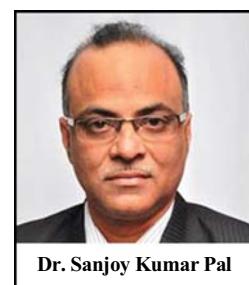


The Ayurvedic Bhasma: The Ancient Science of Nanomedicine

Sanjoy Kumar Pal*

School of Animal & Range Sciences, Haramaya University, Dire Dawa, Ethiopia

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Dr. Sanjoy Kumar Pal

Abstract: Nanomedicine is the relevance of nanotechnology in the area of healthcare, diagnosis of disease, cure and prevention of disease. Nanotechnology covers the diverse area of matters at dimensions between approximately 1 to 100 nanometers. Nanotechnology has enormous applications in drug delivery field. Nano drug delivery systems can reduce the drug consumption and side-effects by lowering the deposition of the active agent in the non targeted sites. Ayurveda is thousands of years old holistic system of Indian medicine. Various herbs, metals and non-metals preparations are used as medicine in Ayurveda. In the Ayurvedic description, several metallic preparations called *Bhasma* are in clinical use since 8th century AD. The Puta system of Ayurveda describes that metals or minerals should be heated at high temperature for melting and then it quench in suitable media like herbal juices or decoction for specified times. The *Bhasma* (incinerated metals) is obtained by repeating these methods several times. In this process the toxic effects of the metals are not only nullified but are transformed into biologically active nanoparticles. When various *Bhasmas* viz. *Swarna bhasma*, *Makshika bhasma*, *Abhrak bhasma*, *Tamra bhasma* and *Louha bhasma* were subjected to analysis under electron microscope it was found that they were similar to nanocrystalline materials possessing similar physico-chemical properties. The therapeutic effect of *Bhasma* may be attributed to large surface area of materials and small particle size by which they can easily transported into cell nucleus and to specific target sites as desired.

Keywords: Ayurveda, *Bhasma*, nanomedicine, nanosize, patent, safety.

INTRODUCTION

In the last 30 years material science has progressed widely with the applications of nanomaterials. Nanomaterials and structures possess very unique features owing to their small size, as compared with larger bulk materials, making them suitable candidates for novel applications [1]. Nanotechnology has been the focus of considerable attention in medicine due to the facility with which nanostructures interact with the body at the molecular scale [2]. Pharmacokinetics and bio-distribution of active ingredients can be improved remarkably with nano drug delivery systems by targeting them to the specified site, thereby efficacy and bio availability can be improved and drug toxicity will be reduced. For achieving this researchers exploited the drug in the body in a controlled manner from the site of administration to the targeted area [3]. Ayurveda is one of the oldest systems of medicine, practiced in Indian sub-continent [4].

Ayurveda is a well-established science of ancient Indian heritage. The word Ayurveda implies the meaning “science of life”. This science is trusted and established through thousands of years. At the time of *Charaka* and *Sushuruta* medicinal plants were primarily used for the preparation of remedial agents. In 8th century AD the Indian alchemist *Nagarjuna* first introduced the use of metals and

minerals like - *Swarna* [gold], *Rajat* [silver], *Tamra* [copper], *Abhrak* [mica], and *Makshika* [pyrites], *Rasa* [mercury] as medicinal agent. The branch of Ayurveda dealing with herbo-metallic preparation is known as *Rasa Shastra* [5].

ANCIENT AND CURRENT ASPECT OF NANOTECHNOLOGY

In the ancient time it may be a serendipitous discovery that when metals, minerals like gems like gold, silver, copper, mercury, lead, iron, arsenic etc. are heated to red hot/burned several times and then mixed with herbs and other medicinal agents drastically altered the effectiveness of certain Ayurvedic medicines without producing any toxic or harmful side effects. The scientist of ancient times had limited knowledge that continuous burning and cooling of metals / minerals / gems (in some case which was more than 100 times) changed the physical and chemicals properties of the parent metal. The nano size particles were totally different from original particles in chemical composition and structure (Fig. 1). It not only increased the surface area but the nano size also helped the drugs to reach the target site efficiently. The scientists of the ancient time did this process to get rid of the toxic effect of the metal/minerals; however, the end result was remarkable. The drugs developed in this method were not only more effective but had quick action and required smaller dosage. They became more palatable and also had longer shelf life. Hence, the use of metals and minerals became the strength of Ayurvedic therapeutics. The ashes that were obtained after calcined preparation of metals

