Chapter 17
Nanometals in Bhasma: Ayurvedic Medicine

Dilipkumar Pal and Vinod Kumar Gurjar

Abstract Bhasmas are unique Ayurvedic metallic preparations with herbal juices or fruits, known in the Indian subcontinent since the seventh century BC and widely recommended for treatment of a variety of chronic ailments. More than 18 Bhasmas based on calcium, iron, zinc, mercury, silver, potassium, arsenic, copper, tin, and gemstones were analyzed for up to 18 elements by instrumental neutron activation analysis method, including their C, H, N, and S contents. In addition to the major constituent elements found at percent level, several other essential elements such as Na, K, Ca, Mg, V, Mn, Fe, Cu, and Zn have also been found in μg/g amounts and ultratrace (ng/g) amounts of Au and Co. The Bhasmas are biologically produced nanoparticles and are taken along with milk, butter, honey, or ghee thus; this makes these elements easily assimilable, eliminating their harmful effects and enhancing their biocompatibility. Particle size (1–2 μm) is reduced significantly, which may assist absorption and assimilation of the drug into the body system. Standardization of *Bhasma* is utmost necessary to confirm its identity and to determine its quality, purity safety, effectiveness, and suitability of the product. But the most important challenges faced by these formulations are the lack of complete standardization by physiochemical parameters.

Keywords Ayurveda • *Bhasma* • Nanoparticle • Nanotechnology • *Lauha Bhasma* • *Shankha Bhasma* • Nanomedicine

Abbreviations

AFM	Atomic Force Microscopy
Ag	Silver
Au	Gold
CaO	Calcium Oxide

D. Pal (✉) • V.K. Gurjar
Institute of Pharmaceutical Sciences, Guru Ghasidas Vishwavidyalaya (A Central University), Koni, Bilaspur 495 009, Chhattisgarh, India
e-mail: drdilip71@gmail.com

M. Rai, R. Shegokar (eds.), *Metal Nanoparticles in Pharma*,
DOI 10.1007/978-3-319-63790-7_17

DLS	Dynamic Light Scattering
EDAX	Elemental Analysis with Energy Dispersive X-Ray Analysis
GIT	Gastro-Intestinal Tract
ICP	Inductively Coupled Plasma
NIH	National Institute of Health
NPs	Nanoparticles
PbS	Lead Suilphide
PXRD	Powder X-Ray Diffraction
TEM	Transmission Electron Microscopy
XPS	X-ray Photoelectron Spectroscopy

17.1 Introduction

Nanotechnology is a recent technology and is being used in almost all industry for the development of cost-effective and eco-friendly products. The term "nanotechnology" was first defined by Tokyo Science University, Norio Taniguchi, in a 1974 paper as follows: "Nanotechnology" mainly consists of the processing of, separation of, consolidation of, and deformation of materials by one atom or one molecule. It is anticipated to open some new aspects to fight and prevent diseases using atomic scale tailoring of materials (Geetha et al. 2016). The ability to uncover the structure and function of biosystems at the nanoscale stimulates research primary to improve biology, biotechnology, medicine, and healthcare. The size of nanomaterials is similar to that of most biological molecules and structures; therefore, nanomaterials can be helpful for both in vivo and in vitro biomedical research and applications. Nanotechnology is currently employed as a tool to discover the darkest avenues of medical sciences in several ways like imaging, sensing, targeted drug delivery and gene delivery systems, and artificial implants. The new-age drugs are nanoparticles of polymers, metals, or ceramics, which can combat conditions like cancer and fight with human pathogens like bacteria and other microorganisms (Pandey and Pandey 2013; Othayoth et al. 2014). This emerging technology has multiple possible applications and thus affects various technological domains including advanced materials, biotechnology and pharmacy, electronics, scientific tools, and industrial manufacturing processes. The emergence of nanotech has been enabled by the development of specialist instruments, which in turn facilitated the observation and management of nanostructures at the atomic or molecular scale, as well as the discoveries of new nanomaterials. Nanotech offers also new opportunities in rapid development of neatness techniques (so-called "top-down" approach, involving decomposition into the smallest manageable entities) and building macrostructures (so-called "bottom-up" approach, allowing reengineered materials at nanolevel and using them in developing new and improved products) (Miyazaki and Nazrul Islam 2007).

Nanotechnology, being so promising and lurking with possibilities, doesn't escape this bitter truth. Owing to their various applications in the field of medical

science, the sad fact is that these potentially dwarf particles can expose negative effects to our body's system. Nanoparticles (NPs) can potentially cause adverse effects on organ, tissue, cellular, subcellular, and protein levels due to their abnormal physicochemical properties (e.g., small size, high surface area-to-volume ratio, chemical composition, electronic properties, surface structure reactivity and functional groups, inorganic or organic coatings, solubility, shape, and aggregation behavior). Metal NPs, in particular, have received increasing attention due to their widespread medical, consumer, industrial, and military applications. But these metal-based NPs have been confirmed to show tremendous toxicity, though the same material is relatively inert in its bulk form (e.g., Ag, Au, and Cu). Metals at the nanoscale level owing to their difference in bulk form properties can pose potential harmful biological interactions. Scientific validation and the documentation of Ayurvedic drugs are very crucial for its quality evaluation and worldwide acceptance. Metal nanoparticles have a high specific surface area and a high fraction of surface atoms and have been studied extensively because of their unique physicochemical characteristics including catalytic activity, optical properties, electronic properties, antimicrobial activity, and magnetic properties (Shahverdi et al. 2007). Nanotechnology promises important improvements of advanced materials and manufacturing techniques, which are significant for the future competitiveness of national industries (Miyazaki and Nazrul Islam 2007).

Therapeutic usefulness of Ayurvedic herbs may be improved with high quality, which can be achieved by uniqueness, purity, safety, drug content, and physical and biological properties. Ayurvedic medicines need to be explored with the modern scientific approaches for its validation. Therefore, an effort has been made in the present chapter to highlight the essential aspects that need to be considered for the promotion and development of Ayurvedic medicine. Size reduction is one of the basic unit operation having important applications in pharmacy. It helps in improving solubility and bioavailability, reducing toxicity, enhancing release, and providing better formulation opportunities for drugs. Drugs in the nanometer size range enhance performance in a variety of dosage forms. The recent status of nanotechnology in pharmaceutical field includes development of nanomedicine, tissue engineering, nanorobots, biosensors, biomarkers, etc. Pharmaceutical nanotechnology provides opportunities to improve materials and medical devices and help to build up new technology where existing and more conventional technologies may be reaching their limits (Varshney and Shailender 2012).

17.2 Distinctive Features of Nanoscience and Nanotechnology

Nanoscience and nanotechnology are extensively seen as having enormous potential to many areas of scientific research such as physics, chemistry, material sciences, biology, and engineering and technological applications (such as healthcare and life sciences, energy and environment, electronics, communications and

computing, manufacturing, and materials) because of its nanoscale where the materials' properties are significantly different from those of the same materials in bulk or macroscopic form. Nanotechnology encompasses the work of nanoscale science and enlarges understandings of interactions in the atomic or molecular scale and the capacity to characterize and control materials using nano-tools (Miyazaki and Nazrul Islam 2007).

Nanotechnology has a multidisciplinary character, affecting multiple traditional technologies, scientific disciplines, and industries. Additionally, through the nanotech revolution, boundaries between previously distinctive disciplines such as mechanics and chemistry begin to blur, stimulating knowledge transfer and cross-fertilization (Nicolau 2004). Many scientists believe that nanomaterials will induce a new generation of consumer products, based on miniaturized computer chips, nanoscale sensors, and devices for sorting DNA molecules and integrating microsystems and biotechnology (Ikezawa 2001). Nanotechnology innovation can be characterized as evolutionary from micro to nano. An important feature of nanotech is that it is not restricted to the realm of advanced materials, extending also to manufacturing processes, biotechnology and pharmacy, electronics and information technology, as well as other technologies (Miyazaki and Nazrul Islam 2007).

17.3 Nanotechnology in Medicine

Nanotechnology has been setting benchmarks for the last two to three decades, but the origins of this technology achieve back to ancient history. Today, nanoparticles of both metallic and nonmetallic origin are under research and development for applications in different fields of biology/therapeutics (Sengupta et al. 2014). Applying nanotechnology for treatment, diagnosis, monitoring, and control of diseases has been referred to as "nanomedicine." While the application of nanotechnology to medicine appears to be a relatively recent development, the basic nanotechnology approaches for medical application date back several decades (Singh et al. 2008).

