Chapter 11 Toxicity of *Bhasmas* and Chelating Agents Used in *Ayurveda*

Shruti Pandey and Anand Chaudhary

Abstract The use of metals in medicine is not new to this world. It has been used by both modern and traditional systems of medicines. Perhaps, the *Ayurveda* stood first for using metals in medicine. The *Ayurvedic* pharmaceutical processes are used to convert metallic properties of metals into medicinal properties defined as *Bhasma* in *Ayurveda*. If these metals in their ionic/metallic forms accumulate in body tissues, then severe damage and toxicity may occur. But *Ayurveda acharyas* proposed some therapy and agents like cilantro, boron, and garlic which were used to remove toxins, produced from intake of improperly prepared *Bhasma*. These so-called agents may be termed as chelating agents of *Ayurveda* because certain researches showed that these agents help to chelate metal ions from the body. These herbs have antioxidant property which helps to chelate these metallic ions as well as helps to restore the normal functioning of tissues.

Keywords Ayurveda • Bhasmas • Toxicity • Chelating agents Antioxidants

11.1 Introduction

The Indian traditional system of medicine, i.e., *Ayurveda* dating back to about 5000 years B.C., has literature which states that drugs originated from plant, animal, metal, and mineral sources were used in healthcare system (Galib et al. 2011). The use of different forms of metals to restore the normal, healthy physiology of the body either by direct administration of essential metals or by chelating out excess metals, or using them as carriers for targeted drug delivery or for targeting biomolecule for diagnostic, are all techniques that may be classified under the general headings of metallo-pharmacology. Metallo-pharmacology is an area of thrust

S. Pandey (☑) · A. Chaudhary Department of Rasa Shastra and Bhaishjya Kalpana, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005, India e-mail: shruayu@gmail.com

where clinical trials are being conducted worldwide for the use of metals in therapeutics. For example, clinical trials for silver and zinc biotics have been carried out to assess its efficacy for a wide variety of human problems like malaria, burn wounds respiratory tract infections, etc. (Pathad and Lokhande 2014). On the requirement of metals for the body physiological functions, these can be classified into two categories—essential and nonessential. Lemire et al. (2013) classified metals into essential and nonessential on the basis of their utilization for body. Essential metals that are required for the normal physiology and function of organisms these include sodium, magnesium, calcium, iron, copper, zinc, etc. while non-essential metals have no known biological function for an organism these include mercury, arsenic, lead etc. Any reason, either environmental or medicinal which disturbs the homeostatic balance of essential metal ion in the body, can result in a shift from that equilibrium state to a condition of either shortage or excess and it is a latter state that causes the toxicity of essential metals. Toxicity is a measurement to which any substance or mixture of substance can harm or damage an organism. Metal toxicity is the harmful effect of certain metals in certain dose on an organism. Metal toxicity occurs when metals form poisonous soluble compounds in living body (Flora and Pachuari 2010). However, if these metals accumulate in the body, in concentrations sufficient to cause poisoning, then serious damage may occur. Some metals are toxic when they form poisons soluble compounds. Often heavy metals are thought as synonymous of toxins, but lighter metals may also be toxic in certain circumstances (Lemire et al. 2013).

Ayurveda is the science made up of Veda (knowledge) and Ayush (life), i.e., knowledge of life. An Ayurvedic system adopts a holistic approach toward health care by balancing the physical, mental, and spiritual functions of the human. The use of metallic preparations to cure diseases is a precise characteristic of this system. The metallic preparations play a vital role in the treatment of different diseases. Processed metals like mercury, gold, silver, lead, zinc, copper, etc. were used very frequently by Ayurvedic acharyas in different disease conditions with great authority. It is mentioned in the Ayurvedic texts that these elements either essential metals or non essential metals (Table 11.1) are detoxified during the highly complex manufacturing processes (Sodhana—purification process, Marana—incinerated ash) before the use of therapeutic purpose. Charaka Samhita, one of the pioneer texts of Ayurveda, has indicated ample of references regarding the use of metals in different forms for different clinical purposes. These metallic preparations are termed as Bhasma. Rasashastra (vedicchemistry) is one of the parts of Ayurveda, which deals with herbomineral/metals/nonmetals preparations called Bhasma. Rasayana (immunomodulation and antiaging

Table 11.1 List of essential and nonessential metals

S. No.	Name of metals	Name of metals		
	Essential metals	Nonessential metals		
1	Calcium	Mercury		
2	Zinc	Lead		
3	Copper	Gold		
4	Iron	Silver		

quality) and *yogavahi* (ability to target drugs to the site) are characteristics of a properly made herbomineral/metals/nonmetals preparation, which is also nontoxic, gently absorbable, adaptable, and digestible in the body. *Bhasma* is an *Ayurvedic* metallic/mineral preparation, treated with herbal juices or decoction and exposed for certain quantum of heat as per *puta* system of *Ayurveda*, which itself is well known in Indian medicine system since eighth century A.D. and widely recommended for the treatment of many disease conditions. *Bhasma* is claimed to be biologically produced mixtures of nanoparticles and macroparticles, which are prescribed with several other medicines of *Ayurveda* (Chaudhary and Singh 2010). These *Bhasmas* prescribed to patients either in single form or in combination with herbal preparations (Herbomineral formulations). They are given to patients in the very low dose form (Galib et al. 2011). These *Bhasmas* do contain metals as an integral component; if not used by following proper *Ayurvedic* pharmaceutics processes, then it may show symptoms of toxicity. The *Ayurvedic* Seers were well versed about this fact and documented the toxic effects in their respective classics.

