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REVISITING ANCIENT THERAPEUTIC POTENTIAL OF AYURVEDIC BHASMA

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ABSTRACT: With the advent of nanotechnology, it has become important to realize the immense potential of ayurvedic bhasma which had been there for centuries. The study of ayurvedic bhasma as nanomedicine is an important interdisciplinary research area in need of contributions from material science, chemistry, pharmacology, *etc*. Such a research will definitely help in the characterization and standardization of these bhasmas which is a very complex problem. However, this system is not getting recognition in other parts of the world. Among the various reasons listed for lack of popularity of ayurveda, is non-availability of 'standards' for ayurvedic medicine particularly when prepared on large scale in modern pharmaceutical plants, matching the convenience palatability of modern dosage forms. Many times, it is reported that the preparation, particularly those mineral based are found to contain toxic substances exceeding permissible limits. There has been a lot of hue and cry regarding the safety and efficacy of the bhasmas, especially after publication of certain reports in print media. Further, the commercial pharmacies not adhering to the traditional methods adopt short cut methods and use of adulterated / substandard material augmented the apprehensions in public over their utility. It is therefore needed to explore the same with a multidisciplinary approach, the present study is contemplated. The present review is aimed at finding out the ways and means to standardize the manufacturing processes and develop standardization methods after they have been formed.

INTRODUCTION: The present era is the era of nanotechnology which is currently employed as a tool to explore the different areas of medical sciences like imaging, sensing, drug delivery, gene delivery system and artificial implants to name a few [1]. It has been the focus of considerable attention in medicine due to the ease with which the drug in the form of nanoparticles, interact with the human body at the molecular scale [2]. Ever since the discovery of nanotechnology, there has been considerable research oriented towards the synthesis of nanoparticles.

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There are a number of approaches for the synthesis of nanoparticles as mentioned in **Fig. 1**.

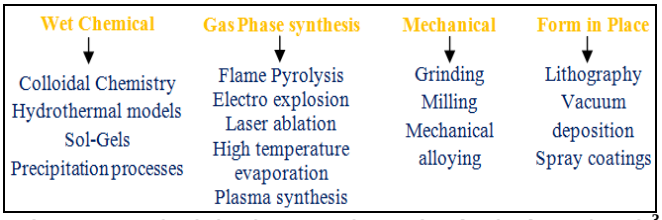

FIG. 1: METHODS OF SYNTHESIZING NANOPARTICLES [3]

Apart from the above mentioned approaches, a lot of research has been reported for the synthesis of nanoparticles using natural biological system to minimize or eliminate the use of hazardous substances [4].

In this context, it has become necessary to revisit the ancient counterpart of nano in the form of ayurvedic bhasma [5, 6].

1.1. Bhasma as Nanoparticles: The use of ayurvedic bhasma as nanomedicine is nothing new in our country as this system of medicine has been known since 7th century A.D. and widely recommended for the treatment of different chronic ailments [7]. It has been known to follow holistic approach towards health care by maintaining a balance between the physical, mental and spiritual health of the human body.

Bhasma is a well-known potent preparation of ayurveda which literally means 'ash'. These are unique metal base preparation made by sophisticated pharmaceutical processes incorporating herbs and converting them in to suitable form. Conversion of metals into Bhasma is a unique process mentioned under Rasashastra. Bhasmas are complex organometallic compounds of metals or minerals obtained by repeated incineration with different medias and are well known for its effectiveness, smaller dose and long shelf life [8].

In ancient times, the ayurvedic physician (vaidya) used to prepare different types of bhasmas on small scale. They were very much aware of the fact that the continuous burning and cooling of metals/minerals which they were doing to remove the toxic effects of the metals/minerals in fact changed the physical and chemical composition of the bhasma particles.

In a way, it not only increased the surface area, but also helped the medicine prepared in this manner to reach the target site efficiently. Thus, they become more palatable with longer shelf life [9].

Recent studies have claimed that the herbomineral formulations of ayurveda constituting bhasmas to be equivalent and in tune with nanotechnology [10]. Also, the nanoparticles in the form of bhasma have been found to have an advantage over other preparations in terms of their stability, lower dose and easy availability [11]. In this way, the use of metals and minerals in the form of bhasma particles became the strength of ayurveda [9].

1.2 Process of Bhasma Preparation: Basic preparation of any bhasma involves the following steps as shown in **Fig. 2**.

Sarkar *et al.*,[5] have described the above mentioned methods in detail as follows:

Putaka Method: During this method, after shodhan and jarana, metal is exposed to bhavana process, which involves the use of specific plant extract for different metals. From this levitated doughy mass, Chakrikas (pellets) are prepared and taken into earthen crucibles faced together, and junction is sealed by mud smeared clothes. Then heat is applied into this apparatus (Sharava Samputam) using traditional Puta (heating grade) or electric muffle furnace for a specific time. This method is known as Putapaka in parlance of ayurveda. After burning for specific time these materials are cooled down in an apparatus, Sharava Samputam. After repeating these procedures for particular time, prepared Bhasma (incinerated metal) is collected.

Kupipakwa Method: In this method, bhasma of different metals are prepared by subjecting these metals (gold, silver, copper, *etc*.) to four step procedures, *i.e.* Shodhan, Kajjali preparation, Bhavana and Kupipakwa. After Shodhan, 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 levitated by particular liquid media for certain period. It is allowed to dry and then 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 and sublimed product is collected from neck and bhasma is collected from the bottom of bottle and ground to powder form.

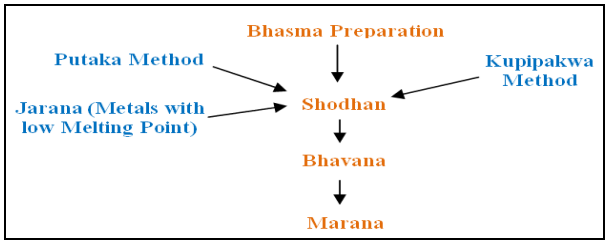

FIG. 2: STEPS INVOLVED IN PREPARATION OF BHASMA

The following steps are followed in the above two methods.