*Address correspondence to this author at the School of Animal & Range Sciences, College of Agriculture & Environmental Sciences, Post Box: 138, Haramaya University, Dire Dawa, Ethiopia; Tel: +91-9867705500; E-mail: sanjoypal@yahoo.com

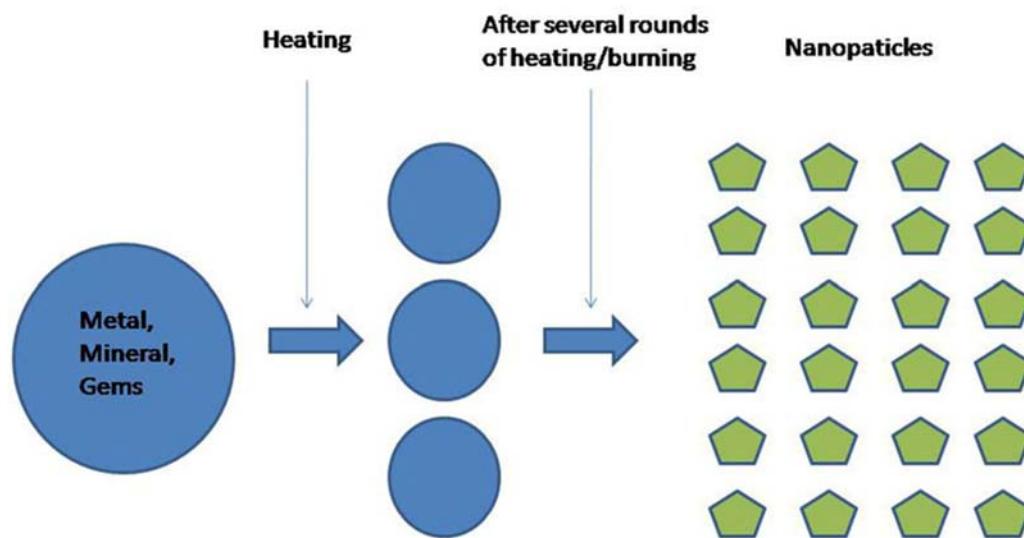


Fig. (1). Schematic diagram of how toxic metal, minerals and gems turn into non-toxic nanoparticles after several rounds of heating and burning.

and minerals were prepared by triturating and macerating in herbal extracts was known as *Bhasma*.

However, the real significance of nanomedicine and its potential was realized only recently. Though there are many use of nano medicine, however, the primary applications of nanomedicine at present time include diagnosis of various diseases which are difficult to spot with the presently available conventional techniques in addition to crafting proficient and biosafe drug delivery systems for site specific targeting with ultimate goal of treatment of diseases [6]. Moreover, nanomedicines can also be utilized to investigate cellular movements and molecular variations which are often related to pathological conditions with the promise of building fabricated cells, enzymes and genes [7]. Nanomedicines can also be described as carrier systems in the nanometric scale carrying drugs, imaging agents, diagnostic agents, antibodies and others [8]. The nanotechnology has proven to be a state of the art technology for medical scientists which enable them to reduce drug carrier size for an efficient line of attack against ailments. The foreseen enormous scientific and commercial potential of nanotechnology in the area of human health care lies in developing significantly effective medical treatment strategies [9]. One major advantage of nanotechnology is its flexibility which enables the nanomedicines to take various shapes such as liposomes, dendrimers, nanoparticles, nanocrystals etc. so as to the meet the needs of desired or required biomedical applications [10].