In contemporary science, there is an alternative for treatment of metal poisoning namely chelation therapy, which is a technique that involves the administration of chelating agents to remove metals from the body. In this therapy, there is the use of chelating agents to detoxify poisonous metal agents such as mercury, arsenic, iron, etc. by converting them to a chemically inert form that can be excreted without further interaction with the body. Chelation therapy is a medical procedure that involves the administration of chelating agents to remove metals or heavy metals from the body. The few chelating agents which are used in contemporary sciences are EDTA, 2,3-Dimercaprol, and meso-2,3-dimercaptosuccinic acid. Chelating agents must be administered with care as it has a number of possible side effects including death. Some of the risks while using chelating agents in contemporary science (Angle 1996) are as follows:

- 1. Chelators bind to heavy metal or metal particles, but they can also bind to important minerals in the body, such as calcium and iron, which are essentials for human body.
- 2. Although chelating agents can be beneficial in cases of heavy metal poisoning, sometimes these may be critical if acts otherwise. The use of disodium EDTA instead of calcium EDTA has resulted in fatalities due to hypocalcemia.
- 3. Side effects of chelation therapy include dehydration, low blood calcium, harm to kidneys, increased enzymes as would be detected in liver function tests, allergic reactions, and lowered levels of dietary elements.
- 4. When administered inappropriately, chelation therapy brings the risk of cancer, neurodevelopment disorder, and even death.

Ayurveda viewed health as a state of many-sided equilibrium. It is achieved through dietary regimen and medications. The ancient scholars of Ayurveda while practicing these Bhasmas came to know about the ill effects of these medicines on human body, which may be caused due to the use of Bhasmas, made from improper processed metals and minerals. Sometimes, these Bhasmas show toxic signs in the

body if not used by following proper *Ayurvedic* pharmaceutics processes. The ancient seers of *Ayurveda* at the same time advised to administer various natural substances in the form of antidotes such as honey, ghee, cow's milk, garlic, coriander, turmeric, and coconut water to remove ill effects or toxicity occurred from these medicines, i.e., *Bhasmas* (Choube 2000). These natural antidotes may be considered as chelating agents of *Ayurveda*, which are not only helpful to remove the toxic effects of metal and minerals without causing any side effects but also protect the loss of essential elements from the body.

This chapter mainly emphasized on procedures of *Ayurveda* used for removal of metal and mineral toxicity caused by improperly prepared medicines of *Ayurveda*, i.e., *Bhasmas*. This chapter deals with all the process of *Ayurvedic* clinical practices and pharmaceutical process, and diet regimen given to the patients while treatment. These are aimed to maintain the balance of human body to keep it free from disease and related adverse effects of medicines. All these processes of *Ayurveda* are closer or equivalent to chelation therapy of contemporary sciences.

11.2 Assertions of Contemporary Science, *Ayurvedic* Pharmaceutics and Therapeutics for Chelation

11.2.1 Remedies for Removal of Toxic Element/Metal Poisoning

There are certain methods through which toxicity of metals can be removed from body (Pandey and Chaudhary 2016).

11.2.1.1 Chelation

Certain foods, herbal drinks, and herbs actively bind to a range of minerals or metals. They are then excreted or washed away from the body.

11.2.1.2 Saturation

Sufficient and wide range of minerals in the diet and cells becomes saturated with the variety of minerals they need. Toxic minerals are then likely to be excreted rather than taking up. Some minerals are also antagonistic to each other, and a high level of one prevents the uptake of another.

11.2.1.3 Antioxidants

A diet high in antioxidant nutrients and enzymes protect from toxic minerals.

11.3 General Antidotes or Chelating Agent of Ayurveda

Tankan (borax), Gandhak (sulfur), Saindhava Lavana (rock salt), Churnodaka (limewater), Triphala Kwath, Arjuna (Terminalia arjuna), Maricha (black pepper), Kumari Swarasa (aloe vera juice), coriander, ginger juice honey, turmeric, lemon juice, cow's milk, goat's milk, cow's ghee, cow's urine, etc. are some common antidotes, which are used to subside the toxic symptoms and to remove the toxic effects of administration of improper processed metals and minerals (Choube 2000).