Shodhan: The principal objective of shodhan is to remove unwanted part from the raw materials and separate out impurities. It is the process of

purification and detoxification by which physical and chemical impurities and toxic materials are eliminated. The shodhan process deals with samanya shodhan and vishesh shodhan [12].

Samanya Shodhan can be done by Dhalana (liquefying and pouring) method in Tila (*Sesamum indicium*) Taila (oil), Takra (butter milk), Go-mutra (Cow's urine), Kanji (sour gruel), Kulattha (*Dolichus biflorus*) kwatha (decoction).

Specific Shodhan: can be done by same Dhalana process, but in this process, specific liquid medias are required for specific metal.

Bhavana: It helps to make the metal and mineral particles become finer and change into organo-metallic compounds. This is done by mixing shodhit metal with specific plant extracts.

Marana: It is the process in which metals and minerals are made into paste with various drugs and juice. A change is brought about in the chemical form or state of the metal. This makes it to lose its metallic characteristics and physical nature. Metals can be converted into powder or other form suitable for administration. It is carried out by heating the metal in presence of mercury, plant extracts, and sulfur.

For metals having low melting point, process followed is different as under:

Shodhan---Jarana-- Bhavana

Jarana: Metals are melted and mixed with some plant powder and are rubbed by an iron ladle on inner surface of pot until metal become a complete powder form.

2. Need for Standardization: Standardization is a measurement for ensuring the quality and is used to describe all measures, which are taken during the manufacturing process and quality control leading to a reproducible quality [13]. It will also make sure the safety, effectiveness and acceptability of the product. Ayurvedic system of medicine is one of the time tested system and widely accepted one in our country. However, this system is not getting recognition in other parts of the world. Though the system has an holistic approach to treatment of disease, and claim to remove root cause of the disease, is cheap and universal, depend entirely on nature for its curative agents, mostly collected from the surroundings, yet the system needs to be popularized through special measures. Even the believers of the system are switching to modern system of medicine. Among the various reasons listed for lack of popularity of ayurveda, is non-availability of 'standards' for Ayurvedic medicine particularly when prepared on large scale in modern pharmaceutical plants, matching the convenience palatability of modern dosage forms.

Many times, it is reported that the preparation, particularly those mineral based are found to contain toxic substances exceeding permissible limits. Many of the 'Bhasma' either used alone or used with various herbs are excellent therapeutic agents in the hands of expert Ayurvedic physician. However, when tested, some of these may have excessive amount of toxic metal. These toxic substances might have come by not adhering to the procedures described in literature, particularly during industrial production.

In modern times, scaled up technologies are used to manufacture these products on large scale. Also, there has been lot of concerns raised regarding the safety and efficacy of the bhasmas, especially after publication of certain reports in print media. Further the commercial pharmacies not adhering to the traditional methods adopt short cut methods and use of adulterated / substandard/ spurious material augmented the apprehensions in public over their utility. Tripathi had pointed out the importance of multidisciplinary approach to standardize the bhasma, particularly in the light of reported presence of heavy metals in ayurvedic preparation[14].

Also, inferior quality of raw material, lack of authentication of raw material, non-availability of standards, no quality control parameters adulteration and deviations in standard manufacturing practice either intentionally or unintentionally, leads to the production of inferior quality products, which not only raise the concern over the their efficacy but also their safety [15]. It is therefore needed to explore the same with a multidisciplinary approach, the present study is contemplated. It is worthwhile to investigate these preparations for metallic contamination and

determine their physico-chemical standards when prepared in small quantities according to traditional prescribed method and when the same is prepared in large quantities in modern pharmaceutical industries, special emphasis has to be laid on how these preparation methods affect the size of the particles and oxidation state of the metals in the 'Bhasma'. These methods should be a combination of both classical and modern methods of analysis. Thus, standards need to be prepared with respect to raw material, manufacturing process and the end products.

2.1 Characterization of Bhasma particles: After the bhasma particles have been synthesized, characterizations are done to confirm the formation of these bhasma particles. Characterization of bhasma particles has to be done by both classical and modern methods of analysis. The important aim of analytical study is to know the particular chemical configuration and to point out the physicochemical changes and effect of different samskara (Nirvapa, Bhavna, Marana *etc.*)[16].

2.1.1 Classical Standardization Methods:

2.1.1.1 Physical Parameters:

(1) Colour (Varna): A specific color is mentioned for each bhasma. Alteration in colour suggests that the bhasma is not prepared properly. This is because a particular metallic compound is formed during bhasma preparation and every chemical compound possesses specific colour. However, colour of the bhasma sometimes depends on the materials used during the method of incineration [17].

(2) Nishchandratvam: 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 to check whether luster is present or not; if luster is still present, it indicates further incineration [18].

(3) Varitara: Varitara test is applied to study lightness and fineness of bhasma, by checking the 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 slowly on stagnant water surface from short distance. Properly incinerated bhasma will float on water surface [19].

(4) Unama test: This test is further assessment of Varitara test. A grain of rice is to be kept carefully on the layer of floated Bhasma. Observe whether grain float or sinks. If grain remains as it is on the layer, then bhasma can be considered as excellent (properly prepared) [19].

(5) Rekhapurnata: This test is applied to study fineness of bhasma. Bhasma particle should be of minimum size for easy absorption and assimilation in the body. A pinch of bhasma is rubbed in between thumb and index finger. If the bhasma particle enters into the creases of these fingers; it indicates that the metal is incinerated properly.

This test indicates the fineness of the particles. Finer the particle, fastest the absorption and quickest the action; is the fundamental principle of pharmacology *i.e.* If the medicine is reduced to Nano particles, better therapeutic activities can be expected [19].

(7) Anjana Sannibha: 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.

(8) Taste (Niswadu): Metals in their natural form have specific taste. During niswadu, a pinch of bhasma is placed on the tongue and if is tasteless *i.e.* absence of metallic taste, it indicates the properly formed bhasma.

(9) Nirdhuma: A pinch of bhasma is sprinkled on the ignited charcoal and observed. The prepared bhasma can be considered as proper if it does not yield fumes over fire. Apart from the above mentioned physical parameters that are taken in to consideration for the testing of properly synthesized bhasma, some other physical standardization methods are also mentioned in the literature which are mentioned as follows:

(1) Determination of Total Ash: 1 gm of formulation is taken in silica crucible and incinerated at a temperature of 450 ºC until free from carbon and cooled and weighed [20].

