

SAFETY AND TOXICITY PROFILE OF SOME METALLIC PREPARATIONS OF AYURVEDA

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ABSTRACT:

Metals and minerals are used profusely in practice of *Ayurveda* after proper incineration by the name of *Bhasma*. Some metals and minerals have the potency to produce toxic effects in human being. In this paper safety and toxicity profiles of *Tamra Bhasma* (incinerated copper, Cu), *Lauha Bhasma* (incinerated iron, Fe), and *Yashada Bhasma* (incinerated Zinc, Zn) has been presented, which reveal no serious deleterious effects on body function as a whole.

Key Words: Toxicity, Metal, *Ayurveda*, *Tamra* (Copper), *Lauha* (Iron), *Yashada* (Zinc).

INTRODUCTION:

The *Ayurvedic* system of medicine has been in vogue since the *Vedic* period or even earlier. In principle this system advocates a holistic approach to the human health care i.e. a balance between the physical, mental and spiritual functions of the human body. It is the sum total of the knowledge, skills and practices based on the theories, beliefs and experiences. This system of medicine involves the use of plant parts, animal products, minerals and metals.

Long historical use of practices of *Ayurvedic* system of medicine, including experience passed on from generation to generation, has demonstrated the safety and efficacy of this system. However, so many research works have been carried out to provide additional evidence of its safety and efficacy profile. But the quantity and quality of the safety and efficacy data on *Ayurvedic* medicines

are far from sufficient to meet the criteria needed to support its use worldwide.

Institute for Post Graduate Teaching and Research in Ayurveda of Gujarat Ayurved University is the pioneer institute in the field of research on *Ayurvedic* medicines. This institute has given enormous efforts since last fifty years in research in *Ayurvedic* medicines with special emphasis on metallic and mineral preparations. In this present paper, the studies on safety and toxicity profile of *Tamra Bhasma* (incinerated copper), *Lauha Bhasma* (incinerated iron), and *Yashada Bhasma* (incinerated zinc) have been enlightened.

RECENT PUBLICATION REGARDING REACTIVITY OF SOME AYURVEDIC PREPARATIONS:

An article entitled “Ayurveda – The Death Metal Soup” was published in ‘Outlook Express’ magazine highlighting effects of some *Ayurvedic* preparations containing lead (Pb) and arsenic (As). This article also mentioned the permissible limit of some heavy metals and enlisted some heavy metals containing *Ayurvedic* preparations.

In ‘Energy Monitor Journal’, an article had been published entitled “Scenario of ‘Pb pollution and children’ in Mumbai: Current air quality standard vindicated” presented current situation of lead (Pb) pollution in Mumbai and cases of lead (Pb) poisoning due to ingestion of lead (Pb) containing *Ayurvedic* preparations¹.

The latest exclusive article, which had shaken the *Ayurvedic* world, was published in Journal of American Medical Association entitled “Heavy metal content of Ayurvedic herbal medicinal products”. This article was mentioned some *Ayurvedic* formulations containing heavy metals and permissible limits of these in human being and presented some case reports on adverse effect of some *Ayurvedic* herbal formulations containing heavy metals².

ANCIENT CONCEPT REGARDING METAL PHARMACOLOGY:

Therapeutic effectiveness of the *Ayurvedic* drugs have been established and well documented by the great Acharyas in the form of classics attributed to them. However lot of changes have occurred in our living milieu since the time these classics were written and impact of these changes on the therapeutic efficacy of the preparations formulated has not been ascertained. Further

the art of preparing the preparations requires certain amount of expertise and no much information is available about the likely impact of improper preparation on the expression of biological activity including possibility of production of undesirable effects.

Gold preparations are generally used in general debility, poisoning, etc. and as immunomodulator³. But improperly prepared *Swarna Bhasma* (incinerated gold) may causes emaciation, many other diseases even death⁴. Silver preparations are generally prescribed in epilepsy, spleenomagaly, etc. and as nervous tonic⁵. But defectively prepared *Rajat Bhasma* (incinerated silver) may leads to fever, constipation, etc.⁶ *Tamra* preparations are used systematically in abdominal pain, respiratory distress, obesity, skin disorders, etc.⁷ And vomiting, dyspepsia, excessive perspiration, fainting attack, skin disorders may occur, if improperly prepared *Tamra Bhasma* (incinerated copper) is taken.⁸ Like wise the adverse effect of other metals used therapeutically in *Ayurveda* like *Parada* (mercury), *Lauha* (iron), *Vanga* (tin), *Naga* (lead), *Yashada* (zinc) are also describe in management of their adverse effects are also mentioned (presented in Table 1).