11.4 Purification Materials (*Shodhana* Drugs) Versus Chelating Agents

The use of metals as medicine is a multistep process. Metals need to be treated with various natural agents, including heat in various complex and multistep processes, and then only a metal is converted into a medicine (Chaudhary and Singh 2010). First, these metals are detoxified during the highly complex manufacturing processes (Sodhana- purification/potentiation processes) by different natural agents from herbal, animal, and mineral origin which are described in Ayurvedic texts (Choube 2000) (Table 11.2). The respective branch of Ayurveda where these processes take place called Rasa Shastra (Metallic Ayurvedic pharmaceutics). General rule for removing toxic elements from the human body is quite logical in Ayurveda; any substance used for the purification of metals automatically has potent antidote properties attached to it. So, for removing toxicity of metals from body, same purification agents are used. For example,

Table 11.2 Drugs used in purification process of metals (Shodhana process) versus chelating agents

S. No.	Metals	Drugs used for purification process of metals
1.	Swarna (Gold)	Saindhava lavan (Rock salt), Swarna gairik (Ochre), and Nimbu swaras (Lemon juice)
2.	Raupya (Silver)	Agastya swaras (Juice of Sesbania grandiflora Pers.), Nimbu swarasa, Lead, and Borax
3.	Tamra (Copper)	Nimbu swarasa, Saindhava lavan, Nirgundi (Vitex negundo Linn.) swarasa, Ark milk (milky latex of Calotropis gigantea R.Br.ex Ait.), Cow's urine
	Swarnamakshika (Copper pyrite)	Nimbu swarasa, Triphala*
	Tuttah (Copper sulfate)	Nimbu Swarasa, Cow's urine

(continued)

S. No.	Metals	Drugs used for purification process of metals
4.	Lauha (Iron)	Triphala decoction, Sea salt, Cow's urine
	Mandur (Iron oxide)	Cow's urine, Triphala decoction
	Vimal (Iron pyrite)	Meshashringi, nimbu swarasa
	Gairik (Haematite)	Cow's milk and Cow ghrita (Clarified butter)
	Kasisa (Ferrous sulfate)	Nimbu swarasa, Bhringaraj swarasa (Juice of Eclipta alba Hassk)
5.	Yasad (Zinc)	Limewater, Nirgundi root swarasa, Ark milk, Cow's milk
6.	Parad (Mercury)	Garlic (Allium sativum), Limewater
	Hingul (Cinnabar)	Nimbu swarasa, Adraka swarasa (Juice of Zingiber officinale)
7.	Naag (Lead)	Nirgundi swarasa, churnodaka (limewater) Haridra powder (Curcuma longa), Cow's urine, Cow's ghee, Honey
8.	Arsenic	
	Hartala (orpiment)	Kushmand swarasa (Juice of Benincasa hispida Cogn.), Limewater, Borax, Nimbu swarasa, Triphala decoction, Sesame oil
	Manhashila (Realger)	Adraka swarasa, Bhringraj swarasa, Goat urine. Limewater, Nimbu swarasa
	Gauripasan (Arsenious oxides)	Karvellaka (Momordica charantia Linn.), Cow's milk, Borax water

Table 11.2 (continued)

- 1. Raw *Vimal* (Iron pyrite) gets purified in *Meshshringi* (*Gymnema sylvestre*) juice while performing the pharmaceutical process of *Shodhana*. If its toxicity occurs in the body, then *Meshshringi* is recommended with sugar for 3 days to remove its toxicity from the body (Choube 2000).
- 2. Raw *Hartala* (Arsenic trioxide; As₂S₃) gets purified with *Kushmand Swarasa* (*Benincasa hispida Juice*) and to remove its toxicity *Kushmand Swarasa* is recommended with *Jeerak* (*Carum carvi*) and honey (Sharma 1998).
- 3. Raw *Gauripasan* (Arsenious oxide; As₂O₃) gets purified with *Tankan* (borax) and cow's milk and to remove its toxicity from body, the same is recommended (Sharma 1998; Jha 2000).

11.5 Ayurvedic Concepts Concerning Metal Pharmacology

The pharmacology of metals, which are used as medicine, has been described in *Ayurvedic* treasures. Some of them are mentioned here in terms of their pharmacological actions, related adverse effect, and its management (Upadhyay 1994; Sharma 1998; Choube 2000).

^{*}Triphala (Three fruits)—Fruit of *Terminalia chebula* Retz., *Terminalia belerica* Roxb., *Emblica officinalis* Gaertn—all taken in equal quantities.

11.5.1 Rasa Aushadhi (Mercurial/Metallic/Mineralic Medicinal Compounds)

11.5.1.1 Pharmacological Actions

Aphrodisiac, Antiaging, Immunomodulator, Increases Intellect, Memory, Tissue Element, and eradicate disease caused by vitiated *doshas* (Humoral Principles, Viz., *Vata, Pitta, Kapha*).

11.5.1.2 Adverse Effects

Fainting, Vomiting, Diarrhea, Dyspnoea, etc. even Death.

11.5.1.3 Management of Adverse Reactions

Coriander sativum with sugar candy and Piper nigrum with clarified butter should be repeated for 7 days.