(2) Acid Insoluble Ash: Total ash is boiled for 5 minutes with dilute HCl. Insoluble matter is collected, washed, ignited and weighed [20].

(3) Water Soluble Ash: Total ash is boiled for 5 minutes with 25 ml of distilled water cooled and collected the insoluble matter on ash less filter paper. Washed and ignited at 450 ºC. Subtract the weight of insoluble ash and the percentage is calculated [20].

(4) Determination of Loss on Drying: The samples are taken in china dish and placed in hot air oven and the weight is observed in every half an hour till same weight is observed, weight loss is due to the removal of water and volatile ingredients[20].

(5) Determination of pH: Aqueous solution is prepared and measurements are carried out at 25 ºC using pH meter [20].

2.1.1.2 Chemical Parameters: Along with physical parameters, chemical parameters are also mentioned in the ancient classics. Few of them are as follows:

(a) Apunarbhava: The incinerated metal is to be mixed with equal quantity of seeds of *Abrus precatorius*, guda, gunja, madhu, ghee and tankana, kept in musha, sealed with another musha and sandhi bandhana to be done. This samputa is to be subjected to intense heat. After self-cooling, the product from the musha is collected and analyzed. The presence of free metal in the product indicates that the metal is not incinerated properly.

(b) Niruttha: This test is also similar to that of apunarbhava test and is applicable for all the metals. Incinerated metal is to be added with equal quantity of silver and this complex is heated in a musha under intense heat. After self-cooling the silver is to be examined for changes in weight and colour. If the metal is properly incinerated there will not be any change in the weight of the silver.

2.2 Modern Standardization Methods: [15] Adulteration/substitution as well as presence of free particles will have an effect on the quality and safety of the drug. It becomes obligatory to adopt modern analytical methodology to determine the important chemical constituents present in the drug qualitatively and quantitatively. This will make understanding and interpretation of pharmacological action of any drug easier and better. Some of the frequently followed modern analytical methods are discussed as under.

(a) SEM (Scanning Electron Microscopy): SEM is used to study the morphology and elemental composition of the bhasma samples. This is used to investigate particle size, shape and structure of bhasma sample. SEM shows very detailed three dimensional images at much high magnifications (up to x 300000) as compared to light microscope.

(b) EDAX (Energy dispersive X-ray spectroscopy): EDAX study helps to reveal accurate elemental analysis of the sample and enable us to explore major, minor and trace elements present in the sample [16]. EDAX is a technique to analyze the chemical components in a material under SEM. This method detects the X-rays produced as the result of the electron beam interactions with the sample. SEM-EDAX is many times used to obtain morphological information of the surface and identification of chemical composition.

(c) TEM (Transmission Electron Microscopy): Transmission Electron Microscopy (TEM) is a characterization tool for directly imaging nanomaterial to obtain quantitative measures of particle and/or grain size, size distribution, and morphology.

(d) DLS (Dynamic Light Scattering): It is known as Photon Correlation Spectroscopy, this technique is one of the most popular methods used to determine the size of particles. Such structural information is absolute necessary for the bhasmas containing heavy metals like lead, mercury *etc.*

(e) ICP-MS (Inductively Coupled Plasma-Mass Spectrometry): Inductively Coupled Plasma Mass Spectrometry or ICP-MS is an analytical technique used for elemental determination in the bhasma sample. It detects various elements up to ppm or ppb level.

(f) XRD (X-Ray powder Diffraction): It is one of the most powerful techniques for qualitative and quantitative analysis of crystalline compounds. The information obtained includes types and nature of crystalline phase present, structural make-up of

phases, degree of crystalline, amount of amorphous content, micro strain & size and orientation of crystallites.

(g) XPS (X-ray Photoelectron Spectroscopy): This technique quantitatively measures the elemental composition, atomic concentrations and chemical states of elements present at a samples surface. XPS can detect all elements with an atomic number greater than 3, therefore, Hydrogen and Helium are not possible to detect.

(h) FTIR (Fourier Transform Infra-Red spectroscopy): The Principle of FTIR is based on the fact that bonds and groups of bonds vibrate at characteristic frequencies. A molecule that is exposed to infrared rays absorbs infrared energy at frequencies which are characteristic to that molecule. The resulting FTIR spectral pattern is then analyzed and matched with known signatures of identified materials in FTIR library.

3. Standardization methods used for the Preparation and Characterization of Some Bhasma: The following section discusses the various standardization methods followed by researchers over the years for the preparation and characterization of some bhasma. Recent literatures have shown that researchers have identified the importance of modern analytical methods for quantitative evaluation of the formed bhasma particles, although the classical methods of evaluation called the bhasma pariksha cannot be ignored as they help in qualitative evaluation of bhasma particles. A combination of both the methods could be very handy in identification of proper bhasma particles.

Preparation of Mukta Shouktic Bhasma: Dubey *et al*., had prepared biomedicine Mukta shouktic bhasma (MSB) through special calcination of mother of pearl. The raw material of mukta shouktic (mother of pearl) is an organomineral matrix containing calcium carbonate in aragonite form.

Shodhan: The mother of pearl fragments was gently crushed to smaller fractions using an agate mortar and pestle. Pieces of mother of pearl were first cleaned with hot water to remove dirt material. The mother of pearl fragments were then immersed in lemon juice (nimbus swarasa) and boiled for 90 min in a specially prepared hanging sealed earthen pot (dolayantra). This process was known as boiling (swedana). The solution was filtered off to get the cleaned mother of pearl fragments (shodhit mukta shouktic), which were subjected to first calcination. For calcination the cleaned mother of pearl fragments were placed in sealed earthen pot (sarava samputta) and subjected to ignition in a traditional furnace (gaja-puta). The stable intermediate can be stored in sealed earthen pot until further use.