THERAPEUTIC USE OF BHASMAS

Though *Rasa Shastra* is a very important branch of Ayurveda since 8th century; however, report of large scale randomized clinical trials involving *Bhasmas* are less. One of the reasons for this may be the fact that *Rasa Shastra* is well tested science; hence, there was no need of fresh proof. However, few properly conducted clinical studies indicated that nutritional anemia in nonpregnant adolescent girls can be improved by a daily dose of *Sootshekhar Rasa* (250 mg)

plus *Sitopaladi Churna* (400 mg) [11]. Another clinical study of *Kukkutanda twak bhasma* reveals statistically significant improvement in *Swetapradara*, an important gynecological disorder [12]. Likewise, '*Swarna Bhasma*' has shown some response in the treatment of solid tumor [13], and certain herbo-minerals preparations were found to be effective in leukemia [14, 15]. *Swarna Bhasma* also has antioxidant/restorative effects against global and focal models of ischaemia (stroke). *Nāga bhasma* (lead calx) is a potent metallic formulation mainly indicated in the treatment of *Prameha* (diabetes) [16]. Use of some *Bhasmas* is given in Table 1.

STEPS USED TO PREPARE BHASMAS

Bhasmas are being prepared by *Putapaka* method and *Kupipakwa* method [17].

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 quenched in suitable liquid media for required times. *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. Then heat is applied into this apparatus (*Sarava Sampatam*) 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, *Sarava Samputa*. After repeating these procedures for particular time finally prepared *Bhasma* (incinerated metal) is collected.

Table 1. Marketed *Bhasmas* products and their uses (Adopted from [18]).

Name	Ingredients	Uses
<i>Navrattankalp amrit ras</i>	Calcined ash of expensive gems, minerals like ruby, sapphire, emerald, cat's eye stone, pearl, coral, silver, gold, iron, zinc	Cancers of all types, anemia, complication of diabetes
<i>Heerak Bhasma</i>	Diamond	Useful in cancers, immunity disorders, crippling rheumatoid arthritis, bone marrow depression
<i>Tsrailokya chintamani ras</i>	Diamond, gold, silver, iron	Severe respiratory tract infection, marrow depression, ovarian cysts, uterine fibroids
<i>Swarna basant mali ras</i>	Gold, <i>piper-nigrum</i> , white pear powder	Tonsillitis, fevers, cough, bronchitis, decreased immunity, cancers, autoimmune disorders
<i>Kamdudha ras</i>	Ochre, <i>Tinospora cordifolia</i> , mica (calcined)	Hyperacidity, headache, fever, blood pressure
<i>Vasant kusumakar ras</i>	Gold, silver, coral	Complications of diabetes, neuropathy, general weakness
<i>Kumar kalian ras</i>	Gold, iron, mica, copper pyrite, red sulfide of mercury	General debility in children, fever, respiratory tract infections
<i>Tamra Bhasma</i>	Copper, mercury, sulfur	Anemia, jaundice, digestive disturbance, abdominal disorders
<i>Loha Bhasma</i>	Iron, cinnabar	Enlargement of liver, anemia, jaundice
<i>Vaikrant Bhasma</i>	Manganese, sulfur (Tourmaline)	Diabetes, can be used in place of diamond ash in case of poor patients
<i>Loknath ras</i>	Mercury, sulfur, conch shell	Diarrhea, respiratory disorders, immunity disorders, cancers, ovarian cysts
<i>Abhrak Bhasma</i>	Calcined purified mica ash	Respiratory disorders, diabetes, anemia, general weakness
<i>Swarna Bhasma</i>	Ash of gold (Calcined gold)	Improves body immunity, general weakness, anemia, energetic
<i>Rajat Bhasma</i>	Silver ash (Calcined silver)	Irritable bowel syndrome, acidity, pitta disorders
<i>Ras raj ras</i>	Red sulfide of mercury, mica, gold, iron, silver, with <i>aniasomnifera</i> , <i>Syzygium aromaticum</i>	Paralysis, hemiplegia, rheumatism, insomnia, stroke
<i>Shwaskuthar ras</i>	Black sulfide of mercury, aconitum ferox, sodium bicarbonate, <i>piper nigrum</i> , <i>Trikatu'</i>	Cough, pneumonia, bronchitis
<i>Swarnmakshik Bhasma</i>	Copper pyrite (calcined), mercury, sulfur	Anemia, jaundice, stomatitis, chronic fever
<i>Kaharva pishti</i>	Amber of succinate (trinkantmani), <i>rosa centifolia</i> (rose)	Bleeding
<i>Yogender rasa</i>	Red sulfide of mercury, gold (calcined), magnetic iron, mica, <i>myristica fragrans</i>	Polio, paralysis, muscular weakness, insomnia, headache
<i>Bolbadh ras</i>	Black sulfide of mercury, <i>Tinospora cordifolia</i> , <i>Commiphora mukul</i>	Bleeding
<i>Praval pishti</i>	Purified powder of corals	Calcium deficiency, blood pressure, insomnia, agitation
<i>Praval panchamrit</i>	Powder of corals, pearls, conch Shells	Richest source of natural calcium agitation, acidity, burning sensation
<i>Jaharmohra pishti</i>	Powder of serpentine orepithite	Natural source of calcium, useful in burning sensation, acidity, heart burn
<i>Sarvatobhadra Vati</i>	Mercury, sulfur (purified and calcined), with gold	Renal failure, nephrotic syndrome, dialysis, high urea and creatinine
<i>Mukta pishti</i>	Pearls powder (moti pishti)	Calcium, cooling and soothing, blood pressure, acne, headaches, acidity, ulcers, heat disorders