11.5.2 Swarna Bhasma (Medicinal Gold Preparations)

11.5.2.1 Pharmacological Actions

Aphrodisiac, Cardiac Stimulant, Immunomodulator, it increases Longevity, Memory, Attentiveness, and eradicate the diseases caused by all three vitiated *Doshas*.

11.5.2.2 Adverse Reactions

Illness, Weakness, Impotency, and leads to imbalance of homeostasis and even Death.

11.5.2.3 Management of Adverse Reactions

Powder of Terminalia chebula with sugar candy for 3 days.

11.5.3 Raupya Bhasma (Medicinal Silver Preparations)

11.5.3.1 Pharmacological Actions

Aphrodisiac, Antiaging, and Immunomodulator. It increases Potentiality, Intellect complexion.

11.5.3.2 Adverse Reactions

Anemia, Fever, Weakness, Itching, Constipation, Headache, Cervical Lymphadenopathy, Oligospermia, and reduce Potency.

11.5.3.3 Management of Adverse Reactions

Honey and sugar for 3 days.

11.5.4 Tamra Bhasmas (Medicinal Copper Preparations)

11.5.4.1 Pharmacological Actions

Rejuvenator, Wound healer, Emaciator, Purgative, Immunomodulator. Alleviates disorder caused by *Kapha* and *Pitta*.

11.5.4.2 Adverse Reactions

Vomiting, Fainting, Hallucination, Skin Disorders, Spasmodic Pain, Hyperlipidimia, Delirium, Anorexia, Impotency, and even Death.

11.5.4.3 Management of Adverse Reactions

Coriandrum sativum with Sesbania grandiflora given with sugar candies.

11.5.5 Lauha Bhasmas (Medicinal Iron Preparations)

11.5.5.1 Pharmacological Reactions

Approdisiac, Antiaging, Emaciating, Immunomodulator. Increase Complexion, Appetite, Potentiality, and eradicate diseases caused by vitiated *Kapha* and *Pitta*.

11.5.5.2 Adverse Reactions

Angina, Skin Disorders, Urolethiasis, Spasmodic Pain, Burning Sensation, Weakness, and even Death.

11.5.5.3 Management of Adverse Reactions

Powder of *Embelia ribes* with juices of *Sesbania grandiflora* and patients should be exposed to sunlight. Fruit pulp of *Cassia fistula* and powder of *Elettaria cardamomum* seeds should be given repeatedly.

11.5.6 Naag Bhasmas (Medicinal Lead Preparations)

11.5.6.1 Pharmacological Actions

Appetizer, Aphrodisiac, Immunomodulator, Urinary tract disease, and in disease caused by vitiated *Vata* and *Kapha*.

11.5.6.2 Adverse Reactions

Emaciation, Jaundice, Oedema, Peri-Anal Fistula, and Dyspepsia.

11.5.6.3 Management of Adverse Reactions

Swaran Bhasma and Terminalia chebula with sugar candy for 3 days.

11.5.7 Yasad Bhasmas (Medicinal Zinc Preparations)

11.5.7.1 Pharmacological Actions

Ophthalmic Nourisher, Immunomodulator, Increase Strength, Potentiality, Intellectual Power and disease caused by vitiated *Kapha* and *Pitta*.

11.5.7.2 Adverse Reactions

Diabetes, Indigestion, Vomiting, and Hallucination.

11.5.7.3 Management of Adverse Reactions

Terminalia chebula with sugar candies for 3 days.

11.5.8 Haratala Bhasmas (Medicinal Orpiment Preparations) (Arsenic Compounds)

11.5.8.1 Pharmacological Actions

Immunomodulator, Increase Strength and Digestive Power, Rejuvenative, and Increase Complexion.

11.5.8.2 Adverse Reactions

Diabetes, Pyrexia, Blisters on skin, and even Death.

11.5.8.3 Management of Adverse Reactions

Cumin seeds and sugar candies for 3 days.

11.5.9 Manhashila Bhasmas (Medicinal Realgar Preparations)

11.5.9.1 Pharmacological Actions

Immunomodulator, Increase Strength and Digestive Power, Rejuvenative, and Increase Complexion.

11.5.9.2 Adverse Reactions

Calculi, Dysuria, Burning Micturition, and Constipation.

11.5.9.3 Management of Adverse Reactions

Cow's milk with honey for 3 days.

11.5.10 Gauripasan Bhasmas (Medicinal Arsenious Oxides Preparations)

11.5.10.1 Pharmacological Actions

Respiratory disorders, Aphrodisiac, Digestive disorders, and Fevers.

11.5.10.2 Adverse Reactions

High dose can cause death.

11.5.10.3 Management of Adverse Reactions

Tankan (Borax), Godudha (Cow's milk) with Goghrita (Cow's Ghee), and Karvelaka (Momordica charantia).