17.4 Nanotechnology in Ayurveda

Nanotechnology has been the focus of significant attention in medicine due to the facility with which nanostructures interact with the body at the molecular scale. Pharmacokinetics and biodistribution of active ingredients can be improved remarkably with nano-drug delivery systems by targeting them to the specified site; thereby efficiency and bioavailability can be improved, and drug toxicity reduces. In eighth 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 agents (Conde et al. 2014). The branch of Ayurveda dealing with herbo-metallic preparation is known as *Rasa*

Shastra. One major gain of nanotechnology is its flexibility, which enables the nanomedicines to take different shapes such as liposomes, dendrimers, nanoparticles, nanocrystals, etc., so as to the meet the needs of desired or required biomedical applications (Pal 2015).

17.5 Types of Metal Nanoparticles

Concept of reduction in particle size of metals is prevailing since *Charaka Santhita* (1500 BC). For a metallic preparation of *Lauhadi Rasayana*, the tip of iron is heated to red hot and quenched in some liquid media immediately until flakes of iron become fine powder form. Nanotechnology has ability to work at these levels to produce larger structures with new molecular organization (Sarkar and Chaudhary 2010). The invention of nanoparticles is not less than a miracle due to the distinctive properties that offer innovative and life-changing products and technologies in the fields of medicine. Nanotechnology is however also questioned in terms of safety for humans and also animals, plants, and ecosystem at large. There has been an exponential increase in this field with a wide variety of products, which are questioned for safety by many international organizations (Palkhiwala and Bakshi 2014). Particles of "nano" size have been shown to exhibit improved or novel properties including reactivity, greater sensing capability, and increased mechanical strength. The nanotechniques offer simple, clean, fast, efficient, and economic process for the synthesis of a variety of organic molecules and have provided the thrust for many chemists to switch from traditional method (Arivalagan et al. 2011).

Nanoparticles are the new approach to the scientists in the field of biomedical and commercial application. Nanotechnology is the field of advanced technology for medicine and imaging of various critical diseases. It is built as nanodevices and particles on the scale of 10^{-9} m, whereas size of the cell is 10 μm, and cell organelles have size in nanometer range. Nano-sized particles can easily enter into the cell and take part in the cell metabolism. Metal nanoparticles now are being applied in the field of drug delivery and imaging. Scientists are trying to develop noble nanoparticles, which can release the drug at exact site of targeted tissue and to be able to escape from the degradation system of the body. Metal nanoparticles have characteristics, small size and unique chemical properties, which are the important features for future development for various therapeutics and imaging (Yadav et al. 2016).

Ayurvedic nanomaterials, especially the gold *Bhasmas*, have unique physicochemical properties such as biocompatibility and ease of surface fictionalization. The most chronic illnesses, including cancer, diabetes, and cardiovascular and pulmonary diseases, are mediated through constant inflammation and it has the potential to delay the suppressing chronic inflammation and prevent and treat various chronic diseases, including cancer. The Ayurvedic *Bhasmas*-coated nano-tablets have been studied for their anticancer activity (Amin et al. 2009). The formulations in the "Bhasma" have nanoparticles. It is surprising for many researchers that 5,000-year-old Indian medical system have the knowledge of nanoscience and

technology. *Charaksamhitha* is the oldest classical way of Ayurveda with the thought of reduction in particle size of metals. The *Bhasmas* are used for treatments of various diseases in Ayurveda for the past several centuries in the form of nanotechnology; some of the common properties in the Ayurvedic *Bhasmas* are "Rasayana" (immune-modulation and antiaging quality) and "Yogavahi" (ability of drug carry and targeting drug delivery). They were prescribed in minute dosage (15–250 mg/day) (Othayoth et al. 2014).

17.6 Bhasma: An Ayurvedic Medicine

The traditional medicinal system practicing in India for several centuries is well known as Ayurveda. According to this medicinal system, metal-based drugs known as "Bhasma" involve the modification of a metal into its mixed oxides. During these transformations, the zerovalent metal state gets converted into a form with higher oxidation state, and the most important aspect of this synthesis (traditionally known as "Bhasmikarana") is that the toxic nature (i.e., systemic toxicity causing nausea, vomiting, stomach pain, etc.) of the resulting metal oxide is completely destroyed while inducing the medicinal properties into it. The important step implicated in the procedure for making "Bhasma" is repeated treatment (Wadekar et al. 2005). *Bhasmas* are such kind of dosage forms which gained their position as effective formulations for any disease compromising the aspects of nanotechnology and overcoming the limitations of usual dosage forms (Rasheed et al. 2014).

Bhasmas are particulate matters that are thought to be readily assimilated in the body's system. They are highly inert in nature because of insolubility. *Bhasma* is important in maintaining optimum alkalinity for good health, neutralizing harmful acids that lead to illness, because *Bhasma* does not get metabolized so they don't produce any harmful metabolite, rather it breaks down heavy metals in the body (Hareshwar et al. 2017). Most of the *Bhasmas* are mixed with cardamom, cinnamon, ghee, and honey and are taken orally. In clinical practice, *Bhasma* is not reported to have any serious untoward effects. Although honey is one of the most frequently suggested vehicles in Ayurvedic texts, royal jelly, another honeybee product, is apparently not mentioned. Honey is considered as highly nutritious with nine elements (lithium, sodium, potassium, rubidium, magnesium, iron, manganese, copper, and zinc) reported in a recent study in which metal profiles have been used for its classification. Natural food users claim that royal jelly very quickly lowers blood sugar when taken orally by diabetic patients. In fact, it contains a polypeptide that is similar to bovine insulin. The crude royal jelly and a fraction that co-migrates chromatographically metabolize glucose in vitro incubation with rat adipose fat tissues. The molecule is about 5,000–6,000 Da, contains disulfide bonds, and has an amino acid composition similar to that of bovine insulin (Kumar et al. 2006). Traditionally used *Bhasmas* and their ingredients are summarized in Tables 17.1 and 17.2.

Table 17.1 Bhasma and their ingredients

Bhasma	Ingredients
Abhrak Bhasma	Mica
Halthiana Bhasma	Charcoal of elephant tusk
Jasada Bhasma	Zinc oxide
Lauha Bhasma	Iron oxide
Mandura Bhasma	Iron oxide
Mayrapicha Bhasma	Ash of peacock feather
Mukta Bhasma	Oxide of pearl
Naga Bhasma	Lead
Parade Bhasma	Mercury compound
Pravala Bhasma	Oxide of coral
Rajat Bhasma	Silver oxide
Shankha Bhasma	Oxide of conch *Bhasma*
Muktashukti Bhasma	Oxide of pearl, oyster shell
Talaka Bhasma	Arsenic sulfide
Tamra Bhasma	Cupric oxide
Vanga Bhasma	Tin compound

Source: Pal et al. 2014

Table 17.2 Ayurvedic Bhasma ingredients, dosage, and uses

Name	Ingredients	Dosage	Uses
Navratan kalpamrit ras	Calcined ash of expensive gems, minerals like ruby, sapphire, emerald, cat's eye stone, pearl, coral, silver, gold, iron, zinc	62.5 mg twice daily	Cancers of all types, anemia, complications of diabetes
Heerak Bhasma	Diamond	12.5–25 mg twice daily	Useful in cancers, immunity disorders, crippling rheumatoid arthritis, bone marrow depression
Trailokya chintamani ras	Diamond, gold, silver, iron	62.5 mg twice daily	Severe respiratory tract infections, bone marrow depression, ovarian cysts, uterine fibroids
Swarna basant malti ras	Gold, *Piper nigrum*, white pearl powder	62.5 mg twice daily	Tonsillitis, fevers, cough, bronchitis, decreased immunity, cancers, autoimmune disorders
Kamdudha ras	Ochre, *Tinospora cordifolia*, mica (calcined)	250–500 mg twice daily	Hyperacidity, headache, fever, blood pressure
Vasant kusumakar ras	Gold, silver, coral	62.5–125 mg twice daily	Complications of diabetes, neuropathy, general weakness

(continued)

Table 17.2 (continued)

