Historical Review of Copper-based Ancient Ayurvedic Medicine: Tamra Bhasma

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Abstract:- Copper has been widely used for various purposes since the Vedic periods. It plays a vital role in human physiology and has been used to treat different ailments in its mineral forms. Tamra Bhasma, the oldest medicinal form of copper, has been used in Ayurveda for centuries. In the traditional practice of Ayurvedic pharmaceutics, copper is converted into its safe and effective nanomedicine form, Tamra Bhasma. This literature review provides a comprehensive analysis of (Tamra), covering its traditional uses, copper pharmaceutical processes, therapeutic applications, pharmacological activities, safety profiles, and reports on the structural identification of Tamra Bhasma. This examination extends from the Vedic and Samhita periods to recent developments.

Keywords:- Copper, Tamra, Bhasma, Ayurveda, Rasa Shastra

I. INTRODUCTION

Review studies shed light on existing theories and frameworks, revealing gaps, inconsistencies, and areas for future research. These studies also open doors for interdisciplinary approaches to tackle important research problems. By promoting innovative thinking, review studies can pave the way for new research fields and fresh perspectives on existing issues.

The ancient pharmaceutical processes of *Rasa Shastra* offer valuable insights into traditional methods for preparing therapeutic materials. Today, with advancements in chemistry, physics, and material science, we have the opportunity to comprehend this ancient knowledge using modern scientific terms. By incorporating recent literature, scientific theories, tools, and techniques, we can bridge the gap between traditional and contemporary understanding. A comprehensive review study is crucial for this effort. It assists researchers in establishing a solid theoretical foundation and expanding their thought processes, allowing them to proceed with greater clarity and innovation.

The present literature review offers a thorough analysis of *Tamra* (Copper). It covers its traditional uses, pharmaceutical processes, and therapeutic applications, as well as safety profiles and reports on the structural identification of *Tamra Bhasma*. This examination extends from the *Vedic* and *Samhita* periods to recent developments.

II. HISTORICAL BACKGROUND OF COPPER (TAMRA) [1, 2]

- *Vedic Period:* The *Vedas*, as ancient Indian scriptures, cover diverse topics including religious rituals, philosophy, mathematics, astronomy, and ethics, making them a rich repository of knowledge reflecting the early Indian civilization. Traces of *Vedic* wisdom can be found in almost all branches of science, highlighting their interdisciplinary nature and enduring significance.
- *Rigveda:* In the *Rigveda*, the word "*Ayas*" (Rigveda 1-11-68) is often mentioned in conjunction with "*Tamra*," suggesting a reddish metal, likely copper. These references typically relate to various ornaments and decorative items utilized during that era. The use of "*Ayas*" in association with "*Tamra*" hints at the early understanding and utilization of copper as a material for crafting ornamental objects, reflecting the technological advancements and cultural practices of the time (Rigveda 5-58-2; 5-53-4; 8-47-15).
- *Yajurveda:* In the *Yajurveda*, the term "*Tamra*" is frequently mentioned (Shukla Yajurveda 23/37). However, copper is denoted by the name "*Shyamam*" due to its characteristic color.4 Additionally, "*Sisam*" is used interchangeably with "*Tamra*" in the *Shukla Yajurveda* (Shukla Yajurveda 23/37). Originally, both "*Tamra*" and "*Lohitayas*" were used to refer to copper, but over time, "*Tamra*" gained more popularity and became the preferred term.
- Atharva Veda: In the Atharva Veda, the term "Tamra" is indeed prevalent and is also denoted as 'Ayas' and 'Shyamam' (Atharvaveda 1-34-6; 1-34-7; 20-8-31). Additionally, references to other metals and alloys such as brass and bronze can be found. Iron is symbolically represented as "blood," while copper, denoted as "Shyamam," is likened to "flesh" (Atharvaveda 11-3-74) These symbolic associations indicate the significance attributed to various metals within the cultural and philosophical framework of the Atharva Veda.
- Brahmanas: In the Shatapatha and Gopatha Brahmanas, copper is termed "Lohayasam" (Shatapatha Brahmana 5/4/1/1/2) for its red hue and was used in arrow-making (Shatapatha Brahmana 2/3/4/5). Mythologically, "Tamra" is said to have originated from

Lord Indra's umbilicus. The *Shatapatha Brahmana* mentions Lord Prajapati creating all ores, called "*Apakva Dhatu Ayas*," within the earth's womb (Shatapatha Brahmana 6/1/1/13). These mythological and symbolic interpretations reflect the reverence and significance attributed to copper in ancient Indian culture and mythology, as well as the understanding of its origins and uses.