11.6 Pathya and Apathya (Wholesome Diet and Unwholesome Diet) and Chelating Concepts

The ancient seers of *Ayurveda* found that drugs of different origins (herbal, metal, or animal) in addition to codes of conduct and dietary regulations are suitable tools to maintain health and eradicating disease (Galib et al. 2011). There is a concept of wholesome diet and unwholesome diet, which go along with the treatment (Choube 2000). These diets somehow reduce the chances of toxicity of metals or heavy metals. It is a method for reducing heavy metal or metal exposure via the inhibition of absorption from the gastrointestinal tract. They have a key role in reducing the gastrointestinal tract absorption of these elements. These herbal diets may actively encourage mobilization and excretion of metals which further give a hand in reducing an individual's overall exposure. Hence, the underlying principle behind using herbal diet is as follows.

- Lessen gastrointestinal uptake of free metal ions (when taken with wholesome diet).
- 2. Passively assist excretion of toxic intermediates/elements from the body.
- 3. Diets which are contraindicated may boost the uptake by making more soluble intermediate products or may cause any adverse reaction with the metal ions in the body.

11.6.1 Description of Definitive Diets in Ayurveda While Treatment with Bhasmas-Specific Metallic Preparations

11.6.1.1 Rasa Aushadhis (Medicinal Mercurial/Metals/ Minerals Preparations)

Wholesome diet: Milk, Rock salt, Clarified butter, Curd, Butter, *Phaseolus aureus* seeds, *Crocus sativus* stigma, *Zingiber officinale* rhizome, and *Cyperus rotundus* root.

Unwholesome diet: These herbs are strictly avoided during mercurial therapy. *Benincasa cerifera* fruit, *Dolichus biflorus* seeds, *Cucumis utilissimus* fruit, *Solanum nigrum* fruit, *Momordica charantia* fruit, *Carthamus tinctorius* seeds, *Citullus vulgaris* fruit, and *Musa sapientum* fruit.

11.6.1.2 Swarna Bhasmas (Medicinal Gold Preparations)

Wholesome diet: Milk, Sugar unctuous foodstuffs.

Unwholesome diet: Aegel marmelous fruit and all herbs included in mercury unwholesome diet.

11.6.1.3 Tamra Bhasmas (Medicinal Copper Preparations)

Wholesome diet: Milk with sugar candies, sweet food with clarified butter.

Unwholesome diet: Sour foodstuffs are strictly avoided.

11.6.1.4 Lauha Bhasmas (Medicinal Iron Preparations)

Wholesome diet: Honey, Milk, Sweet food, Clarified butter, Triphala (Three fruits —Fruit of *Terminalia chebula* Retz., *Terminalia bellerica* Roxb., and *Emblica officinalis* Gaertn—all taken in equal quantities.).

Unwholesome diet: Sesame oil, Wine, Sour food, Fish, Brinjal, Bitter gourd.

11.6.1.5 Medicinal Arsenic Preparations

Wholesome diet: Sweet food and rock salt (in place of other salts). Unwholesome diet: Salt, sour, pungent, and exposure to sunlight.

11.7 Researches on References of Ayurvedic Chelating Agents

Each and every medicine system has its own line of the treatment for removing toxin or poison caused by their respective medicines or by any other mean, present in the body. In *Ayurveda*, poisoning/toxicity can be treated by some of the natural agents. Antidotes or chelating agents are described in *Ayurveda* classics, which help to remove poison caused by metals. Some researchers have been done on various antidotes of *Ayurveda*, which clearly shows that they have potential to remove toxicity caused by metals from any source. These agents had already been practiced by ancient scholars. Some of those researches are described below.

11.7.1 Haritaki (Termenilia chebula)

Sarkar et al. (2012) revealed in their research that methyl extract of *Termenilia chebula* possess both reducing power and iron chelating activity. It has the ability to reduce the toxic level of iron in iron overload mice and hence protect liver from oxidative stress and fibrosis. Iron overload causes a signified increase of hydroxyproline, a marker of liver fibrosis and Ferritin. Extract significantly reduced the hydroxyproline content in iron intoxicated mice, thus signifying the hepatic fibrosis inhibit potency of fruit extract and also decreases the level of Ferritin because of its reductive release activity. It was concluded from the research that extract can reduce hepatic iron content in treated mice and supported its chelating potency.

11.7.2 Aragvadh (Cassia fistula)

Cassia fistula was evaluated for chelating effect (Dinis et al. 1994). The presence of chelating agents in the ethyl acetate extract of *C. auriculata*, *C. absus* and *C. fistula* disrupts the ferrozine—Fe²⁺ complex formation (Jayaraman et al. 2014).

11.7.3 Karvellaka (Momordica charantia)

In one of the studies, toxicity in rat was induced by lead, and the animals were treated with ethanolic extract of *Momordica charantia*. The oral administration of lead nitrate induced bone marrow injury. There was reduction in the serum erythrocyte count, total leukocyte count, lymphocyte count, mean corpuscular volume, and mean corpuscular hemoglobin concentration. The extract normalized all the above parameters with the neutrophils count was also decreased. Thus, this study

showed that ethanolic extract of *M. charantia* has a satisfactory effect on toxicity induced by lead (Ehimigbai et al. 2015).