PREPARATION OF DHATU BHASMA (INCINERATED METAL):

Ayurvedic system of medicine is the only one out of all traditional medicine system of various civilizations, where importance of metals for curing ailments was first recognized. Metallic preparations are mainly termed as ‘*Bhasma*’ and obtained by repeated incineration of metal with herbal extracts or juice.

For this purpose, after procurement of metals, these are made into coarse powder by hammering. Then these are subjected to *Shodhana* (purification) procedure according to traditional *Ayurvedic* references. For this, the metals are heated to red hot or melted and quenched in particular liquid media for specified times. Then these *Shodhita* metals are subjected to *Marana* (incineration). The *Shodhita* metals are then mixed with specific drugs for incineration (*Maraka Dravyas*) and are levigated (*Bhavana*) by particular liquid media for specified time. *Chakrikas* (pellets) are prepared from levigated doughy mass and taken into earthen crucibles faced together, and the junction is sealed by mud smeared clothes. This apparatus, called as *Sarava Samputam* is subjected for heating in traditional *Putapaka* (heating grade) or electric muffle furnace. Heating of materials continue to this apparatus is called as *Putapaka* in parlance of *Ayurveda*. Burning is continued for a specific time limit and when cooled down the apparatus is taken out and open to get the incinerated metallic powder. These procedures are repeated for particular time and finally the prepared *Bhasma* (incinerated metal) is collected.

TOXICITY STUDY:

Objective:

To evaluate the acute and chronic toxicity profile of the prepared *Bhasmas* (*Tamra*, *Lauha* and *Yashada*) (incinerated copper, iron and zinc) on experimental animal.

MATERIALS AND METHODS:

Animal: Charles Foster strain albino rats of either sex weighing between 180g to 250g were used for these experiments. They were obtained from the animal house attached to the pharmacology laboratory. They were

housed in breeding cages at an ambient temperature with a natural day and night cycles. The animals had free access of pellet feed and tap water.

Drugs:

Tamra Bhasma: The copper wire was collected and subjected for *Shodhana* (purification) according to traditional *Ayurvedic* procedures. The purified metal then mixed with drugs for incineration (*Shuddha Hingula*, purified cinnabar, and *Shuddha Gandhaka*, purified sulphur) and levigated by lemon juice, pellets were prepared and subjected for heat treatment (*Putapaka*). These procedures were repeated for 6 times, and then prepared *Tamra Bhasma* was collected and stored.

Lauha Bhasma: The scraps of wrought iron were purified (*Shodhana*) according to traditional procedures of *Ayurveda*. The purified metal was mixed with 1/12 th part of *Shuddha Hingula* (purified cinnabar) as drug for incineration and was levigated by *Kumari Swarasa* (aloe gel). Pellets were prepared and subjected for heat treatment (*Putapaka*). These procedures were repeated for 7 times.

Yashada Bhasma: After purification (*Shodhana*) amalgam of purified zinc was prepared by mixing with same part mercury (*Parada*), then same part of *Shuddha Gandhaka* (purified sulphur) was mixed and triturated. The mixture was subjected to heat treatment. These procedures were repeated for 8 times.

Drug and dose: Drug (*Tamra Bhasma*, *Lauha Bhasma*, *Yashada Bhasma*) suspensions were prepared by adding few drops of 5% gum acacia solution in distilled water. The dose for experimental study of the test drugs were calculated by

extrapolating the human dose to animal dose based on body surface area ratio.

Study protocol:

Acute Toxicity Study: Acute toxicity of *Tamra Bhasma*, *Lauha Bhasma* and *Yashada Bhasma* were evaluated by administering single oral dose of 5 times, 10 times, 20 times and 40 times more than the therapeutic dose of test drug suspensions.

Chronic Toxicity Study: Chronic toxicity of *Tamra Bhasma*, *Lauha Bhasma* and *Yashada Bhasma* were assessed by administering 5 times more than therapeutic equivalent dose of test drugs suspension through oral route by No. 3 simple rubber catheter for 45 days.

RESULTS:

Acute Toxicity Study: The animals of all the test drug groups did not manifest any signs of toxicity and no exitus (death) was observed upto 40 times more than the therapeutic equivalent dose. From this it can be mentioned that the approximate LD₅₀ values are more than 40 times of therapeutic equivalent dose.

