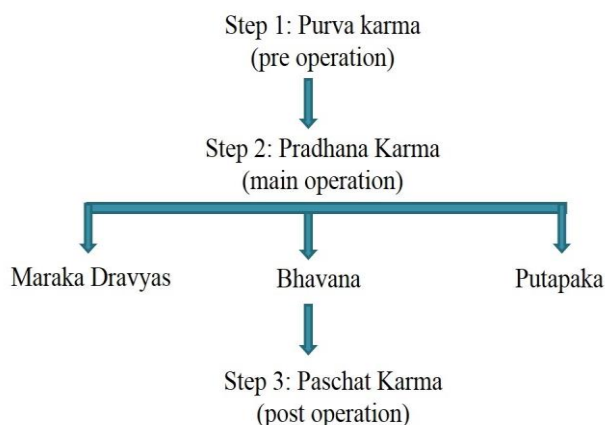


Figure 1 Process of Bhasmikaran

Purva karma

Shodhana encompasses purification of raw material, usually mineral ore/metal fillings. Metals are heated to elevated temperatures until red hotness and suddenly immersed in water or seaseem oil. This process removes most of the visible and hidden impurities. It also enhances the therapeutic action of the drug, by converting some of its desirable characteristics.

Pradahana Karma

Marana is the main procedure carried out to obtain Bhasma. It involves three important steps: Maraka Dravyas, Bhavana, Putapaka [11]. The purified raw material is subjected to incineration or calcination with some additional drugs or herbs known as Maraka Dravyas or maraka gana drugs. Maraka gana drugs supplemented during this process plays role in crumbling of metallic / mineral constituents. For example,

mercury amalgamates with many metals and finely disperses the particles into distinct elements. The acquired substances are ameliorated to finer organo-metallic compounds in the process of *Bhavana*, a wet grinding process. In the next stage, the particles are heated for several times to conceive them more brittle and fine powder in the *Putapaka* method.

Paschat Karma

This step is post-operative process carried out to enhance the Bhasma quality and to improve its therapeutic properties.

Bhasma pariksha (Physico-chemical analysis)

Certain ayurvedic parameters assess the physical and chemical properties of Bhasma [12,13].

Physical properties

Varana or the color of the final product differs for different bhasmas. *Varitara* reflects the floating property of bhasma. The as prepared bhasma floats on the water, exhibiting the characteristics of lightness and fitness. *Rekhpurnata*; a small amount of bhasma is rubbed in between the index and thumb fingers. If the bhasma can fill the furrow of the fingers, the particles are determined to be finer and smaller. *Nishchandra* is the lusterless property of bhasma ascertained under sunlight. In general, metals have trait of lustering. Nevertheless, the incinerated bhasma should be lusterless, which is an important criterion in therapeutic application. *Anjana Sannibha*, signifies the smoothness property of bhasma. Higher the smoothness, lower the irritation observed within the body when administered.

Chemical properties

Gatarasatva exhibits tastelessness property of the incinerated bhasma. *Apunarbhava*, designates the irreversible nature of the Bhasma. *Niruttha* speculates the irrecoverable attribute examined using a silver leaf. Pre-weighed amount of silver leaf blended with bhasma has to be heated and cooled. No net change in the weight of silver leaf after processing indicates that bhasma has no regain capacity. *Amala pariksha and Aksharatwa* indicates the sour taste and lack of alkaline taste in the prepared bhasma. *Avami*; a pinch of bhasma on oral administration should not create vomiting sensation. Handmade techniques were followed due to lack of characterization techniques for accessing their nano-size.

Magnificent properties of nano-bhasmas

Bhasma are nano-crystalline materials that are confirmed by the quality assessment parameters of ayurvedic era. Over the past few years, bhasmas were re-discovered and their nano size was confirmed with the advanced techniques. Bhasma has immunomodulation and anti-aging properties commonly known as *Rasayana* and has targeted drug delivery known as *Yogavahi*. They are biodegradable and biocompatible which are explained by the terms, *Rasibhavana, Shighravayapti* of the ayurvedic period [14]. Besides the main metallic elements (Ag, Fe, and Au), it contains other elements such as Ca, Mg, V, Mn, Cu etc. which plays role in improving the health.