Bhavana: The intermediate obtained after the first calcination was then treated with Aloe vera gel and triturated using an automated mortar and pestle at 1000 rpm. The total time of trituration was 8 hrs. The mixture was pressed in the form of cakes (Chakrikas) and dried in the shade for 48 h. These dried cakes were immediately subjected to further processing, Marana the cakes were calcinated to obtain the intermediate. The procedure was repeated two times [21].

Physicochemical evaluation of the synthesized biomedicine using XRD (X-ray diffraction) confirmed the presence of calcite as the major crystalline phase in the sample, while TG (Thermo-gravimetric) studies showed gradual weight loss up to 43% between temperature 800 and 900 ^{o}C due to gradual conversion of calcium carbonate to calcium oxide. DLS (Particle size analysis with Dynamic light scattering) showed that size of MSB particles ranged between 1.22 and10.20 μm having a mean particle size of 22.52 ± 0.45 μm. 6%of the particles were also found to have a particle size less than 50 nm. TEM (Transmission electron microscopy) showed that the particles are irregular rod shaped. The TEM photomicrograph of MSB showed the appearance of 15 - 50 nm particles in the sample.

SEM (Scanning electron microscope) showed the morphology of MSB samples to be remarkably different from that of standard calcite. This simply means that repeated calcinations cycles were necessary to stabilize the particles to a minimum particle size. The element analysis through ICP and EDAX revealed the presence of heavy metals like chromium, lead, and cadmium in MSB. Other heavy metals like arsenic, mercury, and tin were below the detection limit of the ICP analysis. TGA analysis showed weight loss up to 600^{o}C, which

may be attributed to the loss of moisture content of the crystal. A gradual weight loss up to 43% w/w was also observed between 800 and 900 ºC due to gradual conversion of calcium carbonate to calcium oxide.

Preparation of Naga Bhasma: Nagarajan *et al*., had prepared Naga bhasma by following procedure:

Shodhan: Involved the quenching of metal thrice sequentially in sesame oil, butter milk, cow's urine, sour rice gruel and horse gram decoction. This was aimed at rendering the metal to a form capable of reacting with herbal ingredients to be added during the later stages of preparation.

Jarana: Purified lead was stirred well under heating with tamarind and peepal bark powder to reduce the metal to the powdered form in a process.

Marana: The powdered form of lead was ground well with Arsenic di sulfide and sour rice gruel until a doughy mass was obtained which was made into round shaped discs. These discs were sun dried well before being subjected to 50 cycles of Arddha gajaputa and 10 cycles of Puta [22].

Physicochemical evaluation through TGA (Thermo gravimetric analysis) showed that Naga bhasma sample was thermally stable until 900 °C which indicated the absence of free organic molecules. FTIR (Fourier transform infrared spectroscopy) analysis showed that the entire sample contains organic moieties in the form of complex. Particle size analysis was done to determine the particle size and pore volume of Naga bhasma. Surface area analysis was carried out to check the presence of micron size particle and to find out the specific surface area of Naga bhasma.

EDAX (Energy dispersive X ray analysis) was done to check the presence of arsenic along with lead. Electron microscopy study showed the bhasma content particle in micron and sub-micron range. XRD (X-ray powder diffraction) analysis showed that lead was present in lead oxide phase.

The authors have revealed the presence of batch to batch variation in the samples prepared by the same manufacturer, which has been attributed to lack of good standards for preparation of bhasma.

Preparation of Lauha bhasma (Iron ash): Pavani *et al*., had synthesized iron oxide Nano particles (Lauha bhasma) using iron filings as a precursor material by subjecting it to normal and special purification to obtain the final product as Lauha bhasma, which is present in γ- phase.

Normal purification and Special purification: Are modern synthesis techniques which were used to produce final product, Lauha bhasma.

Normal Purification process: It involved three sub steps: In the first step of purification process, 40 grams of iron filings were taken in a beaker, using 20 ml of sesame oil as quenching medium, immerse for 30 minutes and filter by Filtration setup. Then so obtained filtrate was heat treated at 530 - 560 °C for 30 minutes by which the filtrate was completely dried. Each of the quenching process was repeated for seven times with each treating liquid, by using Fresh medium every time.

Special Purification: The product obtained from normal purification was taken in a beaker and immersed in 20 ml of panchgavya for 24 hours. It was then washed with panchgavya for 6 times by filtration process. Thereafter 2 grams of triphala decoction was added and again immersed in panchgavya for 2 h. The product obtained from special purification was exposed to sunlight for 24 hours.

Heat treatment: Finally the product was heat treated in iron pan. Add 3 grams of triphala, at 95-100°C to dry for 1hour. Again 0.5 grams of triphala was added at 900 °C to dry for 2 hours, then the final product obtained was Lauha bhasma [23].

Physicochemical evaluation through XRD (X-ray diffraction) analysis showed transformation of iron oxide from α- to γ- phase and this γ-phase remains constant, that indicated the face-centered cubic structure for iron oxide Nano particles. FTIR (Fourier Transform Infrared Spectroscopy) spectra indicated three vital peaks, the spectra displayed broad absorption around 3733.83 cm^{-1} was assigned as OH stretching, H-O-H bonding at1632.56cm^{-1} and the main Fe-O stretching was observed at 577.94 cm^{-1} indicating the presence of iron oxide nanoparticles. TGA, DTA (Thermo Gravimetric) and (Differential Thermal Analysis) showed that at temperature range from 500 - 800 °C; the weight

loss is about 0.2603% which showed very low percentage of weight loss and indicated high purity in the sample. TEM (Transmission Electron Microscopy) analysis indicated presence of well dispersed and perfect cubic structure of the sample and the presence of spherical structure of iron oxide nanoparticles.

Preparation of Yashada Bhasma: Santhosh *et al*., had prepared yashada bhasma by following procedure:

Samanya Shodhan: (general purification) was done by the Dhalana (liquefying and pouring) method in Kanji (sour gruel), Takra (butter milk), Kulattha (Do-lichus biflorus) kwatha (decoction), Go-mutra (Cow's urine) and Tila (*Sesamum indicium*) Taila (oil). Dhalana was carried out three times in each liquid media. After Samanya shodhan.

Vishesha Shodhan: (specific purification) was carried out in Churnodaka (lime water) for seven times. After shodhan, the metal became more brittle.