11.7.4 Lahsuna (Allium sativum)

The sulfhydryl-containing compounds have the ability to chelate metals. Garlic which has water-soluble organosulfur compounds, S-allylcysteine, and lipid soluble compounds like diallyl-sulfide, etc. shows supporting factors against heavy metal poisoning due to its possession of chemicals containing organosulfur groups, volatile oils, enzymes, carbohydrates, and amino acids; garlic was extensively exploited to treat the metal-induced toxicities. Recent studies support the fact that garlic contains compounds capable of detoxifying lead, cadmium, methylmercury, phenylmercury, and arsenic. The sulfur-containing amino acids methionine and cysteine, N-acetylcysteine, an acetylated analog of cysteine, the methionine metabolite S-adenosylmethionine, α -lipoic acid, and the tripeptide glutathione all contribute to the chelation and excretion of metals from the human body. The clastogenic effects of the heavy metals were also reduced by administration of garlic. Fatal effects caused by metal accumulation and mitochondrial injury were effectively reduced by garlic (Flora and Pachuari 2010).

11.7.5 Dhanyak (Coriandrum sativum)

It is a popular culinary and medicinal herb, gained attention when soup was reported to enhance mercury excretion following dental amalgam removal. In different research studies, it decreased the lead absorption into bone. It has the ability to remove toxicity caused by heavy metals like mercury. In particular, coriander seems to be the only chelating agent that can remove these metals from the central nervous system. It helps to remove mercury, lead, and other heavy metals. Coriander contains antioxidants, with the leaves having the highest levels (Sears 2013).

11.7.6 Mandukparni (Centella asiatica)

Saxena and Flora (2006) reported in their research study that extract of *C. asiatica* was administered with DMSA (meso-2,3-dimercaptosuccinic acid) against experimental lead intoxication in rats. It was found that combined administration was most effective in reducing biogenic amines, oxidation stress besides reducing body lead burden. Thus, supplementation of herb extract during chelation could be recommended for achieving optimum effects of chelation therapy.

11.7.7 Shigru (Moringa oliefera)

Efficacy of combined administration of *M. oliefera* powder extract with a thiol chelator monoisoamyl DMSA post-arsenic exposure in mice was studied. Arsenic exposure caused a significant decrease in blood glutathione with increase in the production of ROS in blood and soft tissues. Combined administration of MiADMSA with *M. oliefera* proved better than all other treatment in the recovery of most of the above parameters, accompanied by more pronounced depletion of Arsenic. The results suggest that concomitant administration of *M. oliefera* during chelation treatment with MiADMSA might be a better treatment option than monotherapy with the thiol chelators in chronic arsenic toxicity (Mishra et al. 2009).

11.7.8 Haridra (Curcuma longa)

Another interesting domain of investigation is curcumin metal chelation capacity, bearing probable correlation with its cytoprotective potency. In one of the studies, curcumin derivatives were investigated and designed as potential neuroprotective agents, acting as metal chelators with improved stability at physiological pH and increased cytotoxic activity with respect to curcumin (Ferrari et al. 2014). Thus, the skill of curcumin to chelate metal ions such as iron and copper could be a useful feature for detoxifying body from metal toxicity.

11.7.9 Nimbu (Citrus limon) and Antioxidant

Ascorbic acid (present in sour fruit viz., lemon, etc.) having antioxidant activity is used as chelator for metal toxicity (Kleszczewska 2001; Tamafo et al. 2017). The lemon juice (*Nimbu swarasa*) is used in *Ayurveda* for purification process of many metals (Table 11.2). These are presumed to play a key role in minimizing the damage from oxidative products, including free radicals. Vitamin C and other antioxidants including bioflavanoids also support metal binding induction of reactive oxygen species by metals, and subsequent depletion of antioxidant cell defenses can result in disruption of the antioxidant balance in tissues. This balance can be overcome by either reducing the metal interacts with biomolecules or inducing oxidative damage or by bolstering the cell's antioxidant defenses through endogenous supplementation of antioxidant molecules. These antioxidants when given either alone or in combination with a chelating agent proved to be effective in mobilizing metal from soft as well as hard tissues. Many studies on the effects of vitamin C on lead intoxication have been performed. Vitamin C attenuates the oxidative damage and histopathological changes induced by CdCl₂ in the lungs and

brain of rats. It has been reported to act as chelating agents for lead, with a similar potency to that of EDTA (Kleszczewska 2001).

11.7.10 Tannins

Triphala is an Ayurvedic medicine used at many places in the purification process of metals. Triphala consisting of fruits of three herbs, viz., Terminalia chebula, Terminalia bellerica, and Phyllanthus emblica. The main phytoconstituent of Triphala is tannin, which is present in abundant amount in Triphala. Phenols can affect the biological availability or activity of metal ions by chelating the metal (Dinis et al. 1994). One of the research studies was designed to find out the chelating capacity of tannin for copper, iron, and zinc ions in which percentage of bound metal ions were calculated. The studies revealed that tannin was able to chelate these ions. Thus, it is recommended that tannins may also have high affinities for metals (Karamac 2009).