Instrumental facilities for assessing the nanosized Bhasma

The availability of chemical analysis in 19th century [15] and the advancements of instrumental facilities to detect nano sized particles resulted in vast exploration of bhasmas. The common analytical parameters and recently developed techniques are tabulated in Table 2. Particle size, morphology, elemental analysis and toxicity studies were the major parameters used in characterization studies. Recent explorations on microscopic techniques like Transmission Electron Microscopy, Scanning Electron Microscopy and other techniques such as Nuclear Magnetic Resonance (NMR), X-Ray Diffraction Spectrometer (XRD), Chromatographic techniques such as High Performance Liquid Chromatography (HPLC) flagged a path for better understanding of Ayurvedic bhasmas [16–19].

Table 2: Instrumental facilities available for characterization of Bhasma

S.No	Instrument Name	Uses	Reference
1	Transmission electron microscope (TEM) and High Resolution TEM (HR TEM)	Particle size and size distribution	38,39
2	Scanning Electron Microscope SEM and HR SEM		
3	Dynamic light scattering	Particle size	39
4	Zeta potential	Stability	39
5	X-ray Diffraction (XRD)	Phase and lattice structure	40–42
6	X-ray Photoelectron Spectroscopy (XPS)	Elemental analysis	40
7	Energy Dispersive X-ray analysis (EDX)	Chemical nature of the particles	38
8	Electron Probe Micro analyzer (EPMA)	Distribution of individual elements	43
9	X-Ray Fluorescence (XRF) Spectroscopy		27,44
10	Particle Induced X-ray Emission (PIXE)		45
11	Inductive Coupled Plasma ICP – Elemental analysis	Elemental analysis	46
12	Electronic Spectroscopy for Chemical Analysis (ESCA)	Electronic nature and oxidation state of metal	47
13	Fourier Transform Infrared Spectroscopy (FTIR)	Chemical analysis	40,41
14	Nuclear Magnetic Resonance (NMR)	Structure of compounds	40,41
15	High Performance Liquid Chromatography (HPLC)	Extraction of organic/ biomolecules from the crude material	48
16	Other Chromatographic techniques (GC, Gel permeation)		49

BHASMA FOR CHRONIC NON-COMMUNICABLE DISEASES (NCDS)

The 21st century human health care system focuses on prevention and management of chronic NCDs. Chronic NCD affects the global population with increasing mortality every year and posed to be a challenge to the future world. The common NCD includes cancer, cardiovascular diseases, diabetes and chronic respiratory diseases. It was estimated that 38 million deaths in 2012 globally were due to NCD [20]. World Health Organization framed global targets until 2025 on reducing the mortality rate and prevention of NCD.

Ayurveda could unravel the global crunch on chronic NCDs in all aspects with reliable and efficacy outcomes [21]. Bhasmas used to treat chronic NCDs are listed in Table 3. Ayurvedic documentary evidence and current scientific reports on Bhasmas for treatment of NCDs were available until date. Muktaashukti bhasma contains pearl formulated with aloe vera and vinegar. Muktaashukti bhasma was known to possess anti-inflammatory activity in albino rats [22]. Swarna Bhasma (gold) was proved to be effective against different malignant tumors such as lung, liver, pancreas, gall bladder, and colon with more anticancer activity on rectal cancer [23]. Similarly, Rajat Bhasma used with other herbal formulations was proved to be effective against myeloma and lymphoma [24]. Jasada bhasma (zinc ash) was found to possess anti diabetic activity experimentally proved in Wistar rats [25]. Vanga Bhasma (tin) was scientifically proved to be effective against diabetes mellitus in alloxan induced hyperglycemic rats [26].