Jarana: (roasting) was carried out by using Apamarga panchanga churna (powder of Achyranthes aspera). After Jarana, the metal was converted into a very fine grey shining powder which was deemed fit for Marana. Marana (incineration) the powder was then subjected to.

Marana: by triturating it with Shuddha Parada (purified Mercury) and Shuddha Gandhaka (purified Sulphur) both $1/4^{th}$ quantity of Yashada, to form a black powder, to which one

Bhavana: (triturating in liquid media) each with Kumari swarasa (fresh juice of *Aloe vera*) and Nimbus swarasa (fresh juice of Citrus li-mon) was given and Chakrikas (pellets) prepared. After drying, they were kept in sharava (casseroles), sandhi bandhana (sealing) was done and subjected to Gajaputa (heating system). After two Gajaputas, Yashada bhasma of yellowish color was obtained [24].

Once synthesized, the yashada bhasma was tested with both ancient and modern analytical parameters to know how the basic metal was transformed into bio-absorbable bhasma form. It was concluded through ICPAES study that the bhasma contains Zinc in major portion (95.08ppm) and other elements like Sn (0.27), Pb (0.14), Fe (1.69), Ca (1.82), Mg (1.00), Cu, Co and Mn< 0.5 ppm in the final product. Physicochemical evaluation through XRD (X-ray powder diffraction) analysis showed that zinc oxide (ZnO) as final product. SEM (Scanning -electron microscopy) showed the amorphous nature of the bhasma with particle size range 5 –20 micrometer.

Preparation of Abhraka Bhasma: Shetty *et al*., had prepared abhraka bhasma by Nirvapa method with Godugdha (cow milk), dhanyabhrakarana, abhraka marana and Amruteekarana processes. In marana process Erandapatra swarsa was used for trituration and calcination was carried out 23 times [25].

The modern analytical method EDAX (Energy Dispersive X-Ray Fluorescence), revealed the presence of Al,Si, Fe, K, Mg, Na Fe and oxygen. FEG-SEM **(**Field Emission Gun-Scanning Electron Microscopes) studies showed that the particles in Abhraka bhasma in nano meter range least being 213.2 nm. XRD study revealed the presence of Fe_2O_3, Al_2O_3, SiO_2, MgO, Na_2O and K_2O [25].

Preparation of Vanga Bhasma: Chaudhary *et al*., had prepared Vanga bhasma by following procedure:

Shodhan- Samanya and Vishesha: Raw Vanga was heated to red hot stage & then quenched in Tila oil, Takra, Gomutra, Kanji, Kulattha Kwatha respectively 7 times each. Then, Vishesha shodhan was performed and Samanya shodhit vanga was quenched in Nirghundi Kwatha mixed with Haridra powder for 3 times.

Jarana: Shodhit Vanga was put in an Iron vessel & heated over flame till it melted. Then equal quantity of Asvatha bark was added to it and rubbed till it turned into powder form.

Marana: Marana was done with hingul media. Jarita Vanga was put in a pestle - mortar & hingul ($1/8^{th}$) was added to it and levitated with *Aloe vera* pulp. Then contents were dried, cut into pellets & subjected to heating in an electric furnace. This process was repeated 10 times till bhasma was obtained [26].

The vanga bhasma was then characterized by different analytical techniques.XRD (X-ray powder diffraction) analysis was conducted on the sample which showed that vanga bhasma had a crystalline structure. The major component (over 95%) was Tin Oxide, possibly Cassiterite and Aluminium oxide. The predominant peaks in sample (vanga bhasma) correspond to major phase comprising SnO_2. SEM (Scanning Electron Microscopy) showed a characteristic three dimensional appearance and was useful for determining the surface structure of the sample.

It was observed from SEM Figures that particles of Vanga Bhasma showed granular appearance and porous morphology. There was no particular pattern in structure. EDX (Energy-Dispersive X-ray spectroscopy) analytical technique was used for elemental analysis or chemical characterization of the sample.

It showed the presence of Na, Mg, Al, Si, S, and Fe & O in the bhasma. FTIR (Fourier transform infrared spectroscopy) showed that the bhasma was an organometallic compound. Formation of a bond between tin (Sn) and carbon (C) (Sn-C) was formed and appeared at wavelength of 592.08. Bonding at wavenumber 646.14 represented the bond formed between Sn and Oxygen (O).

Preparation of Trivanga Bhasma: Rasheed *et al.*, had prepared Trivanga bhasma using Lead, Zinc and Tin as the ingredients. It is a calcinated metal and mineral based preparation is used to treat diabetes and as Diuretic. A two-step procedure was followed

Shodhan and Marana Shodhan Naga [lead], Vanga [tin] and Yashada were detoxified by adding madhuka Taila. The compounds were then triturated with small amounts of herbal powders such as ashawaganda, sathvari, yastimadhu, tintrivik using akhalvam till a homogenous paste was formed. The obtained mixture was powdered. Marana process transferred to an earthen crucible covered with a lid and sealed with sealing clay. Finally it was kept for calcination. The mixture was blended with Kumari swarasa to form a cake. The cake on drying obtained yellow color Trivanga bhasma [27].

The FTIR (Fourier transform infrared spectroscopy) spectra of the prepared bhasma showed no peak for any organic molecule or bond corresponding it, confirming the absence of organic matter and external organic contamination.

The AAS (Atomic absorption spectroscopy) study showed that the elements Lead, Zinc and Tin are in major concentrations of 4.84%, 9.917% and 5.05%. SEM (Scanning Electron Microscopy) showed difference in size and agglomeration of the particles. 'Trivanga bhasma' showed spongy, relatively compact micro crystalline aggregates with loss of grain boundaries. The average particle size of sample was found to be about 1µ.TGA (Thermo gravimetric analysis) showed complete decomposition at 1253 ºC and 1238ºC respectively.

Lead, Zinc and Tin, when heated in presence of air were converted to Lead oxide, Zinc oxide and Tin oxide, after then these are converted as lead sulphide, zinc sulphide and tin sulphide. XRD (X-ray powder diffraction) pattern suggested that the drug was present in crystalline form. AFM (Atomic Force Microscopy) analysis confirmed spherical morphology with an average particle size of 60nm. The spherical morphology was due to the aggregation of the nano crystals of the metallic oxides.