Name	Ingredients	Dosage	Uses
Kumar kalyan ras	Gold, iron, mica, copper pyrite, red sulfide of mercury	62.5–125 mg twice daily	General debility in children, fever, respiratory tract infections
Tamra Bhasma	Copper, mercury, sulfur	62.5–250 mg twice daily	Anemia, jaundice, digestive disturbance, abdominal disorders
Lauha Bhasma	Iron, cinnabar	125–250 mg twice daily	Enlargement of liver, anemia, jaundice
Vaikrant Bhasma	Manganese, sulfur (tourmaline)	62.5–125 mg twice daily	Diabetes, can be used in place of diamond ash in case of poor patients
Loknath ras	Mercury, sulfur, conch shell	62.5–125 mg twice daily	Diarrhea, respiratory disorders, immunity disorders, cancers, ovarian cysts
Abhrak Bhasma	Calcined purified mica ash	125–250 mg twice daily	Respiratory disorders, diabetes, anemia, general weakness
Swarna Bhasma	Ash of gold (calcined gold)	12.5–62.5 mg twice daily	Improves body immunity, general weakness, anemia, energetic
Rajat Bhasma	Silver ash (calcined silver)	62.5–125 mg twice daily	Irritable bowel syndrome, acidity, pitta disorders
Ras raj ras	Red sulfide of mercury, mica, gold, iron, silver, *Withania somnifera*, *Syzygium aromaticum*	62.5–125 mg twice daily	Paralysis, hemiplegia, rheumatism, insomnia, stroke
Shwas kuthar ras	Black sulfide of mercury, *Aconitum ferox*, sodium bicarbonate, *Piper nigrum*, "Trikatu"	125–250 mg twice daily	Cough, pneumonia, bronchitis
Swarn makshik Bhasma	Copper pyrite (calcined), mercury, sulfur	125–250 mg twice daily	Anemia, jaundice, stomatitis, chronic fever
Kaharva pishti	Amber of succinite (Trinkantmani), *Rosa centifolia* (rose)	125–250 mg twice daily	Bleeding
Yogendra rasa	Red sulfide of mercury, gold (calcined), magnetic iron, mica, *Myristica fragrans*	62.5–125 mg twice daily	Polio, paralysis, muscular weakness, insomnia, headache
Bolbadh ras	Black sulfide of mercury, *Tinospora cordifolia*, *Commiphora mukul*	125–250 mg twice daily	Bleeding

(continued)

Table 17.2 (continued)

Name	Ingredients	Dosage	Uses
Praval pishti	Purified powder of corals	125–250 mg twice daily	Calcium deficiency, blood pressure, insomnia, agitation
Praval panchamrit	Powder of corals, pearls, conch shells	125–250 mg twice daily	Richest source of natural calcium, agitation, acidity, burning sensation
Jahar mohra pishti	Powder of serpentine orephite	125–250 mg twice daily	Natural source of calcium, useful in burning sensation, acidity, heart burn,
Sarvatobhadra Vati	Mercury, sulfur (purified and calcined), with gold	62.5–125 mg twice daily	Renal failure, nephrotic syndrome, dialysis, high urea and creatinine
Punarnava mandoor	Iron ore ash, *Boerhavia diffusa*, *Picrorhiza kurroa*, *Embelia ribes*	125–250 mg twice daily	Diuretic, anemia, swelling around joints, blood pressure, liver cirrhosis, ascites
Akik pishti	Agate stone calcined	125–250 mg twice daily	Heat/pitta diseases, blood pressure, acidity, ulcers
Mukta pishti	Pearl powder (motipishti)	62.5–125 mg twice daily	Calcium, cooling and soothing, blood pressure, acne, headaches, acidity, ulcers, heat disorders
Vriht vat chintamani ras	Herbs and minerals for vitiated vata-calcined mercury, sulfur (purified), and other metals and minerals	62.5–125 mg twice daily	Stroke, paralysis, parkinsonism, epilepsy, tetany, muscle stiffness, joint pains

Source: Pal et al. 2014

17.7 Importance of Bhasma

1. Maintain optimum alkalinity for optimum health
2. Provide easily absorbed and usable calcium
3. Cleanse the kidneys, intestines, and liver
4. Maintain stronger bones and healthier teeth
5. Alleviate insomnia and depression
6. Regulates rhythmic heart beating
7. Maintain arrhythmias and mineral balance
8. Help metabolize iron in body
9. Aid nervous system
10. Break down heavy metals and drug residues in the body
11. Neutralize harmful acids that lead to illness
12. Achieve a healthy alkaline level by neutralizing acid
13. Protect body from free radical damage (Pal et al. 2014)

17.7.1 Therapeutic Applications of Bhasmas

Although *Rasa Shastra* is a very important branch of *Ayurveda* since the eighth century report of large-scale randomized clinical trials involving *Bhasmas* is less. One of the reasons for this may be the fact that *Rasa Shastra* is a well-tested science; therefore, there was no need of fresh proof. However, a few properly conducted clinical studies indicated that nutritional anemia in nonpregnant teenager girls can be improved by a daily dose of *Sootshekhar Rasa* (250 mg) plus *Sitopaladi Churna* (400 mg). Another clinical study of *Kukkutandatwak Bhasma* reveals statistically significant improvement in *Swetapradara*, an important gynecological disorder. Likewise, "Swarna Bhasma" has shown some responses in the treatment of solid tumor, and certain herbo-mineral preparations were found to be effective in leukemia. *Swarna Bhasma* also has antioxidant/restorative effects against global and focal models of ischemia (stroke). *Naga Bhasma* (lead calx) is a potent metallic formulation mainly indicated in the treatment of *Prameha* (diabetes) (Pal 2015). Traditionally used Ayurvedic *Bhasma*, their ingredients, dosage, and uses have been summarized in Tables 17.2 and 17.3.

Table 17.3 Bhasmas, description and utility

Bhasma	Description	Utility
Calcium	Pearls and ghee (milk preparation)	Cough impotency, eye disorders, tuberculosis, spree, nervine sedative, used in hyperacidity, asthma, cough and nervous excitement in growing children and pregnant women
1. Mukta moti	Pearls and rose water pearls	
2. Muktashukti	Conch shell	
3. Praval pishti		
4. Shankh		Respiration, cough, heart diseases, stomach, liver, intestine
		Antacid, used in cough, phthisis, scrofulous, affections, spermatorrhea
		Pulmonary hemorrhage and calcium deficiency
		Antiperiodic, carminative, and analgesic, used in colic flatulence and tympanites
Iron	Magnetic iron (purified)	Spree, stomach disorders, anemia, diabetes, blood disorders, restorative
5. Vanaspati yog Lauh	Magnetic iron (purified), ash of incinerated magnetic iron	Hematinic, astringent, jaundice, disorders of liver and spleen
6. Kant Lauh	Ash of incinerated purified ferric oxide	Antirheumatic, hematinic, and used in anemia
7. Mandoor	Ferrum (purified), incinerated and potentiated, rubbed with trifala decoction	Alterative, hematinic, diuretic, used in anemia, edema, chlorosis, rickets, and jaundice
8. Trifala Yog Lauh		Strengthening the body, deficiency of iron, anemia, indigestion

(continued)

Table 17.3 (continued)

Bhasma	Description	Utility
Zinc	Zinc/ShudhYashad	Dysentery, sweating, phthisis, tuberculosis, diabetes, hypoglycemic, astringent used in urinary disorders
9. Yashad	Zinc carbonate/ash of incinerated purified zinc carbonate	
(a) Baidyanath		
(b) Deshrakshak		
10. Kharpar		Antacid, bone strengthening,
Mercury	Mercury	Physical disorders, strengthening the body, fever, malaria, asthma
11. Siddha Makardhwaj		
12. Parad	Mercury	Syphilis, genital disorders, rejuvenation
Silver	Silver	Wasting, nerve disorders, brain functions, eye disorders, tuberculosis
13.Rajat		
Potassium	Potassium nitrate, alum, ammonium nitrate (crystal powder)	Acidity, calculi, urinary tract infection, enlargement of prostate
14. Swet Parpati		
Arsenic	Arsenic	Nervine tonic, asthma, leukoderma, paralysis, and impotency
15. Kushta khas		
Copper	Ash of incinerated purified copper	Acidity, ascites, jaundice, piles, leprosy, leukoderma, asthma, tuberculosis, cough, skin diseases, obesity, chronic bloating, spleen and liver enlargement, cirrhosis
16. Tamra		
Tin	Tin	Asthma, cough, sweating, blood disorders, diabetes, diuretic and urinary antiseptic, semen disorder, syphilis, and gonorrhea
17. Vanga		
Stone	Ash of incinerated purified	Heart-related disorders, blood pressure, vomiting, burning sensation (pitta) cholera, antidote to poison, provides strength, potency, and vigor
18. Jahar Mohra Khatai Pishti	Serpentine orephite	Anemia, ascites, asthma, tuberculosis, diabetes and cancer, substitute of diamond Bhasma
19. Vaikrant	Ash of incinerated purified	
	Tourmaline	

Source: Kumar et al. 2006

17.7.2 Bhasmas as Nanoparticles

A scientific analysis of *Swarna Bhasma* by TEM and AFM has demonstrated that the principle ingredient of *Swarna Bhasma* is globular gold nanoparticles of 56–57 nm. Atomic absorption spectroscopy and IR spectroscopy studies reveal that *Swarna Bhasma* is devoid of any other heavy metal or organic material. Likewise, *Ras Sindoor* (sublimed mercury compound) contains mercury sulfide (crystalline; size, 25–50 nm). This is an organic macromolecule derived from plant extract. Several macro-/trace elements may be present in different amounts, which are bio-available and accountable for adding to medicinal value of *Ras Sindoor*. Study reveals in physicochemical characterization of *Jasada Bhasma* by XPS, ICP, EDAX,

DLS, and TEM that the particles are in oxygen-deficient state and many of them are in nanometer size range. This reports size range of *Jasada Bhasma* might impart its therapeutic property (Pal 2015).