11.7.11 Glutathione (GSH)

GSH is a protein found in foods. Food rich in GSH is asparagus, walnuts, avocado, and raw milk of goat (Weirzbicka et al. 1989). GSH is another powerful chelator involved in cellular response, transport, and excretion of metal cations and is a biomarker for toxic metal overload (Heba 2017). The detoxifying processes naturally generate large amounts of free radicals, which combats by making antioxidant enzymes, glutathione-S-transferase (GST), glutathione peroxides (GPOX), and superoxide dismutase (SOD). These endogenous antioxidants are GSH and selenium-dependent. GSHs in the diet are precursors to these antioxidant enzymes (Sears 2013). GSH is able to bind, transport, and store several metals, thus affecting metal homeostasis in biological systems. GSH has been shown to protect against Hg²⁺-mediated toxicity in isolated proximal tubule fragments from rabbits and proximal tubular cells from rats. The bile appears to be a main excretory pathway for some metal-GSH complexes. GSH can chelate metals and reduce their toxicity (Aseth et al. 2016). Goat milk is used in different purification processes of metals in Ayurveda as well as antidote in toxicity caused by improperly prepared Bhasma (Choube 2000).

11.7.12 Cow's Urine

This agent is used at many places in *Ayurvedic* classics for purification process of metals. In recent study, it was found that cow's urine exhibits antitoxic activity

against cadmium chloride and can be used as a bioenhancer for zinc. Mature male mice, exposed to cadmium chloride only, showed 0% fertility rate. However, the animals given a combination of cadmium chloride, cow's urine, and zinc sulfate showed 90% fertility rate with 100% viability and lactation indices. Besides this, the fertility index was also found to be 88% in the group treated with cadmium chloride and cow's urine. This result showed the chelating capacity of cow's urine (Singla and Kaur 2016). Chelating action of cow's urine is quite possible because of its antioxidant activity. The antioxidant status of redistilled cow's urine is contributed mainly by volatile fatty acids (1500 mg/L) as revealed by the GC-MS studies. These fatty acids and other antioxidants might cause the observed protective effects.

11.7.13 Madhu (Honey)

Gluconic acid is the carboxylic acid formed by the oxidation of the first carbon of glucose with antiseptic and chelating properties. It is found in plant and honey. The gluconate ion chelates calcium, iron, and other heavy metals. Aqueous gluconic acid solution contains cyclic ester glucono delta lactone structure which chelates metal ions and forms very stable complexes (Paul et al. 2017). It has already been mentioned that in most of the toxicity cases of metals, viz., silver, arsenic honey is used with other herbs like cumin, cilantro, etc. to remove metal toxicity symptoms from the body.

11.7.14 Boron

A study published on boron in experimental and toxicology pathology showed that heavy metal treatments increased the frequencies of sister chromatid exchange micronuclei in the DNA of lymphocytes and the plasma malondialdehyde level, whereas the tested boron compounds significantly reduced the genotoxic effects induced by low doses of heavy metals (Turkez et al. 2012). Their results revealed that the protective roles of boron compounds occurred with the effectiveness of their antioxidant capacity. In conclusion, these compounds could be useful in the development of functional food and raw materials of medicine. In *Ayurvedic* literature also borax is used as antidote/chelating agent in toxicity caused by arsenic compounds (Table 11.2).

11.8 Conclusions

Toxicity is the degree to which a substance can damage an organism. *Ayurvedic* acharya's kept bird's eye on the use of these *Bhasma* on patients. The therapeutic action and the adverse effects are based on the keen observations, theories, beliefs,

and experiences of the ancient *acharyas*. These concepts may also reply the needless hue and cry existing regarding the toxicity of the metallic *Bahamas*. A central concept of toxicology is that the effect of a toxin is dose-dependent. For example, in a very toxic substance such as snake venom, there is a dose below which there is no detectable toxic effect, which itself is used in snake poisoning. *Bhasmas* cause toxicity only when they are improperly prepared, with greater dose and duration level may cause various adverse effects.

The cations, anions, ligands, etc. are the basis of chelation therapy, which are used in contemporary science. However, these terms were not known/discovered at the classical treasure of *Ayurveda*. In spite of that, various methods and substances were used as antidotes, which played the dynamic role in removing the metal toxicity from the body. These natural antidotes may be considered as chelating agents of *Ayurveda*, which are not only helpful to remove the toxic effects of metal and minerals but also protect the loss of essential elements from the body without causing any side effects. *Bhasmas* have no serious dangerous effect on body function as a whole. However, caution should be taken while preparing these *Bhasmas* and calculating the dose and duration during clinical practice.