Preparation of Tambra Bhasma: Jagtap *et al*., had prepared Tambra bhasma by two steps process:

Samanya Shodhan: of Tambra was carried in Kanji (sour gruel), Kulattha Kwatha (decoction of horse gram), and Takra (buttermilk) liquid media for 7 times.

Vishesha Shodhan: of Tambra was carried out in freshly collected Gomutra.

Marana: was done in an Electrical Muffle Furnace.

Samaguna Kajjali: Equal to the amount of Shuddha Tambra was taken in mortar and Nimbus Swarasa Bhavana (wet trituration with lemon juice) was given. When paste like consistency appeared, the mixture of Shuddha Tambra was added in it and triturated.

After drying in shade, it was kept in Sharava (earthen saucer) and covered by another Sharava and junction was sealed by double fold of Multany mitty smeared clothes. It was subjected for Puta in EMF. On the next day, after (self-cooling) Sharava Samputa was removed, material was collected and triturated. This process is done for three times [28].

Physicochemical evaluation through PSD (Particle size distribution) analysis showed 10% of the material was found below 2.83 µm whereas maximum material was below 124.30 µm. Small particle size enhances the absorption. Bhasma analyzed under SEM (scanning electron microscope) showed particle size less than 2µm. In XRD (X ray diffraction) prominent peaks of CuS were seen, which confirmed that final product was sulfide form of copper.

Presence of oxides could not be denied because other peaks were also present. Furthermore, in ICP-AES (Inductively coupled plasma- atomic spectrometry) 58.56 wt. % of copper against 22.48 wt. % of sulfur was present. As the procedure of Tambra shodhan was carried out in an iron pan 0.31 wt. % of iron was traced in Bhasma. Heavy metals like cadmium, selenium were not detected while others like arsenic, lead and mercury are present in traces.

Preparation of Praval Bhasma: Mishra *et al*., had prepared praval bhasma by following two steps procedure

Shodhan and Marana:

Shodhan: Praval was boiled in Dolayantra with Sarjikasalila for 3 h followed by second step *via* Marana.

Marana: Purified praval was grounded with kumari swarasa (25 mL) and flat thin chakrikas (pellets) were prepared. The chakrikas were air-dried in shade and kept in a sharava samputa. The joint of both vessels were sealed with the help of mud and dried in sun light. Finally the sealed vessel was subjected to Gajaputa. The temperature reached to the maximum of 930°C during the process. After once ignition of Gajaputa, it was allowed to quench itself. The Sharava samputa was removed from Gajaputa assembly, opened and the Chakrikas were again triturated with Kumari swarasa. Again the flat thin Chakrikas (pellets) were prepared, air-dried in shade and kept sharava samputa (earthen vessels) and finally subjected to Gajaputa. The process was repeated in triplicate. This process produced the praval bhasma [29]. Physicochemical characterization of praval bhasma with the use of instrumental techniques such as FTIR energy bands appearing in final product spectra shows a significant shift in infrared vibration frequency as well as intensity when compared with the raw material, which was indicative of formulation of bhasma. The XRD analysis revealed that raw material contains $CaCO_3$ whereas in case of final product of bhasma, CaO is identified. SEM analysis revealed the difference in particles size of bhasma (10-15 µm) and raw material (100-150 µm). The EDAX (Energy dispersive X- ray) analysis showed presence of different concentration of carbon in both the samples.

Preparation of Mandur Bhasma: Rajurkar *et al*., had prepared Mandur bhasma by following procedure:

Samanya Shodhan: The raw material used for the preparation of Mandur bhasma was heated till red hot and dipped in 5 different liquid media such as sesame oil, butter milk, cow urine, Kanji and Horse gram decoction respectively. The process was repeated 7 times in each liquid media.

Vishesha Shodhan: was carried out using triphala decoction.

Bhavana: It was the process of wet grinding in which shodhita Bhasma were grounded with particular liquid media for specific period. The Bhavana was done using.

Bhanupak Process: The shodhita Bhasma was mixed with 400 ml of Triphala decoction and kept under sun light till complete evaporation of liquid. For getting more brittle and fine particles, on complete drying of mixture again 100 ml decoction of Triphala was added and dried under sun light. This process was repeated 7 times. Marana (Incineration): The levitated doughy mass was subjected to heating in electric muffle furnace at constant temperature [30]. Physicochemical evaluation through XRD (X-ray diffraction) pattern shows that iron oxide is mainly present in the form of Fe_2O_3 and Fe_3O_4.

It is observed that the iron content in the raw material decreased in final product. The EDAX (Energy dispersive x-ray spectroscopy) analysis indicates that elements other than iron are incorporated in the bhasma during various processes.

The SEM (Scanning electron microscopy) image clearly shows the change in morphology and decrease in particle size of the final product. FTIR (Fourier transform infrared spectroscopy) analysis shows the major peaks samples at 1525.74 cm^{-1}, 2332.8 cm^{-1} and 3738.18 cm^{-1} with different intensities [30].

Preparation of Kasisa Bhasma: Yadav *et al*., had prepared Kasisa bhasma by following procedure:

Shodhan: was done by 3 hours Swedan in Bhringaraj Swarasa for 3 hours. At 80 - 90°C, Kasisa gets completely dissolved in water. Hence, after complete Swedana when Kasisa pottali was removed, it was observed that Kasisa was completely dissolved in Bhringaraja Swarasa and only small quantity of sand remained in pottali. The dissolved Kasisa allowed to remaining in the steel container for 24 hours.

After this period, some Kasisa accumulated at the bottom, which was collected and allowed to dry in a steel tray under sunlight. Remaining Bhringaraja Swarasa was heated and vaporized to half of its level. Then, it was kept in separate steel tray and allowed to dry under sun light. After 4 days, Kasisa in its crystalline form was obtained. Marana was done by seven times Bhavana to purified Kasisa with Kanji and small cakes of nearly 4 - 5 cm in diameter and 0.3- 0.4 cm in thickness were prepared and allowed to dry. Dried cakes were taken in Sharava. Sandhi bandhana was done and kept in muffle furnaces [31].