17.7.2.1 Swarna Bhasma

Nobel metals and their compounds as a therapeutic agent, mainly of gold, have a long and distinguished history in medicine. *Swarna Bhasma* has a unique place in the Ayurvedic system of medicine. It is an integral part of Ayurveda, which describes its usage for the treatment of patients with various chronic disorders (Thakur et al. 2017). Containing gold particles, it has shown its anticancer activity. Since ancient times, *Swarna Bhasma*, prepared from gold, is used in Ayurvedic treatment of TB, infertility, asthma, tissue wasting, poisoning, etc. The last few years have witnessed extremely rapid development of nanotechnology, which seamlessly integrates many disciplines including biotechnology, medicine, chemistry, engineering, materials science, and physics. As the size of matter decreases from micrometric to nanometric dimensions, it exhibits novel physical and chemical properties because of increase in surface to volume ratio. Gold nanoparticles have found wide range of applications for diagnosis and targeted drug delivery in nanomedicine because of their chemical stability, surface chemistry, and unique optical properties. Some reports suggest that *Bhasmas* that are metallomedicines in powder form contain nanoparticles. It is suggested that because of nanometric dimensions of these particles, they may provide physiological basis of their action (Das et al. 2012; Rathore et al. 2013).

Swarna makshika is a mineral having different therapeutic uses and has been used since long in Ayurveda. *Swarna makshika* is used for the treatment of anemia, insomnia, convulsions, and skin diseases. It is also used as a single constituent formulation or in multi-ingredient formulation. Swarna makshika contains iron. *Bhasma* contains Fe_2O_3, FeS_2, CuS, and SiO_2 (Rathore et al. 2013).

Swarna Bhasma (incinerated gold) acts as *Vrishya* (aphrodisiac), *Hridya* (cardiac stimulant), and *Rasayana* (immunomodulator). It increases *Valya* (potentiality), *Kantikara* (complexion), *Ayushkara* (longevity), and *Medha Smriti Mati Pradam* (intellect, memory, and attentiveness). It diminishes disorders caused by all the three vitiated *doshas* and is used in the management of poisoning (*Visha Mukti).* *Swarna Bhasma* is indicated in *Yakshma* (tuberculosis), *Unmada* (schizophrenia), *Jwara* (fever), *Shoka* (grief), *Pandu* (anemia), *Shwasa* (dyspnea), *Kasa* (cough), *Krimi* (worm infestation), *Aruchi* (anorexia), *Chakshuroga* (ophthalmic disorders), and *Visha* (poisoning) (Prajapati et al. 2006; Sarkar et al. 2010).

17.7.2.2 Rajat Bhasma

It has been shown that *Rajat Bhasma* based on Ag acts on the brain and nervous system through a nutritive mechanism. In lower doses, it acts as an anxiolytic, but in higher doses (10–20 mg/kg), it reduces behavioral despair. It is also

recommended for eye disorders and tuberculosis. *Rajat Bhasma* contained 23.4 % Ag in addition to As (14.2 %), P (5.14 %), and Na (1.28 %), with Mn (183 μg/g) and Au (140 ng/g) in trace amounts. It also showed 19.9 % S, suggesting the possibility of silver sulfide (Ag_2S) or other sulfides (possibly As_2S_5) in addition to C (0.63 %) and H (0.25 %) resulting from some minor organic constituents such as polycyclic aromatic hydrocarbons (Kumar et al. 2006).

Rajat Bhasma (incinerated silver) possesses *Vrishya* (aphrodisiac), *Vayasthapana* (antiaging), *Lekhana* (scraping), and *Rasayana* (immunomodulator) properties. It increases potentiality (*Vaya*) and intellect *(Medha).* It eradicates diseases caused by all the three vitiated *doshas. Rajat Bhasma* is used in *Prameha* (diabetes), *Switra* (vitiligo), *Yakshma* (tuberculosis), *Pandu* (anemia), *Shwasa* (dyspnea), *Kasa* (cough), *Nayanaroga* (ophthalmic disorders), *Arsha* (piles), *Trishna* (thirst), *Shosha* (emaciation), and *Visha* (poisoning) (Sarkar et al. 2010).

17.7.2.3 Parada (Mercury) Bhasma

Mercury is used in therapeutics in a compound *(Murchtai)* form. These mercurial compounds are called *Murchita Parada* and possess *Vrishya* (aphrodisiac), *Vardhakya Harana* (antiaging), and *Rasayana* (immunomodulatory) properties. These increase potentiality (*Valakara*), intellect, memory, attentiveness, complexion (*Buddh*, *Smiriti*, *Prabha*, *Kanti Pradam*), and tissue elements (*Dhatu*). These eliminate diseases caused by all the three vitiated *doshas (humoral principles)* even restricting death *(MrityuNasaka).* Mercurial preparations are used in *Pandu* (anemia), *Shwasa* (dyspnea), *Kasa* (cough), *Kamala* (jaundice), *Jwara* (fever), *Shula* (spasmodic pain), *Mutrakriccha* (nephritis), *Vamana* (vomiting), *Udara Pida* (acute abdomen), *Krimi Dosa* (worm infestation), *Atisara* (diarrhea), etc. (Sarkar et al. 2010).

17.7.2.4 Tamra Bhasma

Copper is one such metal in the Ayurvedic system of medicine, which is used for preparation of *Tamra Bhasma* and is recommended in the dose of 10–30 mg for an adult (70 kg body weight; 0.2 mg/kg) to manage liver disorders, gastrointestinal tract (GIT) disorders, old age diseases, leukoderma, cardiac problems, and various other free radical-mediated disorders, besides alone or as herbo-mineral compositions. Deficiency of copper in the body causes weight loss, bone disorders, microcytic hypochromic anemia, hypopigmentation, graying of hair, demyelination of nerves, etc. (Pattanaik et al. 2003).

Ayurvedic *Tamra Bhasma* is derived from metallic copper that is recommended for different ailments of the liver and spleen, abdominal pains, colitis, heart problems, anemia, tumors, loss of appetite, dropsy, eye troubles, and tuberculosis. Recently, pharmacological investigations have been reported on the use of *Tamra Bhasma* for treatment of gastric ulcers and secretion and management of lipid peroxidation in the liver of albino rats and free radical-scavenging properties. Patil

et al. (1987) examine the effect of *Tamra Bhasma* on lipases and lypolytic activities in CCl_4-induced hepatic injury in rats. In case of *Tamra Bhasma*, crystallite size of CuO is found to be higher than that of a standard copper oxide, causing the reduction in its surface area. The preparation process of *Tamra Bhasma* involves repeated calcination cycles, thus facilitating agglomeration and hence bigger crystallites (Wadekar et al. 2005; Waghmare et al. 2016).

It's used for its rejuvenating and antioxidant property; it is also having beneficial effect as aphrodisiac agent. It is known to have properties of maintaining body circulation and tonicity. *Tamra* is included in the group of *Lauha/Dhatu* (metals). It is classified in *Sar Sadharana Lauh* group. Apart from availability of *Tamra* in native form, its different mineral and animal sources (earthworms and feathers of peacock) are also mentioned in the classics (Rai et al. 2008).

17.7.2.5 Abhrak Bhasma

Abhrak Bhasma, a herbo-mineral product of Ayurveda, acts as a tremendous antimicrobial agent. It acts as a synergistic agent, restoring the libido of men. Being a life-promoting drug, it helps in proliferation and synthesis of the sperms. It has a property of oleation. *Abhrak Bhasma* is called as a wonder drug due to its curative property in various ailments. It is the *Bhasma* of the mineral, mica. It contains Fe as a major element and Ca, K, and Si in low concentrations. Its synthesis involves repeated calcinations which transforms the metallic state into corresponding oxide form. It is widely used for the treatment of hepatic dysfunction, leukemia, sex debility, azoospermia, cystic fibrosis, postencephalic dysfunction, and cervical dysplasia (Buwa et al. 2001; Yadav et al. 2016).