Chronic Toxicity Study:

Effect of test drug preparations on body weight and other ponderal parameters:

The mean body weight of the albino rats in different test drugs treatment groups were recorded before and after drug treatment and weight of the vital organs were taken after scarification. The effect of the test drugs pertaining to the ponderal parameters have been presented in Table- 2. Body weight of rats was increased in all the test drugs treated groups. It was increased significantly ($P < 0.05$) in *Yashada Bhasma* treated group

and increased marginally in *Tamra Bhasma* and *Lauha Bhasma* Treated groups. No apparent changes in weight of the vital organs were noticed in all the test drug treated groups in comparison to control group. Only the weight of testes was decreased significantly ($P < 0.05$) in *Tamra Bhasma* treated group in comparison to control group and weight of thymus and prostate were increased in *Lauha Bhasma* treated group.

Effect of test drug preparations on haematological parameters:

Post treated values of the haematological parameters (Hb%, total RBC count, total and differential WBC count, etc.) in all the test drug treated groups were estimated statistically and have been presented in Table- 3. Statistically non-significant changes were observed on almost all the parameters in the entire test drug treated groups, except in *Tamra Bhasma* treated group haemoglobin percentage (Hb%) was increased significantly ($P < 0.05$), Plateletcrit value, mean platelet volume and platelet distribution width were decreased highly significantly ($P < 0.01$) in *Lauha Bhasma* treated group and in *Yashada Bhasma* treated group mean platelet volume was decreased significantly ($P < 0.05$). All the values were assessed in comparison to vehicle treated control group.

Effect of test drug preparations on biochemical parameters:

Biochemical parameters (blood glucose, serum urea, serum creatinine, etc.) of rats in all the test drug treated groups were estimated statistically after completion of treatment and have been presented in Table- 4. In *Tamra Bhasma* treated group, serum creatinine, serum triglyceride and serum cholesterol were decreased significantly

($P < 0.05$) and blood glucose and serum alkaline Phosphatase were increased significantly ($P < 0.05$). In *Lauha Bhasma* treated group only serum alkaline Phosphatase and serum HDL cholesterol were decreased significantly ($P < 0.05$) and no apparent changes was observed in other parameters. In *Yashada Bhasma* treated group, serum creatinine was decreased significantly ($P < 0.05$) and serum cholesterol was increased highly significantly ($P < 0.01$), no apparent changes were found in other parameters. All the values were calculated in comparison to vehicle treated control group.

Effect of test drug preparations on histopathology of vital organs: Microscopic examination of sections of vital organs (liver, heart, kidney, brain, etc.) from treated groups was observed under microscope at different magnifications. *Tamra Bhasma* caused mild to moderate degenerative changes in most of the vital organs (liver, spleen kidney, etc.). In *Lauha Bhasma* treated group moderate fatty degenerative changes in liver was observed, other vital organs exhibits almost normal cytoarchitecture. *Yashada Bhasma* enhanced increase in the epithelial proliferation in seminal vesicle and ventral prostate and it has the potential of affecting kidney function.

DISCUSSION:

The people become so much health conscious, so naturally the quality consciousness of the drug is also increased. Before taking the medicine they want to assure about the safety and purity of the same, the published articles make them more cautious. And these phenomenons indirectly indicate the need of toxicity study of the *Ayurvedic* medicines.

Now a days it is essential for all the *Ayurvedic* practitioners to know the particulars of toxicity profile of the *Ayurvedic* medicines, which they intend to use in clinical practice. This is very essential especially for the medicines containing metals, minerals and organic poisonous substances.

The toxicity of heavy metals is attributed to their ability to form complexes with important biological radicals like the sulfhydryl, the hydroxyl, the carboxyl, the amino and the imidazole. Inhibition of various enzymes leads to the toxic effects. Attempts were, therefore, made to develop organic compounds which would have a high affinity for the metallic ions. Such drug would combine with the metallic ions to produce relatively non-toxic substances.⁹ The process by which these organic materials impregnated into the metal ions is called as *Bhavana* (levigation).

Metals and minerals that are transformed into drug must have excellent therapeutic efficacy and must be safe. Unfortunately some metals and minerals have the potential to produce adverse effects. Therefore, during transmutation of the metals and minerals to drugs, it is essential to evaluate the margin of safety between the dose level that produces the therapeutic effects and that produces the adverse effects. That is to provide benefit to risk assessment. Animal experimentation is the only way through which this assessment can be made.