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 an 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.

CHARACTERIZATION OF BHASMAS

There are certain characteristic that properly processed *Bhasma* should possess, some of the qualities are mentioned here [18].

1. **Color (Verna):** A specific color is mentioned for each *Bhasma*. *Bhasmas* are found in white, pale, or red colour. The colour of the preparation primarily depends on the parent material.
2. **Lusterless (Nishchandravam):** *Bhasma* must be lusterless before therapeutic application. For this test, *Bhasma* is observed under bright sunlight whether luster is present or not, if luster is still present, it indicates further incineration.
3. **Lightness and Fineness (Varitara):** *Bhasma* floats on stagnant water surface. This test is based on law of surface tension. Properly incinerated *Bhasma* is needed to float on water surface.
4. **Tactile sensation:** Tactile sensation can be absorbed and assimilated in the body without producing any irritation to mucous membrane of gastrointestinal tract.
5. **Particle size:** Prepared *Bhasma* should be in powder form. Particle of *Bhasma* should be like pollen grains of *Pondanus odoratissimus* flower (Ketaki rajah).

BHASMAS AS NANOPARTICLES

A scientific analysis of *Swarna Bhasma* by transmission electron microscopy and atomic force microscopy has demonstrated that the principle ingredient of *Swarna Bhasma* is globular gold particle of 56-57 nm. Atomic Absorption Spectroscopy and Infrared Spectroscopy studies revealed that *Swarna Bhasma* is devoid of any other heavy metal or organic material [19]. Likewise, *Ras-Sindoor* (sublimed mercury compound) is contain mercury sulfide (crystalline; size, 25-50 nm). This is an organic macromolecules derived from plant extract. Several macro/trace elements may be present in different amounts, which are bio-available and responsible for adding to medicinal value of *Ras-Sindoor* [20].

Study reveals in physicochemical characterization of *Jasada Bhasma* by "X-ray photoelectron spectroscopy (XPS), inductively coupled plasma (ICP), elemental analysis with energy dispersive X-ray analysis (EDAX), dynamic light scattering (DLS), and transmission electron microscopy (TEM)" that the particles are in oxygen deficient state and many of them are in nanometer size range. These reported size range of *Jasada Bhasma* might impart its therapeutic property [21].

TOXICITY ISSUES WITH BHASMAS

Ayurvedic medicines are used widely in India, in spite of that their long term safety is till date a question due to presence of toxic metals in them [22]. The American medical research community has sounded a heavy metal warning

against Ayurvedic cures [23]. Manufacturers of Ayurvedic medicines are now facing different problems such as inferior quality of raw material, lack of authentication of raw material, non-availability of standards, deficient in proper standardization method for single drugs and formulations and no quality control parameters [24]. Use of inferior grade of raw material, adulteration and deviations in standard manufacturing practice either intentionally or unintentionally, leads to the production of inferior quality products, which not only rise the concern over the efficacy but also the safety [25]. Because of wide spread use of Ayurvedic medicines it has become necessary to lay down stringent parameters to ensure batch to batch consistency and reproducibility [26].