17.7.2.6 Lauha Bhasma

Lauha Bhasma is an iron-based Bhasma, which is prepared from iron ore by a process known as *Bhasmikaran*. The procedure of preparation involves several steps, which include *Shodan* (purification), *Maran* (powdering), *Chalan* (stirring), *Dhavan* (washing), *Galan* (filtering), *Putan* (heating), and *Mardan* (triturating). The *Shodan* or the purification process removes the unwanted materials from the raw material and makes it suitable for the next step. During this process, the raw material is heated to red-hot condition and dipped into various agents such as oil, buttermilk, cow's urine, and rice gruel and horse-gram decoction (Rajendran et al. 2012). *Lauha Bhasma* is prescribed for the treatment of anemia due to iron deficiency. Consisting of Fe_2O_3 and Fe_3O_4, the preparation of *Lauha Bhasma* involves a rigorous procedure meant to convert the metal in to a fine, nontoxic and bioavailable form (Yadav et al. 2016). According to *Rasaratna Samuchchaya*, *kanta lauha* (magnetite Fe ore) is measured as best raw material variety of Fe for *Lauha Bhasma*. However in the absence of *kanta lauha*, *Teekshna lauha* (Fe turning) is used for the preparation of *Lauha Bhasma* (Singh et al. 2016).

17.7.2.7 Mandura Bhasma

Mandura Bhasma, an iron-containing preparation, has been used in therapeutics of anemia, jaundice, poor digestion, edema, skin diseases, etc. Generally, *Mandura Bhasma* is prepared in two steps: purification, procedure performs by heating to red-hot state and quenching in liquid media like cow's urine or *Triphala* decoction, and calcination, by *puta* system of heating in *Gaja puta* (specific amount of heat given through fixed quantity of fuel). During calcination, purified *Mandura* is levitated with *Triphala* (fruits *of Terminalia chebula Retz*, *Terminalia belerica Rox*, *Emblica officinalis Gaertn*) decoction and *Aloe vera* (*Aloe barbadensis* Mill) juice, etc. Mandura contain iron and silicate and *Mandura Bhasma* uses sensitive tools and techniques. *Mandura Bhasma* contains Fe_2O_3 and SiO_2. *Mandura Bhasma* are uniformly arranged in agglomerates of sizes 200–300 nm as compared to the raw *Mandura* which show a scattered arrangement of grains of sizes 10–2 μm (Mulik and Jha 2011).

17.7.2.8 Hiraka Bhasma

A gemstone *Hiraka* (diamond) is a popular one. The *Bhasma* of *Hiraka* is a well-known organomineral preparation, used for *Rasayana*, *Ayushya*, *Vrishya*, *Tridoshagna*, *Prameha*, *Arbuda*, etc. *Hiraka Bhasma* is not generally available in the market due to lack of standards and high cost, but at the same time it is being manufactured by some physicians and industries in the day-to-day practice of life. Analytically *Hiraka Bhasma* contains Fe_2O_3 as a major compound. Color of the *Hiraka Bhasma* is *malina rakta* which is due to presence of Fe_2O_3 (Zala et al. 2016). *Hiraka Bhasma* prepared from natural diamond is an important drug. It is an excellent remedy for heart troubles, heart pains, contraction of veins, and blood clotting. It is also a powerful tonic and antitumor agent. It's a carbon-based drug. It contains C, O_2, Na, Mg, Al, Si, P, S, K, Ca, Cr, and Fe (Acharya et al. 2014).

17.7.2.9 Jasada Bhasma

Jasada Bhasma is a unique preparation of zinc belonging to this class of *Bhasma*. The *Jasada Bhasma* is zinc oxide with nano- to micron-sized particles. The particles are polycrystalline. Its in-process intermediate on the other hand is mixture of zinc sulfide and oxide, with predominance of sulfide phase. Intermediate too has nano- to micron-sized particles (Chavare et al. 2017). This particular preparation has been successfully used by traditional practitioners for the treatment of diabetes and age-related eye diseases (Bhowmick et al. 2009; Chandran et al. 2016). *Jasada Bhasma* is cited for use in several other conditions including anemia, neuromuscular diseases, and eye diseases and as a wound healing, antimicrobial, and antiaging agent. An early anecdotal study shows antidiabetic activity of *Jasada Bhasma* in diabetic patients. The traditional use of *Jasada Bhasma* is suggestive of antioxidant and

Fig. 17.1 Naga Bhasma (Source: Nagarajan et al. 2014)

immunomodulatory effects. There are sporadic reports on reduction of fasted glucose levels, improved glucose tolerance, and antidiabetic activity in rats treated with *Jasada Bhasma.* In fact, a modern version of *Jasada Bhasma*, viz., zinc oxide nanoparticles, has been systematically investigated for their antidiabetic effect (Umrani et al. 2013).

17.7.2.10 Naga Bhasma

Naga Bhasma (Fig. 17.1) has been used to treat a variety of ailments, and different Ayurvedic formulations containing *Naga Bhasma* are available (Nagarajan et al. 2014a, b); it has its history of medicinal applications dating several centuries back. *Naga Bhasma*, with its principal chemical species being PbS, administered at 6 mg/kg body weight is found to be nontoxic in animal model. Naga Bhasma has specific regenerative potential on germinal epithelium of testes in $CdCl_2$-administered albino rats. In addition to treating diabetes mellitus, it has been prescribed for certain disorders related to the liver, spleen, and skin. Few clinical trials have also shown that *Naga Bhasma* significantly reduces blood glucose level in diabetic patients (Nagarajan et al. 2014a). *Naga (lead)* has been administered in various diseases since *Vedic* period. It has been used in treating diabetes, diarrhea, and spleen and skin disorders and has shown testis regenerative potential on partially degenerated testis (Rajput et al. 2013; Shweta and Thakare 2013).

17.7.2.11 Vanga Bhasma

Vanga Bhasma is a tin-based herbo-metallic preparation given for the treatment of urinary diseases, loss of appetite, and inflammatory disorders, among others (Hiremath et al. 2010). It contains Sn (43.8%) and significant amounts of Ca (7.35 %), Fe (0.3 %), and K (0.88 %) in addition to μg/g amounts of P (720), Mn (257), Zn (67), and In (17.1), but the main content is SnO_2 which is the main

constituent, and indium is a rare element frequently present in stannite and other complex sulfides of tin because of similarities in properties. It also contains C (4.2 %), H (0.64 %), and S (0.15 %), suggesting the presence of some sulfides of tin or organosulfur compounds that might remain chelated with various metals. In Ayurvedic literature, it has been recommended for diabetes, semen disorder, impotency, skin disease, syphilis, and gonorrhea. It is also prescribed for asthma, cough, and blood disorders (Umrani et al. 2013).

17.7.2.12 Praval Bhasma

Praval which is well known as coral in English is used in the form of *Bhasma* and *pisti* in order to cure a variety of ailments since ancient times in Ayurvedic system of medicine. Praval Bhasma is used for treatment of inflammation, cough due to phthisis, unnecessary sweating, cardiac fibrillation, osteoporosis, dysuria, and ligourea. *Praval Bhasma* is also an important ingredient of many formulations such as *Sutika-bharana-rasa*, *Vasantakusumakara rasa*, *Muktapanchamrta rasa*, *Brihat vata chintamani rasa*, *Mahatarunarka rasa*, and *Brahmi vati*. It contains CaO as main ingredient (Mishra et al. 2014). *Praval Bhasma* is well known to increase the intestinal absorption of calcium; it remains to be seen to what extent it would be useful in correcting the metabolic conditions that are beneficial and conducive to bone remineralization (Reddy et al. 2003).

17.7.2.13 Trivanga Bhasma

Trivanga Bhasma is a calcinated metal and mineral based on a trimetallic compound used to treat diabetes and as diuretic and *Napunasakta*, *Prameha*, *Ikshumeha*, *Vandhyatva*, *Swetapradara*, *Vata-Pitta dosha*, and *Shaktivardhaka*. It contains elements like lead, zinc, and tin (Rasheed et al. 2014; Sharma and Singh 1987).

17.7.2.14 Shankha Bhasma

Shankha Bhasma derived from conch shell (Gastropoda, class: Mollusca) is used in the treatment of ulcers, dysentery, dyspepsia, indigestion, and jaundice. The constituent of *Shankha Bhasma* is mainly silicate of magnesia. It induces dose-dependent protection against experimental gastric ulcers. It is known to have antacid property (Pandit et al. 2000).