- *Purana:* In the *Varaha Purana*, the origin of *Tamra* Dhatu is believed from Kartikeya's semen falling upon the earth (Varaha Purana, Chaturvarna Diksha, *Tamra* varnana, 126 Adhyaya 465). It is also described as the derivative of the *Rakta* (blood) and *Meda* (body fat) of Gudakesha, who is slain by Lord Vishnu. These mythological narratives from the *Puranas* provide symbolic interpretations of the origin and nature of copper, associating it with divine beings and cosmic events.
- Sutras: In the Guhya Sutras, bronze and copper are extensively utilized in the preparation of Yantras, indicating their significance in sacred practices and rituals. Acharya Gautama emphasized the superiority of utensils made of Tamra (copper) for holy rituals, underscoring its revered status in religious practices in Dharma Sutras. Tamra was regarded as inherently pure, underscoring its importance not only in religious ceremonies but also in other areas due to its enduring qualities.
- Smritis: In the Smritis, Tamra (copper) was extensively utilized and revered as a symbol of purity. It was employed in various contexts, including for detrimental punishment, coinage, and the creation of sacred pitchers, which were cleansed using acids and alkalis (Yagya Valkal Smriti Vyavhar Page.562/365) Manusmriti provides detailed descriptions of metal extraction procedures, including those for *Tamra*, along (Manusmriti with other metals 5/113-114). Additionally, Manusmriti advises the purification (Shodhana) of metals, including Tamra, through the use of Kshara (alkali), Amla (acid), and Jala (water).

Samhita Period, Sangraha Granthas and Nighantus:

During the period of the Samhitas, the therapeutic use of metals began. In the Charaka Samhita, Tamra (copper) is listed among the six metals (Ch. Su. 1/71). recognized for its poisonous nature (Ch. Su. 1/132) yet prescribed in the treatment of various ailments. Tamra Churna (powder) is used as a Rasayana in the Bhrahma Rasayana Kalpa and for various ailments (Ch. Chi. 1-3/46). Utensils made of Tamra are suggested for skin diseases like Sidhma and Kilasa (Ch. Chi. 7/117-118). Tamra powder is utilized in treating conditions such as Hikka, Shwasa, and Kasa. Anjana (collyrium) prepared in Tamra pots is used for treating Abhishyanda and Timira (Ch. Chi. 17/125). Tamra, along with other Dhatus like gold, is employed in treating conditions like Visarpa and Gulma (Ch. Chi. 21/131). Furthermore, Anjana, Shankh Varti, and Drustiprada Varti are prepared using Tamra powder and other medicinal substances to treat various eye diseases and enhance vision. Tamra is also used in crafting medical instruments such as the nozzles of Basti (enema) and tongue cleaners (Jihva

nirlekhaka) (Ch. Si. 3/7). *Tamra Churna* is utilized to eliminate unabsorbed poison from the *Koshta* (stomach and intestines) (Ch. Chi. 23/239). These references from the *Samhitas* highlight the early understanding and utilization of metals, including copper, in therapeutic practices within ancient Indian medicine.

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In the *Sushruta Samhita*, numerous references regarding the therapeutic use of *Tamra* (copper) for both external and internal applications can be found in various sections. *Tamra* is classified under the main heading *'Trapvadi Gana'* (Su. Su. 38/62), and its pharmacological actions are also mentioned (Su. Su. 46/326), *Tamra* is used for treating conditions such as *Krimi, Pandu*, and *Prameha*.