At higher dose level *Tamra Bhasma* has tendency of producing toxicity. The observed toxic effects were moderate in intensity. There is possibility that these toxic effects may not occur at therapeutic equivalent dose, which is five fold smaller than the administered dose. This aspect needs to be considered. However, it is to be

always kept in mind that higher doses have definite predilection of producing toxicity.¹⁰

In *Lauha Bhasma* treated group, no serious toxicity was found. Only mild impairment in the hepatic functions and hepatic cytoarchitecture was observed. So *Lauha Bhasma* should be considered as safe drug and has a wide range of safety.¹¹ *Yashada Bhasma* has no serious deleterious effect on body functions as a whole, the epithelial proliferation may be indicative of androgenic activity and may not be considered as pathological changes and the changes in kidney function are of moderate intensity, they are likely to be reversible. It has moderate cytoprotective activity by promoting the formation of anti-stress proteins, by promoting the turnover of epithelial tissues in different organs, by

inhibiting lipid peroxidation and DNA fragmentation in target tissues.¹²

All the *Bhasma* (incinerated metallic ash) preparations are the cocktail of many other trace elements. Presence of these elements from conceptual point of view should be important for the expression of biological activity, may be beneficial or toxic.

CONCLUSION:

Analysis of these data of toxicity study reveals these *Bhasma* preparations have no serious deleterious effect on body function as a whole. However, caution should be taken while preparing these preparations and calculating the dose and duration during clinical practice.

TABLE- 1: ANCIENT CONCEPT REGARDING METAL PHARMACOLOGY:

Metallic Preparations	Indications	Adverse Effects	Management
<i>Parada</i> (Mercury, Hg)	In all the diseases with specific <i>Anupana</i> (adjuvant).	<i>Murcha</i> (fainting), <i>Chhardi</i> (vomiting), <i>Atisara</i> (diarrhoea), <i>Shwasa</i> (dyspnoea), etc. even death.	<i>Kanji</i> (sour gruel) + <i>Sarjika Kshara</i> (KNO ₃) + cow's urine + rock salt
<i>Swarna</i> (Gold, Au)	<i>Kshaya</i> (emaciation), <i>Shwasa</i> (dyspnoea), <i>Kasa</i> (cough), <i>Pandu</i> (anaemia), <i>Hridya</i> (cardiac tonic), <i>Rasayana</i> (immunomodulator), etc.	Decrease <i>Oja</i> and <i>Bala</i> (defense mechanism), creates many other diseases even death.	<i>Haritaki</i> (<i>Terminalia chebula</i>) powder + <i>Sita</i> (sugar candy)
<i>Rajata</i> (Silver, Ag)	<i>Madataya</i> (alcohol poisoning), <i>Kshaya</i> (emaciation), <i>Plihodara</i> (spleenomagaly), <i>Apasmara</i> (epilepsy), etc.	<i>Jwara</i> (fever), <i>Vivandha</i> (constipation), <i>Angasada</i> (body ache), etc.	Honey + sugar
<i>Tamra</i> (Copper, Cu)	<i>Pandu</i> (anaemia), <i>Krimi</i> (warm infestation), <i>Sthaulya</i> (obesity), <i>Kustha</i> (skin disorders) etc.	<i>Vamana</i> (vomiting), <i>Shula</i> (spasmodic pain), <i>Kustha</i> (skin disorders), etc. even death.	<i>Dhanyaka</i> (<i>Corindrum sativum</i>) + sugar or <i>Munibrihi</i> (<i>Sesbania grandiflora</i>) + sugar