17.7.2.15 Gemstone Bhasma

Bhasmas based on gemstones, mica, and diamonds find much importance in Ayurveda, but their incineration process is very important. For example, mica (*Abhraka*) is believed to be an excellent rejuvenator for the lungs and for *Rasa*

Dhatu. *Vaikrant* alleviates excess *Vata-Pitta-Kapha*, increases vitality, and can be used as a substitute of diamond Bhasma. *Jahar Mohara* is a mineral stone, also called magnesium silicate and green in color. It is commonly used to neutralize poisonous effects of snakebite, causing vomiting, and is mostly recommended by Unani physicians. Some physicians have used it for heart palpitation, nervousness, depression, and irregular heartbeats (Kumar et al. 2006).

17.7.2.16 Muktashukti Bhasma

Muktashukti Bhasma is a compound consisting of pearl (*moti*), *Aloe vera* Linn (*Guar Patha*), and vinegar (*kanji*). The compound is prepared from the outer covering of the shell (pearl oyster), ground and triturated with *Aloe vera* and vinegar in sufficient amount to make a homogenous paste. Recommended proportions of pearl oyster and *Aloe vera* are in the ratio of 1:4. Medicinal properties have been attributed to this preparation in ancient Ayurveda and Unani systems of medicine. *Muktashukti Bhasma* is used in treatment of tuberculosis, cough, chronic fever, conjunctivitis, abdominal discomfort, biliary disturbances, asthma, heart disease, vomiting, acidity, dyspepsia, dysmenorrhea, general weakness, arthritis, rheumatism, and musculoskeletal disorders. It is recommended in a dose of 125–375 mg twice or thrice daily in treatment of abovementioned disorders (Chouhan et al. 2010; Parmar et al. 2012). Recent studies have shown that adding heated oyster shells to the diet of elderly patient increased the bone mineral density of the lumbar spine. It is one third to one half as potent as anti-inflammatory as the amino salicylic acid. Further, even as *Muktashukti Bhasma* is widely used for its antipyretic activity, there are no scientific reports on antipyretic activity of *Muktashukti Bhasma* (Dubey et al. 2009). Chemically *Muktashukti Bhasma* consists of calcium carbonate, calcium phosphate, aluminum oxide, magnesium oxide, and organic matter. Its ash or paste is used in ancient Ayurvedic medicine to manage various gastric disorders (Chouhan et al. 2010).

17.7.2.17 Varatika Bhasma

Varatika Bhasma is a herbo-mineral formulation coming under the holistic concept of Ayurveda. It is identified as the outer shell of sea animal *Cypraea moneta* Linn or commonly known as money cowry (Rasheed and Shivashankar 2017). It occurs in the coastal areas of the sea (Figs. 17.2 and 17.3). *Cypraea moneta* is commonly known as the money cowry (Fig. 17.4). Chemically it is carbonate of calcium (Pal et al. 2014).

17.7.2.18 Kasisa Bhasma

Kasisa Bhasma is described very briefly in some of the most valuable *Rasa Gransthas* including *Rasa Tarangini*, *Rasaratna Samuchchaya*, and *Ayurveda Prakasha* (Rajput and Tekale 2011).

Fig. 17.2 *Varatika* (before purification) (Source: Pal et al. 2014)

Fig. 17.3 *Varatika* (after purification) (Source: Pal et al. 2014)

Fig. 17.4 Varatika Bhasma (Source: Pal et al. 2014)

Ayurvedic Bhasmas: Toxicity Issues

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. The American medical research community has sounded a heavy metal warning against Ayurvedic cures. Manufacturers of Ayurvedic medicines are now facing different problems such as inferior quality of raw material, lack of authentication of raw material, nonavailability of standards, deficiency in proper standardization method for single drugs and formulations, and no quality control parameters. The 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. Because of widespread use of Ayurvedic medicines, it has become necessary to lay down stringent parameters to ensure batch to batch consistency and reproducibility (Pal 2015).

The use of metals in medicine is often associated with the question of toxicity. Many studies have so far clearly shown that these are nontoxic but exhibit free radical-scavenging activity because of their antioxidant property. The *Bhasmas* are associated with organic compounds and show significant increased superoxide dismutase and catalase activity, two enzymes that reduce the free radical concentration in the body. The preparation and purification of *Bhasmas* undergo elaborate traditional purification procedures and are well mixed with extracts of herbs, fruits, juices, and so forth. The presence of irrelevant elements present at minor or trace levels is the result of the medium in which they are prepared and, thus, might help in enhancing their potentiation. Metallic preparations offer some advantages over plant drugs by virtue of their stability over a long period, lower doses, easy storability, and sustained availability. These have been in use since ancient times and are still considered useful. However, strict quality control by using contamination-free raw materials is necessary (Kumar et al. 2006). Nanoparticles can have many adverse effects at the cellular level. Adverse outcomes may include organelle or DNA damage, oxidative stress, apoptosis, mutagenesis, and protein up-/downregulation. Interestingly, according to some reports, gold nanoparticles have been claimed to be “nontoxic” in nature. In Ayurveda structural and chemical transformation of metal into metal compounds (*Bhasma*) which are bioabsorbable is the main objective of *marana*. Ayurvedic practices aim to avoid toxicity and adverse effects of these products (Rathore et al. 2013).

17.8 Toxicity of the Metal Nanoparticles

Heavy metals in Ayurvedic formulations have been used for centuries with claimed effectiveness and safety. However, concerns are often raised about the toxicity due to heavy metals used in Ayurvedic formulations. On the basis of preference, 18.7 %

of the population uses Ayurveda for normal ailments, 7.1 % in case of sickness, and 5 % in case of serious ailments. A report by the World Health Organization (WHO) indicates that many people in developing countries still rely on herbal medicine. Majority of people believe that herbal medicines are safe and nontoxic, unlike modern chemotherapeutic agents. Individuals usually use herbal medicine for prolonged periods to achieve a desirable effect (Sengupta et al. 2014).

In *Rasa Shastra*, the metals and the minerals are also termed as "Dhatus" and "Updhatus" because of their definite role in biological systems, i.e., they can sustain body tissues by supplementing some of the essential elements to the tissues, whose deficiency causes many unwanted problems or disease in the body. The available Ayurvedic literature emphasizes the need of metals in maintaining the metabolic equilibrium of the human body. These metals are mercury, gold, silver, copper, iron, tin, lead, zinc, etc. Any deficiency, excess, or imbalance in the composition of these metals leads to certain metabolic and anabolic disorders. Equilibrium state of metals in the human body provides the basis for strong immunity. Therefore, any imbalance in the composition of these metals can cause diseases, and equilibrium of these metals is seen as a preconditioning for a normal immune defense and general health. Each time before burning, the metallic powders are processed with fresh herb juices to neutralize their toxicity. One of the numerous tests the *Bhasma* has to pass through is called "Varitar" which means the *Bhasma*, once ready for internal use, floats on water indicating nonexistence of heavy metal in it. The "Bhasma" is then transformed to compound formulas by mixing herbal powders. Special herbal juices are used for processing the compound formula for no more toxic metals and for nontoxic herbo-metallic compounds (Kumar and Gupta 2012).

In a study it has been shown that metal oxide nanoparticles of with particle sizes ranging from 30 to 45 nm have a significant toxicity effect on mammalian cells. Study data indicate toward a more serious concern and issue of teratogenic toxicity exhibited by these particles, which needs to be addressed further carefully before these particles become a part of our day-to-day medicine and other products. Human exposure to nanoparticles can cause severe risks in terms of health, and therefore toxicity issues should be avoided by chemical approaches such as by surface treatment, functionalization, and composite formation. Immune response of nanoparticle exposure is another perspective of nanoparticle interaction that needs to be studied in detail since nanoparticles have immunomodulatory potential and also to stimulate or to suppress the immune system. However, both conditions are undesirable, and the successful nanoparticle-based therapeutics should avoid immunostimulatory or immunosuppressive reactions to the nanomaterials once administered into the body. Nanoparticles can penetrate deeply into the body, having larger surface area because of small size, and possess charge on their surface; therefore, they can cause a greater inflammatory response. Mercury toxicity leads to Alzheimer's disease, Parkinson's disease, gastrointestinal symptoms, renal dysfunction, and neuropsychiatric abnormalities. According to Ayurvedic literature, the toxic effects of Hg are neutralized in the presence of sulfur. Adaptogenic effects

(growth promoting, rejuvenating, and facilitating the learning process) on the central nervous system (CNS) in small doses of 15 mg/kg have been reported. The most renowned of all Hg preparations is *Makaradhwaja*, which acts as rejuvenator (Kumar et al. 2006).