References

Angle CR (1996) Chelation therapies for metal intoxication: toxicology of metals. CRC Press, Boca Raton, FL, pp 487–504

Aseth J, Crisponi G, Anderson O (2016) Chelation therapy in the treatment of metal intoxication. Academic press, London

Chaudhary AK, Singh N (2010) Herbo mineral formulation (Rasaoushadhies) of Ayurveda an amazing inheritance of Ayurvedic pharmaceutics. Ancient Sci Life 30(1):18–26

Choube D (2000) Brihat Rasaraja Sundar. Chaukhambha Orientalia, Varanasi, India

Dinis T, Madeira VMC, Almeida LM (1994) Action of phenolic derivatives (acetoaminophen, salycilate and 5-aminosalycilate) as inhibitors of membrane lipid peroxidation and as peroxyl radical scavengers. Arch Pharmacal Res 315:161–169

Ehimigbai ROA, Grillo DB, Eze GI, Ezeuko VC (2015) Protective effects of ethanolic extract of Mormodica charantia leaf on lead nitrate-induced bone marrow toxicity. J Exp Clin Anat 14:13–17

Ferrari E, Benassi R, Sacchi S, Pignedoli F, Asti M, Saladini M (2014) Curcumin derivatives as metal—chelating agents with potential multifunctional activity for pharmaceutical applications. J Inorg Biochem 139:38–48

Flora SJ, Pachuari V (2010) Chelation in metal intoxication. Int J Environ Res Public Health 7:2745–2788

Galib Barve M, Meshru M, Jagtap C, Patgiri BJ, Prajapati PK (2011) Therapeutic potentials of metals in ancient India: a review through Charak Samhita. J Ayurveda Integr Med 2(2):55–63

Heba AY (2017) Food as method of heavy metal detoxification. Adv Clin Toxicol 2(1):000115
Jayaraman P, Sivaprakasam E, Rajesh V, Mathivanan K, Arumugam P (2014) Comparative analysis of antioxidant activity and phytochemical potential of Cassia absus Linn., Cassia auriculata Linn., Cassia fistula Linn. Indian J Drugs Dis 3(1):298–304

Jha CB (2000) Ayurvediya Rasashastra, Choukhamba Saurabharati Prakashan, Varanasi, India Karamac M (2009) Chelation of Cu(II), Zn(II), Fe(II) by tannins constituents of selected edible nuts. Int J Mol Sci 10(12):5485–5497

- Kleszczewska E (2001) Biological role of reactions of L-ascorbic acid with Metals. Postępy Higieny: Medycyny Doświadczalnej 55(1):81–94
- Lemire JA, Harrison JJ, Turner RJ (2013) Antimicrobial activity of metals: mechanisms, molecular targets and applications. Nature 11:371–384
- Mishra D, Gupta R, Pant SC, Kushwah P, Satish HT, Flora SJS (2009) Co-dminitration of monoisoamyl dimercaptosuccinic acid and *Moring oleifera* seed powder protects arsenic induced oxidative stress and metal distribution in mice. J Toxicol Mech Methods 19(2): 169–182
- Pandey S, Chaudhary AK (2016) Chelation therapy and chelating agents of Ayurveda. Int J Green Pharm 10(3):143–150
- Pathad YV, Lokhande JN (2014) Handbook of metallonutraceuticals. CRC Press, Boca Raton, FL Paul S, Hossen S, Tanvir EM, Afroz R, Hossen D, Das S, Bhoumik NC, Karim N, Juliana FM, Gan SH, Khalil I (2017) Minerals, toxic heavy metals, and antioxidant properties of honeys from Bangladesh. J Chem 2017: Article ID 6101793. https://doi.org/10.1155/2017/6101793
- Sarkar R, Hazra B, Mandal N (2012) Reducing power and iron chelating property of *Termenalia chebula* (Retz.) alleviates iron induced liver toxicity in mice. BMC Complementory Alternetive Med 212:144–167
- Saxena G, Flora SJ (2006) Changes in brain biogenic amines and haem biosynthesis and their response to combined administration of succimers and *Centella asiatica* in lead poisoned rats. J Pharm Pharmacol 58:547–559
- Sears ME (2013) Chelation harnessing and enhancing heavy metal detoxification: a review. Sci World J 2013. Article ID 219840, p 13. http://dx.doi.org/10.1155/2013/219840
- Sharma S (1998) Rasa Tarangini, Motilal Banarasidas, New Delhi, India
- Singla S, Kaur S (2016) Biological activities of cow urine: an Ayurvedic elixir. Eur J Pharm Med Res 3(4):118–124
- Tamafo ADF, Ghogomu JN, Nkungli NK, Mama DB, Younang E (2017) Quantum chemical investigation on the antioxidant activity of neutral and anionic forms of Juglone: metal chelation and its effect on radical scavenging activity. J Chem 2017
- Turkez H, Geyikoglu F, Tatar A, Keles MS, Kaplan I (2012) The effects of some boron compounds against heavy metal toxicity in human blood. Exp Toxicol Pathol 64:93–101
- Upadhyay M (1994) Ayurved Prakash, Chaukhamba Bharati Academy, New Delhi, India
- Weirzbicka GT, Hagen T, Tones DP (1989) Glutathione in food. J Food Compos Anal 2(4): 327–337