<i>Lauha</i> (Iron, Fe)	<i>Pandu</i> (anaemia), <i>Shotha</i> (oedema), <i>Rajyakshma</i> (tuberculosis), <i>Kustha</i> (skin disorders), <i>Rasayana</i> (immunomodulator), etc.	<i>Hripida</i> (angina), <i>Ashmari</i> (urolethiasis), <i>Apasmara</i> (epilepsy), <i>Sotha</i> (oedema), <i>Shula</i> (abdominal colic), etc.	<i>Vidanga</i> (<i>Embelia ribes</i>) + Juice of <i>Agasta</i> (<i>Sesbania grandiflora</i>), or <i>Aragvadha Phala Majja</i> (<i>Cassia fistula</i>).
<i>Vanga</i> (Tin, Sn)	<i>Krimi</i> (warm infestation), <i>Vamana</i> (vomiting), <i>Kasa</i> (cough), <i>Shwasa</i> (dyspnoea), <i>Pandu</i> (anaemia), <i>Prameha</i> (diabetes mellitus), etc.	<i>Prameha</i> (diabetes mellitus), <i>Kasa</i> (cough), <i>Shwasa</i> (dyspnoea), <i>Pandu</i> (anaemia), <i>Shotha</i> (oedema), etc.	<i>Mesashringi</i> (<i>Gymnema sylvestre</i>) powder + <i>Sita</i> (sugar candy)
<i>Naga</i> (Lead, Pb)	<i>Prameha</i> (diabetes mellitus), <i>Arsha</i> (piles), <i>Varna</i> (ulcer), <i>Pradara</i> (leucorrhoea), <i>Sukrakshaya</i> (oligospermia), etc.	<i>Murcha</i> (fainting), <i>Prameha</i> (diabetes mellitus), <i>Pakshavadha</i> (paralysis), <i>Shotha</i> (oedema), etc.	<i>Swarna Bhasma</i> + <i>Haritaki</i> (<i>Terminalia chebula</i>) + sugar
<i>Yasada</i> (Zinc, Zn)	<i>Prameha</i> (diabetes mellitus), <i>Pandu</i> (anaemia), <i>Shwasa</i> (dyspnoea), <i>Netraroga</i> (eye diseases), <i>Vrana</i> (ulcer), etc.	<i>Prameha</i> (diabetes mellitus), <i>Kshaya</i> (emaciation), <i>Vamana</i> (vomiting), <i>Kustha</i> (skin disorders), etc.	<i>Vala</i> (<i>Sida cordifolia</i>) powder + <i>Haritaki</i> (<i>Terminalia chebula</i>) powder + <i>Sita</i> (sugar candy).

TABLE- 2: EFFECT OF BHASMAS ON PONDERAL PARAMETERS:

Parameter	<i>Tamra Bhasma</i>	<i>Lauha Bhasma</i>	<i>Yashada Bhasma</i>
Body Weight	NE	NSI	SI
Liver	NE	NSD	NSI
Thymus	NSD	SI	NSD
Spleen	NSI	NSD	NSI
Kidney	NE	NSI	NSD
Heart	NE	NSD	NSD
Testes	SD	NSI	NSD
Seminal vesicles	NE	NSI	NSD
Prostate	NSI	SI	NSD
Uterus	NE	NSD	NSI

NE: No effect; SD: Significant decrease; SI: Significant increase; NSI: Non-significant increase; NSD: Non-significant decrease.

TABLE- 3: EFFECT OF BHASMAS ON BIOCHEMICAL PARAMETERS:

Parameter	<i>Tamra Bhasma</i>	<i>Lauha Bhasma</i>	<i>Yashada Bhasma</i>
Blood Glucose	SI	NSI	NSI
Serum Cholesterol	SD	NSD	NE
Serum Urea	NE	NSD	NSI
Serum Creatinine	SD	NSI	SD
Serum Triglyceride	SD	NSI	NSI
Serum Bilirubin	NE	NSD	NSD
S. G. O. T.	NE	NSD	NE
Serum Alkaline Phosphatase	SI	SD	NE
Serum Total Protein	NE	NSI	NE
S. G. P. T.	NE	NSI	NSI

TABLE- 4: EFFECT OF BHASMAS ON HAEMATOLOGICAL PARAMETERS:

Parameter	<i>Tamra Bhasma</i>	<i>Lauha Bhasma</i>	<i>Yashada Bhasma</i>
Total RBC count	NE	NSI	NE
Haemoglobin %	SI	NSI	NSD
Haematocrit	NE	NSI	NE
RDW	NE	NSI	NE
MCV	NE	NSD	NE
MCH NE	NSD NE		
MCHC	NE	NSD	NE
Total WBC count	NSD	NSI	NSI
Polymorph %	NSD	NSI	NSI
Lymphocyte %	NSI	NSD	NSI
Eosinophil %	NSD	NSD	NSD
Platelet count	NE	NSD	NSD
Plateletcrit	NE	NSD	NSD
PDW	NE	NSD	NE
MPV	NE	NSD	SD

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