17.9 Physiologically Important Cofactor and Metal Nanoparticles

On a biochemical point of view, cofactors are defined as the ion or molecule which binds to the catalytic site of an enzyme, thereby rendering it active, and are capable of catalyzing cytotoxic reactions. Iron-containing enzymes are mononuclear in nature utilizing molecular oxygen which transfers one or both oxygen atoms to substrates, catalyzing many processes including the biosynthesis of hormones, the metabolism of drugs, DNA and RNA base repair, and the biosynthesis of antibiotics. Magnesium is an important consistent controller of glycolysis and Krebs cycle. Copper exhibits different spectroscopic and chemical properties due to its different ligand environments and coordination number, thereby contributing in various biological processes. Zinc is an essential component of many enzymes involved in many metabolic reactions, thus playing an important role in biological activities (Sengupta et al. 2014).

17.10 Metal Nanoparticles and Physiological Implications

Nanoparticles are just not part of a molecular chess game but have potentially evolved as prodigious tools to interact with biological systems. Nanomedicines and nanotherapeutics are presently hot topics in the researcher's domain owing to their versatile application opportunities and molecular signatures. Uptake of nanoparticles into a broad variety of cells seems to be specific for materials in the range of 50–200 nm. Cellular uptake of nanoparticles has been seen to depend on size, surface properties, cell type, and endocytic pathways, enabling optimization of labeling and selection of cells and nanoparticles for applications in vitro and in vivo. Sunscreens containing metal oxide nanoparticles, mainly zinc oxide, appear transparent on the skin, provide excellent protection against sunburn caused by UV radiation, and are readily absorbed by the skin (Sengupta et al. 2014; Mukkavalli et al. 2017). A study is conducted on the elemental and structural characteristics of the traditional Indian medicine, *Rajat Bhasma* with an average particle size of 350 nm. The PXRD pattern in combination with the elemental analysis indicates a complex, heterogeneous, and nonsymmetric arrangement of atoms within the *Bhasma*. Interaction of these nanoparticles with the different types of biological systems suggested that the *Bhasma* is nontoxic to cells compared to pure silver nanoparticles and facilitates transportation of small and large molecules across epithelial cell monolayer, probably through loosening cell-cell tight junctions.

17.11 Metal Nanoparticles and Biological Applications

Using materials at the nanoscale level provides a range of modification flexibility based on requirements in the biomedical field. Nanoparticles as drug delivery agents not only targeted drug release but also monitor release beside with two or more drugs to give combined effects, lesser side effects, extended half-life of the drug in the systemic solution, and better solubility. Several physiologically important metals for the human body like iron, iron oxides, copper, cobalt, and zinc have found an application in biomedical science. Zinc and zinc oxide nanoparticles are extensively used in sunscreens, biosensors, and cancer therapy and show no adverse effects. The most abundantly used nanoparticle is gold, a recent craze among the researchers, owing to its unique optical signature, flexibility in changes of its properties, easy synthesis, easy surface modification, surface plasmon resonance, fluorescence, and chemical stability, which makes it a potential candidate in the field of biomedical science. It is obvious that in recent years iron and iron oxide nanoparticles are the most abundantly used nanoparticles in the biomedical field. On the basis of their excellent properties for qualifying them as potential biomedical tools at the nanoscale level, iron is also physiologically important to the human body. The other elements such as zinc, cobalt, manganese, selenium, and magnesium are also synthesized and are also of physiological importance. Therefore, these metal nanoparticles can be healthier candidates for biological tools and medicines owing to their human body compatibility and acceptability. Even combinations of physiologically important metals and their use in biomedical science, diagnostics, and medicine may counter the possibilities and limitations of metal toxicity and body rejection (Sengupta et al. 2014).

17.12 Conclusion and Future Perspectives

Nanotechnology is beginning to the change the scale and methods of vascular imaging and drug delivery. Indeed, the NIH roadmap's "Nanomedicine initiatives" envisage that nanoscale technologies will begin to produce more medical benefits within the next 10 years. This includes the progress of nanoscale laboratory-based diagnostic and drug delivery platform devices such as nanoscale cantilevers for chemical force microscopes, microchip devices, nanopore sequencing, etc. The National Cancer Institute has related programs too, with the goal of producing nanometer scale multifunctional entities that can diagnose and deliver therapeutic agents and monitor cancer treatment growth. These include design and engineering of targeted contrast agents that improve the resolution of cancer cells to the single cell level and nanodevices competent of addressing the biological and evolutionary diversity of the multiple cancer cells that make up a tumor within an animal (Sujatha et al. 2016).

At present there are three types of *Bhasmas*: metal based, mineral based, and herbal based. In the 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.

Nanotechnology of tomorrow, to become a next-door technology in our day-to-day life, needs concern and justification about its physiological acceptability and compatibility. A few recommendations and improvements based on biological recognition of these particles can heighten the therapeutic potential and use of them, making them a part of our regular life:

- While designing nano-based products used as a part of human health, more stress should be given to physiologically important metals, which can simply be accepted by the body system, avoiding unnecessary toxicity and being more compatible.
- Studies on biodistribution, retention, and clearance of these particles should be one of the important concerns.
- Need to appraise the role of physiologically important metals, which form an important part of cofactors, and vitamins required for normal physiological function.
- The physiologically important metals which, when used in nanoforms, can be administered along with dietary supplements such as vitamins.
- Initiatives of designing nanoparticles with two or more metals can be probably better by having multi-domain action.
- Even while designing particles with elements more suitable to the body, it should be kept in mind that the total therapeutic system and intake should not exceed the value of recommended dietary intake, which may elevate unnecessary questions of toxicity.
- Initiatives of minimizing toxicity should be taken while synthesizing metal nanoparticles. This can either be done by modifying or functionalizing the nanoparticle to make it more attuned and less toxic.
- Conventional physical and chemical methods of nanoparticle synthesis can be replaced by synthesizing nanoparticles from biological synthesis, "green synthesis," which would be devoid of toxicity and have more body tolerability.
- It would be better if a comparative study on the bulk and nanomaterial of the same dose, route, and other standard physiologic conditions is studied, which will help in developing better nano-based drugs.
- There is a need to reestablish the RDA requirement of humans based on the metal nanoparticle needs of the body.
- A technology and its development can only be successful if both the good and dark side are countered simultaneously, along with keeping in mind the biological aspect, because eventually the technology-based products have to be finally implemented in living systems. A multidisciplinary field like nanotechnology therefore needs special attention in every perspective, especially on the physiological point of view for its success.

References

Acharya P, Ranjan R, Kirar P, Srivastva S, Singh P. Properties of traditional ayurvedic herbo–mineral formulation bhasma. Indian J Adv Plant Res. 2014;1:18–20.

Amin AR, Kucuk O, Khuri FR, Shin DM. Perspectives for cancer prevention with natural compounds. J Clin Oncol. 2009;27:2712–25.

Arivalagan K, Ravichandran S, Rangasamy K, Karthikeyan E. Nanomaterials and its potential applications. Int J Chem Tech Res. 2011;3:534–8.

Bhowmick TK, Suresh AK, Kane SG, Joshi AC, Bellare JR. Physicochemical characterization of an Indian traditional medicine, *Jasada Bhasma*: detection of nanoparticles containing non–stoichiometric zinc oxide. J Nanopart Res. 2009;11:655–64.

Buwa S, Patil S, Kulkarni PH, Kanase A. Hepatoprotective action of *Abhrak Bhasma*, an Ayurvedic drug in albino rats against hepatitis induced by CCl_4. Indian J Exp Biol. 2001;39:1022–7.

Chandran S, Patgiri B, Galib R, Prasanth D. A review through therapeutic attributes of *Yashada Bhasma*. IJPBA. 2016;7:6–11.

Chavare A, Chowdari P, Ghosh S, et al. Safety and bioactivity studies of *Jasad Bhasma* and its in-process intermediate in Swiss mice. J Ethnopharmacol. 2017;197:73–86.

Chouhan O, Gehlot A, Rathore R, Choudhary R. Anti–peptic ulcer activity of *Muktashukti Bhasma*. Pak J Physiol. 2010;6:29–31.

Conde J, Dias JT, Grazú V, Moros M, Baptista PV, de la Fuente JM. Revisiting 30 years of biofunctionalization and surface chemistry of inorganic nanoparticles for nanomedicine. Front Chem. 2014;2:48.

Das S, Das MC, Paul R. *Swarna Bhasma* in cancer: a prospective clinical study. AYU. 2012;33:365–7.

Dubey N, Dubey N, Mehta RS, Saluja AK, Jain DK. Physicochemical and pharmacological assessment of a traditional biomedicine: *Muktashukti Bhasma*. Songklanakarin J Sci Technol. 2009;31:501–10.

Geetha M, Murthy KNC, Basavraj BV, Ahalya N. Pharmaceutical nanotechnology: present past and future. Int J Pharm Sci Nanotech. 2016;9:3061–72.