Table 2. List of some patented *Ayurvedic* medicine.

S. No.	Name of the Patented Medicine
1	Tab. Liv 52
2	Syp. M2 Tone
3	Tab./Syp. Vomitab
4	Tab. Kuka
5	Tab. Cystone
6	Tab. Uricare
7	Tab. Tensonil
8	Tab. Prostol
9	Tab. Mentat
10	Tab. Pigmento (Chark comp.)
11	Ulsorex oint
12	Jalan oint
13	Cap. Rheume D.S
14	Cap. Diabetex
15	Tab. Cephagraine
16	Cephagraine Nasal drops
17	Syp. Dysco
18	Syp. Honeyson
19	Cap Karnim
20	Tab. Abana
21	Tab. Geriforte
22	Tab. Feverx
23	Arthral Oil
24	Catramide Eye drops
25	Netrol drops
26	Otosol Ear drops

PATENTED PRODUCTS

Ayurvedic knowledge is centuries old in Indian sub continent and as per the rules to get a patent it must be new invention, consisting nobility with commercial industrial application [27]. Hence, readymade Ayurvedic formulations

Table 3. Status of ayurvedic patents in India.

S. No.	Name of the Patent	Status of Patent	Patent No./Date
1	A process for the production of a Lactonic glycoside from <i>Nerium indicum</i> Mill. (syn. <i>N. odorum</i> Sol.)	Granted	138350/Dt. 26.09.73
2	A process for the production of an Extract useful in the treatment of Bronchial asthma from <i>Mesua ferrea</i> Linn. Seeds	Granted	139868/dt.04.04.74
3	A process for the production of a Sodium Salt of a natural 2-methyl chromone isolated from the pods of <i>Cassia siamea</i>	Granted	140032/Dt. 04.04.74
4	A process for the isolation of a Pongaflavone from <i>Pongamia pinnata</i> (L.) Pierre (syn. <i>P. glabra</i>)	Granted	140321/Dt. 04.04.74
5	A process for the production of a Benzofuran derivative from kojic acid and catechol	Granted	139869/Dt. 04.04.74
6	AYUSH-56 - Process for preparation of therapeutically active anti-epileptic preparation	Granted	141170/dt. 28.07.1976
7	A process for the preparation of 9,13-Epoxy-6 β-hydroxy-8α-Labdone-16,15, 19,20-diolactone 2 known as Nepetaefolinol from the whole plant of <i>Leonotis nepetaefolia</i> Linn	Granted	147936/Dt. 14.08.78
8	A process for the isolation of Vincristine from <i>Vinca rosea</i>	Granted	150019 /Dt. 12.06.79
9	A process for the preparation of vinblastine from <i>Vinca rosea</i>	Granted	150024/Dt. 12.06.79
10	AYUSH-64 - A process for the preparation of a therapeutically active anti-malarial preparation.	Granted	152863/dt.28.07.1980
11	Ksharsutra - A medicated thread for Anorectal diseases	Granted	186243/dt.15.02.2002
12	A Process for the Preparation of Novel Composition from <i>Swertia chirata</i> Buch. Ham. (Gentianaceae) having Anti-carcinogenic (cancer Preventive) and anti-Tumor (Cancer Therapeutic) Action	Granted	191128/Dt. 26.3.2002
13	A Process for the Isolation of Amarogenitin, Novel Seco-Iridoid Glycoside Possessing Anti-carcinogenic (Cancer Preventive) and Anti-Tumor (Cancer Therapeutic) Action	Granted	191129/Dt. 26.3.2002
14	AYUSH Ghutti -“A herbo-mineral formulation” for cough and cold	Granted	193336/dt. 8.11.2004
15	Pharmaceutical ayurvedic preparation	Granted	US 6,939,567B1/Dt. 06. 09.2005
16	BAL RASAYAN - A process for the preparation of a herbo- mineral preparation for general immunity and strengthening of children	Granted	196916/dt.07.07.2006
17	A herbal preparation for combating stress borne syndrome in extreme cold conditions	Filed	961/DEL/2004/Dt. 27.5.2004
18	AYUSH-UT Ointment - A novel Ayurvedic herbal cream	Filed	1346/DEL/2006/Dt. 06.6.2006
19	AYUSH -SS granules “A process for preparation of an Ayurvedic herbal compound preparation” for post natal care (to enhance the quality and quantity of breast milk in mother having deficient lactation)	Filed	1835/DEL/2008/Dt. 01.8.2008
20	AYUSH LND Tablet “A process for preparation of an Ayurvedic herbal compound preparation”in Gynecological disorders (to prevent Dysfunctional Uterine Bleeding (DUB).	Filed	1834/DEL/2008/Dt. 01.8.2008
21	“A process for preparation of an Ayurvedic herbal compound preparation of AYUSH AG Tablet (Shatamuli Mandura)” for Ante natal care	Filed	2216/DEL/2008/Dt. 22.09.2008