Physicochemical evaluation through TEM (Transmission Electron Microscopy) clearly revealed that prepared Kasisa Bhasma formulation had several crystallites agglomerate into a single particle. It yields submicron size particle structure (1.22 μ). XRD (X-ray diffraction) showed Kasisa in the form of Iron oxide and reaching to Nano crystalline (31 - 56 nm) size by analysis. The present study indicates Kasisa Bhasma was Nano crystallite with submicron size particle. AAS (Atomic absorption spectroscopy) showed the percentage of Fe was significantly high.

Preparation of Swarna makshika Bhasma: Mohaptra *et al*., had synthesized Swarna makshika by following procedure.

Shodhan: it was converted into powdered form. A clean and dry iron pan was heated on a charcoal furnace on which powder of Swarna makshika was poured and subjected to intense heat with frequent addition of lemon juice till the liberation of sulfur fume stopped and it turned red. The process was completed in 3 days.

Marana: Equal amounts of Shuddha Swarna makshika and Shuddha gandhaka were triturated with lemon juice till a homogenous paste was formed. After triturating, small pellets of uniform size and thickness were prepared and dried in sunlight. Pellets were kept inside a sharava and another sharava was inverted over it and was sealed with muds and dried in sunlight.

The samputa was subjected to puta system. The process was repeated using Shuddha Gandhaka in equal proportion to Swarna makshika for the first cycle and then in half the proportion for subsequent 8 cycles. Bhasma of the desired quality was obtained from the above process [32].

XRD (X-ray Diffraction) analysis of raw SM and SM bhasma revealed that raw SM contained $CuFeS_2$, and SM bhasma contained Fe_2O_3, FeS_2, CuS and SiO_2. SEM (Scanning Electron Microscope) studies showed that the grains in SM bhasma were uniformly arranged in agglomerates of size 1 - 2 microns as compared to the raw SM which showed a scattered arrangement of grains of size 6 - 8 microns.

It might be concluded that raw SM was a complex compound which got converted into a mixture of simple compounds having very small particle size after the particular process of Marana. To give a clear picture of the various standard procedures followed for the synthesis and characterization of various bhasmas discussed above, the same has been tabulated in the **Table 1** below.

TABLE 1: STANDARDIZATION OF SOME AYURVEDIC BHASMA

Bhasma and Its Use	Raw material used	Preparation method	Characterization				Stability	Method used	Thermal Stability using TGA
			Physical Nature (Particle Size)	Method Used	Chemical Composition	Method Used			
Muktashouktic bhasma (MSB) [21] Use: In abdominal colic gastritis, useful in treating cardiac diseases, urinary calculi, splenomegaly	Calcium carbonate in aragonite form	Traditional method	Crystal size of the MSB reduced to a value less than that of standard calcite.	XRD	Major element: Ca(40.22 wt %), heavy metals like Cr, Pb & Cd	ICP & EDAX			Small wt. loss up to 600 °C, due to the loss of moisture content, loss up to 43% w/w between 800 °C and 900 °C
			1.22-10.20µm (6% of the particles were found to have size less than 50 nm.	DLS					
			Particles of size 15-50 nm	TEM					
Naga bhasma [22] Use: In the treatment of diabetes, non-healing wounds, piles, diarrhea, jaundice, skin diseases, cough, asthma, whooping cough, bronchitis, abdominal colic, obesity, anemia, rheumatoid arthritis, gonorrhea, leucorrhoea, bleeding, epilepsy	Lead	Traditional method	Lead is present in lead oxide form	XRD	Presence of arsenic along with lead	EDAX			Naga bhasma is stable until 900 °C
					Organic moieties in the form of complex	FTIR			
Lauha bhasma [23] Use: In cardiovascular diseases, gastric complaints, eye disorders, bloating, obesity, diabetes, vomiting, asthma, bronchitis, herpes, abdominal colic, chronic respiratory disorders, liver disorders, piles, fistula, chronic diseases, emaciation, dizziness, delusion	Iron filings	Traditional method	20 nm nano particles are found. Iron oxide is present in spherical structure.	TEM	Broad absorption around 3733.83 cm^{-1} indicate OH stretching, H-O-H bonding at 1632.56 cm^{-1} and Fe-O stretching at 577.94 cm^{-1} indicating the presence of iron oxide nanoparticles.	FTIR			At temperature 500-800 °C the weight loss is about 0.2603%
			Shows transformation of Iron oxide particles from alpha to gamma phase. It shows face centered cubic structure.	XRD					
Yashada bhasma [24] Use: In eye disorders, anemia, diabetes, cough, cold, bronchitis, asthma, night sweating, non-healing wounds, menorrhagia, gonorrhea and urinary constraint.	Zinc metal	Traditional method	Bhasma contain zinc oxide as final Product. It shows amorphous nature of bhasma	XRD	Major element is zinc and other elements are Sn, Pb, Fe, Ca, Mg, Cu, Co and Mg<.5 ppm.	ICPAES			
			Particle size range 5-20 micrometer.	SEM					
Abhraka Bhasma [25] Use: In the treatment of asthma, urinary disorders, and skin diseases	Mica (Biotite)		Studies showed that the grains in Abhraka Bhasma were heterogeneous and in aggregates of particle size between 19 nm and 88 nm.	FEG	Fe (22%) Ca, K and Si with conc. Of 11%, 8% and 13%. Mg (4%), Al (2%) and Ti (1%) as minor elements while Na, Cl, and P were in traces (<1%). Major elements present were O (41%), Si (16%), K	EDXRF			
			The grains were found to be irregular in	SEM					