Hareshwar S, Mayuri D, Raman B. Preparation of *Abhrak Bhasma* and its evaluation on modern parameters. Int J Ayur Pharm Res. 2017;5:30–6.

Hiremath R, Jha CB, Narang KK. *Vanga Bhasma* and its XRD analysis. Anc Sci Life. 2010;29:24–8.

Ikezawa N. Nanotechnology: encounters of atoms, bits and genomes. NRI papers 37. 2001.

Kumar A, Nair AGC, Reddy AVR, Garg AN. Bhasmas unique Ayurvedic metallic–herbal preparations, chemical characterization. Biol Trace Elem Res. 2006;109:231–54.

Kumar G, Gupta YK. Evidence for safety of Ayurvedic herbal, herbo-metallic and *Bhasma* preparations on neuro behavioral activity and oxidative stress in rats. AYU. 2012;33:569–74.

Mishra A, Mishra AK, Tiwari OP, Jha S. In–house preparation and characterization of an Ayurvedic Bhasma: *Praval bhasma*. J Integr Med. 2014;12:52–8.

Miyazaki K, Nazrul Islam N. Nanotechnology systems of innovation—an analysis of industry and academia research activities. Technovation. 2007;27:661–75.

Mukkavalli S, Chalivendra V, Singh BR. Physico-chemical analysis of herbally prepared silver nanoparticles and its potential as a drug bioenhancer. Open Nano. 2017;2:19–27.

Mulik SB, Jha CB. Physicochemical characterization of an iron based Indian traditional medicine: *Mandura Bhasma*. Anc Sci Life. 2011;31:52–7.

Nagarajan S, Sivaji K, Krishnaswamy S, Pemiah B, Rajan KS, Krishnan UM, Sethuraman S. Safety and toxicity issues associated with lead–based traditional herbo–metallic preparations. J Ethnopharmacol. 2014a;151:1–11.

Nagarajan S, Sivaji K, Krishnaswamy S, Pemiah B, et al. Scientific insights in the preparation and characterization of a lead–based *Naga Bhasma*. Indian J Pharm Sci. 2014b;76:38–45.

Nicolau D. Challenges and opportunities for nanotechnology policies: an Australian perspective. Nanotechnol Law Bus J. 2004;1(4):12.

Othayoth R, Kalivarapu S, Botlagunta M. Nanophytomedicine and drug formulations. Int J Nanotechnol Appl. 2014;4:1–8.
Pal SK. The *Ayurvedic Bhasma*: the ancient science of nanomedicine. Recent Patents Nanomedicine. 2015;5:12–8.
Pal D, Sahu CK, Haldar A. *Bhasma:* the ancient Indian nanomedicine. J Adv Pharm Technol Res. 2014;5:4–12.
Palkhiwala S, Bakshi SR. Engineered nanoparticles: revisiting safety concerns in light of ethno medicine. AYU. 2014;35:237–42.
Pandey A, Pandey G. Usefulness of nanotechnology for herbal medicines. Plant Arch. 2013;13:617–21.
Pandit S, Sur TK, Jana U, Bhattacharyya D, Debnath PK. Anti–ulcer effect of *Shankhabhasma* in rats: a preliminary study. Indian J Pharm. 2000;32:378–80.
Parmar KKG, Galib R, Patgiri BJ. Pharmaceutical standardization of *Jalashukti Bhasma* and *Muktashukti Bhasma*. AYU. 2012;33:136–42.
Patil S, Kanase AK, Varute AT. Effect of hepatoprotective Ayurvedic drugs on lipases following CCl_4 induced hepatic injury in rats. Indian J Exp Biol. 1987;27:955–8.
Pattanaik N, Singh AV, Pandey RS, Singh BK, Kumar M, Dixit SK, Tripathi YB. Toxicology and free radicals scavenging property of *Tamra Bhasma*. Indian J Clin Biochem. 2003;18:181–9.
Prajapati PK, Sarkar PK, Nayak SV, Joshi RD, Ravishankar B. Safety and toxicity profile of some metallic preparations of Ayurveda. Anc Sci Life. 2006;25:57–63.
Rai RK, Jha CB, Chansuriya JPN, Kohli KR. Comparative assessment of antihyperlipidaemic action of *Tamra Bhasma*. Indian J Trad Knowl. 2008;7:335–40.
Rajendran N, Pemiah B, Sekar RK, et al. Role of gallic acid in the preparation of an iron–based Indian traditional medicine – *Lauha Bhasma*. Int J Pharm Pharm Sci. 2012;4:45–8.
Rajput DS, Tekale GS. Study on *Bhasma kalpana* with special reference to the preparation of *Kasisa bhasma*. AYU. 2011;32:554–9.
Rajput D, Patgiri BJ, Galib R, Prajapati PK. Anti-diabetic formulations of *Naga Bhasma* (lead calx): a brief review. Anc Sci Life. 2013;33:52–9.
Rasheed SP, Shivashankar M. Preparation and characterization of metal oxide as nanoparticles – *Varatika Bhasma*. Mech Mat Sci Eng. 2017;9:1–6.
Rasheed A, Naik M, Pillanayil K, et al. Formulation, characterization and comparative evaluation of *Trivanga Bhasma*: a herbo–mineral Indian traditional medicine. Pak J Pharm Sci. 2014;27:793–800.
Rathore M, Joshi DS, Kadam SN, Bapat RD. *Swarna Bhasmas* do contain nanoparticles? Int J Pharm Bio Sci. 2013;4:243–9.
Reddy PN, Lakshmana M, Udupa UV. Effect of *Praval Bhasma* (Coral calx), a natural source of rich calcium on bone mineralization in rats. Pharmacol Res. 2003;48:593–9.
Sarkar PK, Chaudhary AK. Ayurvedic *Bhasma*: the most ancient application of nanomedicine. J Sci Ind Res. 2010;69:901–5.
Sarkar PK, Das S, Prajapati PK. Ancient concept of metal pharmacology based on Ayurvedic literature. Anc Sci Life. 2010;29:1–6.
Sengupta J, Ghosh S, Datta P, Gomes A, Gomes A. Physiologically important metal nanoparticles and their toxicity. J Nanosci Nanotechnol. 2014;14:990–1006.
Shahverdi AR, Fakhimi A, Shahverdi HR, Minaian S. Synthesis and effect of silver nanoparticles on the antibacterial activity of different antibiotics against Staphylococcus aureus and Escherichia coli. Nanomedicine. 2007;3(2):168–71.
Sharma PV, Singh VP. Standardization of an Ayurvedic drug: *Trivanga Bhasma*. Anc Sci Life. 1987;6:148–9.
Shweta Z, Thakare GD. Pharmaceutico analytical study of *Naga* (Lead) *Bhasma*. IAMJ. 2013;1:1–4.
Singh M, Singh S, Prasad S, Gambhir IS. Nanotechnology in medicine and antibacterial effect of silver nanoparticles. Digest J Nanomaters Biostruct. 2008;3:115–22.
Singh TR, Gupta LN, Kumar N. Standard manufacturing procedure of *Teekshna Lauha Bhasma*. J Ayurveda Integ Med. 2016;7:100–8.

Sujatha PL, Kumarasamy P, Preetha SP, Balachandran C, Karthick J. Nanomedicine: fate and fortune in future to tailor a device at a billionth of a meter, about half the width of a DNA. Int J Gen Med Pharm. 2016;5:19–24.

Thakur K, Gudi R, Mahesh Vahalia M, et al. Preparation and characterization of *Suvarna Bhasma* parada marit. J Pharm. 2017;20:36–44.

Umrani RD, Agrawal DS, Paknikar KM. Antidiabetic activity and safety assessment of Ayurvedic medicine, *Jasad Bhasma* (zinc ash) in rats. Indian J Exp Biol. 2013;51:811–22.

Varshney HM, Shailender M. "Nanotechnology" current status in pharmaceutical science: a review. Int J Therap Appl. 2012;6:14–24.

Wadekar MP, Rode CV, Bendale YN, et al. Preparation and characterization of a copper based Indian traditional drug: *Tamra Bhasma*. J Pharm Biomed Anal. 2005;39:951–5.

Waghmare AH, Dharkar NS, Waykole YC, et al. Pharmaceutical and physico–chemical study of *Tamra Bhasma* incinerated copper. World J Pharm Pharm Sci. 2016;5:1432–41.

Yadav D, Upadhyay SK, Anwar MF, Unnithan JS. A review on the patents of various metal nanoparticles: preparations and formulations. World J Pharm Pharm Sci. 2016;5:1309–17.

Zala UU, Roa SS, Prajapati PK, Vaishnav PU. A comparative pharmaceutical study of *Hiraka* bhasma. Pharm Sci Monitor. 2016;7:25–7.