are not patentable. However, in the year 2005 Patent Amendment Act passed by the Parliament commenced in Sections 2 and 3 which are as follows: “section 2 of the Patent Act is the definition clause: According to section 2(j) invention means a new product or process involving an inventive step and capable of industrial applications. Inventive step means a feature of an invention that involves technical advance as compared to existing knowledge or having economic significance or both and that makes the invention not obvious to a person skilled in art” [27].

It is reported that till 31st March, 2013, 86 applications were filed by foreign entities and 523 applications were filed by Indian entities. These were mainly for grant of patents for products, formulation, compositions & processes in the field

related to traditional Ayurvedic medicine, medicinal plants and herbal based formulations. Amongst these, only 26 patents have been granted to foreign entities and 93 patents to Indian entities [28].

A list of some formulations that got patented is given in Table 2. A medicine developed for acute promyelocytic leukemia comprising of herbal and ayurvedic bhasma like Silver bhasma, Serpentine stone, *Delphinium denudatum*, *Rosa centifolia*, *Santalum album*, *Onosma bracteatum*, *Hibiscus abelmoschus* also received a national and international patent [14]. The US patent 6939567 has reported treatment of leukemia by ayurvedic metallic Bhasma preparation without any side effects [29]. Another interesting patent by Thakur *et al.* patented *Haritaki, Amla*

and *Bahira* combination mixture product for reducing cholesterol-induced atherosclerosis in rabbits [30]. Table 3 represents some important Indian patents which have been granted or filed in current years. This report has been reproduced from the data base of Central Council for Research in Ayurvedic Sciences, Ministry of AYUSH, Government of India [31].

CURRENT & FUTURE DEVELOPMENTS

At present there are three types of *Bhasmas*: metal based, mineral based and herbal based. In future this composition of *Bhasma* can be modified or new composition of *Bhasma* can be introduced. The method of manufacturing of *Bhasma* can be modified or improved for better quality and nano property. Future application of this Nanomedicine, "Ayurvedic *Bhasma*" is immense in the field of healthcare and treatment. But official guidelines have to be set regarding: standardization, toxicity and safety studies, mass production issues, labeling rules, clinical studies and others.

CONCLUSION

There is no doubt that Ayurveda is one of the oldest systems of medicine. And no medical system can stand such a long period of time if it was not effective. Recent TEM and particle size analysis revealed that *Bhasmas* are in nanometer dimension [4]. Hence, *Bhasma* may be considered as nanomedicine and are free from toxicity in therapeutic doses. However, we have to reinvent this ancient science in the parameters and language of contemporary science. So proper scientific standardization of *Bhasma* should taken-up to maximize the therapeutic potential and properly designed randomized clinical trials should be done to demonstrate the efficacy. There is an urgent need for the practitioners of Ayurveda, scientific research institutions and the industry to work unitary to analyze the risk-benefit aspect of these herbo-mineral/metal based medicines.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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