			shape ranging from spherical to oblong		(13%) and Fe (13%). Al (6%), Mg (5%), Ca (4%) and Cl (1%). Na, P and Ti were found in traces (<1%).			
Vanga Bhasma [26] Use: In the treatment of vomiting, anorexia, premature ejaculation, noctural emission, cough, cold, bronchitis, asthma, emaciation, weight loss, chronic bronchial diseases, and urinary disorders	Tin and some associated materials	Traditional method	Particle size is 12-47 nm in jaritra vanga. Shows the particle size to be around 200-300nm and 28nm. Drug is present in crystalline form Scherer equation by particle size analysis	XRD SEM XRD	In jarana sample presence of SnO_2, Sn and K_2SnO_2	ICP-AES	Raw Vanga shows two downward peaks, observed at 234.3 °C corresponds to the melting point of Vanga	DTA
Trivanga bhasma [27] Use: used in the treatment of urinary tract diseases, UTI, diabetes and also used in female infertility	Lead, Zinc and Tin	Traditional method	No peak for any organic molecule or bond corresponding it, confirming the absence of organic matter and external organic contamination Difference in size and agglomeration of the particles. Shows spongy, relatively compact micro crystalline aggregates with loss of grain boundaries. The average particle size of sample was found to be about 1µ Pattern suggests that the drug is present in crystalline form. Spherical morphology with an average particle size of 60nm.	FTIR SEM XRD AFM	Lead, Zinc and Tin are in major concentrations of 4.84%, 9.917% and5.05%.	AAS	Shows complete decomposition at 1253ºC and 1238ºC respectively. Pb, Zn and Sn, when heated in presence of air were converted to Lead oxide, Zinc oxide and Tin oxide, after then these are converted as lead sulphide, zinc sulphide and tin sulphide	TGA
Tambra bhasma [28] Use: For the treatment of wide array of diseases like peptic ulcer, anemia, skin disorders, dyspnea	Pure Copper	Traditional method	10% of the material was found below 2.83 µm whereas max. material was below 124.30 µm Particle size less than 2µm	PSD analysis SEM	Prominent peaks of CuS & CuO 58.56 wt. % of copper against 22.48 wt. % of sulfur along with traces of As, Pb and Hg	XRD ICP-AES		
Praval Bhasma [29] Use: For the treatment of bloating, splenic disorders,	Coral calx	Traditional method		SEM	Raw material contains $CaCO_3$ whereas in case of final product of bhasma, CaO	XRD		

cough, asthma, anorexia, indigestion, diarrhea, urinary tract disorders					is identified. Different concentration of carbon in both the samples	EDAX		
Mandur bhasmav [30] Use: Natural diuretic, improve blood count, and blood quality, remove toxins from the blood.	Ferric Oxide Calx	Traditional method	Change in morphology and decrease in particle size of the final product	SEM	Lead, Zinc and Tin are in major concentrations of 4.84%, 9.917% and5.05%.	AAS	Shows complete decomposition at 1253 ºC and 1238 ºC respectively.	TGA
					Iron oxide is mainly present in the form of Fe_2O_3 and Fe_3O_4	XRD	Pb, Zn and Sn, when heated in presence of air were converted to Lead oxide, Zinc oxide and Tin oxide, after then these are converted as lead sulphide, zinc sulphide and tin sulphide	
					Major peaks samples at 1525.74 cm^{-1}, 2332.8 cm^{-1} and 3738.18 cm^{-1} with different intensities	FTIR		
Kasisa bhasma [31] Use: Good for liver and spleen disorders, enhancement of hemoglobin, relief from inflammation.	Green Vitriol (Ferrous Sulphate)	Traditional method	Prepared Kasisa Bhasma formulation had several crystallites agglomerate into a single particle. It yields submicron size particle structure (1.22 μ)	TEM	Percentage of Fe was significantly high	AAS		
			Iron oxide and reaching to Nano crystalline (31–56 nm) size	XRD				
Swarna Makshika bhasma [32] Use: Boost immunity, in lungs disease, nervous system diseases, bone joint diseases and heart diseases	Copper and Iron Pyrite		The grains in Swarna Makshika (SM) bhasma were uniformly arranged in agglomerates of size 1-2 microns as compared to the raw SM which showed a scattered arrangement of grains of size 6-8 microns	SEM	Raw SM contained $CuFeS_2$, and SM bhasma contained Fe_2O_3, FeS_2, CuS and SiO_2	XRD		

CONCLUSION: Metals have been found to play a very important role for carrying out various physiological functions inside the human body. Although they are required in trace amount, their deficiency leads to several kinds of health related issues. To overcome these issues, people prefer to take drugs which are easily available and effective but have some adverse effects. Ayurvedic bhasmas on the other hand, are found to be effective even at very low dose without any toxic effect. This is because the concept of Ayurveda is based on the fact that since metals are not compatible with the human body in their natural form, they need to be processed in to a much reduced usable form called 'bhasma'.

These processing involves purification and repeated incineration of these bhasma particles along with mixing with some herbomineral formulations.

This helps in reducing their size which increases their solubility and bioavailability inside the human tissues. However, if these bhasmas are not processed properly, it would cause toxic effects inside the human body. Most of the ancient texts have laid down certain protocols to evaluate these bhasmas based on their particle size, density, physical and chemical stability. But, these tests are only qualitative and do not provide much information on the chemical composition of these bhasmas. Also, people use different protocols to synthesize bhasmas of the same metal and thus compromise with the safety and efficacy of these bhasmas. Thus, there is a need to develop standard operating procedures for the synthesis of various types of bhasmas.

The present review focusses on the standardization methods being used by the researchers for synthesis and characterization of different types of bhasma particle. These bhasma particles function as nanoparticles and this might be the reason that they easily get in to blood circulation or reach up to any molecule in any tissue of the body. Some particles with size of 1µ-3µ might be working as catalyst, but it's only the pharmacological action that can give a clear picture of the actual action of bhasma particles. Also, it is quite obvious from the literature that the researchers who have recently worked in the field of standardization of ayurvedic samples have not been able to reach to a conclusion as to which modern techniques would be suitable for characterization of samples. However, some analytical techniques like the use of XRD, SEM, ICP-MS, TEM and AFM cannot be avoided since they help us to give a clear picture of the formation of bhasma as nanoparticles.

They give us an idea of the chemical composition and chemical form of these particles which can help us correlate the toxicity related issues if found during analysis. Also, the use of some other analytical techniques like TGA and DTA can help give us complete information on the thermal stability of the samples, the type of compounds formed during incineration and can be a direct check on the purity of compound as a quality control.

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