Table 3: Bhasma for NCDs

S.No	Formulations	Bhasma	Disease	Reference
1	Mashika bhasma	Swarnamakshika Bhasma		
2	Mehakalanal Rasa	Vanga Bhasma		
3	Panchanan Rasa	Abhraka Bhasma		
4	Naga Bhasma	Naga Bhasma		
5	Yasada Bhasma	Yasada Bhasma		
6	MehamudgaraRasa	Lauha Bhasma		
7	Trivanga Bhasma	Naga Bhasma, Vanga Bhasma Yasada Bhasma		

8	Vangeswar Rasa	Vanga Bhasma	Diabetes	50-53
9	Chandraprava Vati	Lauha Bhasma		
10	Vedvidya Vati	Kantaluha Bhasma, Abhraka Bhasma, Naga Bhasma		
11	Navayasa Yoga	Lauha Bhasma		
12	Yogeswar Rasa	Naga Bhasma, lauha Bhasma, Tamra Bhasma, Abhraka Bhasma, Vanga Bhasma		
13	Vasanta Tilaka Rasa	Lauha Bhasma, Abhraka Bhasma, Swarna Bhasma, Vanga Bhasma		
14	Megnada Rasa	Swarnamakshika Bhasma, Abharaka Bhasma, Kantaluha Bhasm		
15	Apurbamalinivasanta Rasa	Vaikranta Bhasma, Abharaka Bhasma, Tamra Bhasma, Swarnamakshika Bhasma, Rajat Bhasma, Vanga Bhasma, Lauha Bhasma		
16	Navajeevan	Rajat (Raupya)Bhasma	Cancer	24
17	Kamadudha Rasa	Kapardika (Vaikranta) bhasma, Sankha bhasma		24
18	Basanta Kusumakara Rasa	Prawal Bhasma, Abhrak Bhasma, Raupya Bhasma, Swarna Bhasma		30
19	Swarna bhasma	Swarna bhasma	Heart afflictions	54

CONTROVERSIES OVER BHASMA

There are controversies on ayurvedic bhasmas that they are toxic due to the presence of high amount of metallic particles. Saper et al. observed that some of the ayurvedic medicines of US and Indian origin sold through internet were highly toxic [27]. Similar reports were observed by Ernest and his coworkers [28]. But these bhasma were proved to cure various diseases used over millennia with assured quality, safety and efficacy [29,30]. Current scientific evidences also proves that bhasmas are nontoxic [31,32].

The toxicity observed could be due to the following reasons. Ancient ayurvedic system followed only personalized medicine approach. Ayurvedic medicines are always provided with adjuvants like honey, ghee butter etc. to get rid of detrimental effects of metals and intensify their biocompatibility [33]. This system is in practice until date in ayurvedic and in Siddha medicines. Further, the safety and efficacy of bhasma relies on the methods of preparation. Ayurvedic practitioners gave more preference to the manufacturing process [34] and always followed standard procedures [35,36]. Improper preparation methods resulting in metallic impurities will lead to toxic effects.

At present, various metallic nanoparticles based drugs were proven effective for chronic diseases such as DOXIL® (anticancer drug), magnetic nanoparticle in medical diagnosis (MRI scan) etc. The metallic nanoparticles found to be toxic beyond a particular dosage were coated with herbal constituents or polymers to reduce their toxicity. These reports are sufficient to accept that, Bhasmas used with some adjuvants are to prevent toxic effects. Further, Bhasmas were proved to be non geno-toxic [37].

CONCLUSIONS

Ayurvedic Bhasmas cures diseases in multifactorial approach; they act on a particular disease, besides heals inflammations and prevents toxic side effects. The unexplored potential of Ayurvedic Bhasmas are regaining in current world. However, most of Bhasmas were still unexplored for NCDs and other diseases. Our paper signifies the urge to rediscover the ancient nano-bhasmas for earlier prevention of chronic diseases.

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