Water stored in Tamra pots (Su. Su. 45/13) is said to become free from all toxic effects and is considered beneficial in the treatment of *Paittika* disorders (Su. Ut. 42/105). Sushruta also describes the use of Tamra powder combined with other Dhatus (metals) and Kashayas (decoctions) of drugs from the Salsaradi Gana in the treatment of Prameha (Su. Chi. 12/10). Copper powder, along with other metals, is utilized as an external plaster in cases of Kaphaja Arbuda (Su. Chi. 18/38). Additionally, Tamra powder, combined with herbal powders, is applied to wounds in Upadamsha (Su. Chi. 16/47). Tamra pots are recommended for fermentative preparations such as Soma (Su. Chi. 26/13). Copper is indicated in the preparation of medical instruments like Basti Netra (Su. Chi. 35/12) Further, it is used in Shirovirechana in pot form, in treating Shleshmaja and Raktaj abhishyanda with Anjana (collyrium) (Su.Chi. 40/45; Su. Ut. 11/7; 12/13; 12/46; 12/26; 12/50; 12/46; 12/51), and in curing Praklinnavartma (Su. Ut. 12/53). Other eye diseases like boils and pterygium are also treated with copper-based therapies (Su Ut. 15/26). In the Sushruta Samhita, the Shalakas (probes) prepared by using Tamra Dhatu are preferred for eye procedures (Su. Ut. 18/61). Collyrium made from Tamra is also indicated for treating Timira to improve eyesight (Su. Ut. 18/105; 18/101), eye stability (Su. Ut. 18/85), and in case of paediatric eye diseases (Su. Ut. 16/14) Various external applications of Tamra preparations are recommended for treating eye diseases, but internal use is not indicated.

In the Ashtanga Sangraha, properties of Tamra (copper) and its alloys are detailed, including their use in storing medicines (A. S. Su. 12/14). The pharmacological actions of Tamra are also described within this text (A. S. Chi. 21/101). Moreover, Tamra is part of the Saptadhatus mentioned in the Sharangadhara Samhita (Sha. Sam. M.K. 11/1) and Bhava Prakasha Nighantu (Bh. P. Ni. Dhatuvarga), along with descriptions of its purification and incineration processes. In the Raja Nighantu (Ra. Ni. Suvarnadivarga 1/6-12) and Dhanvantari Nighantu (Dha. Ni. Shhashtavarga 1/6-12), Tamra is ranked third among the group of seven metals, and these texts detail its therapeutic properties as well as any potential toxic effects. Additionally, the therapeutic uses and the pharmacological actions of Tamra are described in the Madhava Dravya Guna (Madhava Dravya Guna 158-164) and Madanpala Nighantu (Ma. Ni. 4/7).

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The *Kautiliya Arthashastra* contains various references concerning copper ores. These detailed descriptions indicate the importance of copper in ancient Indian economy and industry, as well as the sophistication of metallurgical knowledge during that time (Kautiliya Arthashastra 2/18).

A review of Tantric literature indeed suggests that the copper was known for its possible uses during that period, but it was veiled in strict confidentiality similar to mantras. However, this secrecy surrounding the use of metals was eventually lifted by *Nagarjuna*, who advocated for their use openly in his *Rasa* texts. *Nagarjuna's* contributions marked a significant shift, bringing an end to the secrecy surrounding the utilization of *Dhatus* and *Updhatus* (metals and minerals) in various forms.

The *Rasa Hridaya Tantra* provides a comprehensive description of *Dhatus*, including various types of *Tamra*, while the *Rasendra Chudamani* is credited with first describing the method of preparing *Somanathi Tamra Bhasma*. This text also delves into the pharmaceutical processes of *Tamra* and its therapeutic uses in conditions

such as anemia, piles, and different eye diseases (Ra. Chu. 14/61-62). Similarly, the Rasa Prakasha Sudhakara from the 13th century offers insights into the varieties of *Tamra* (R. P. S. 4/40-43), methods Shodhana (R.P.S. 4/36-39; 40-43) Marana, and therapeutic applications (R.P.S. 4/45). The Rasa Ratna Samuchchava discusses the distinctions between good and bad quality Tamra, alongside various purification (R.R.S. 5/49-51) and incineration (R.R.S. 5/53-54; 56-58) methods, including a special process for preparing Somnathi Tamra Bhasma (R.R.S. 5/65-67). Shri Dhundhuka Natha, the author of Rasendra Chintamani in the 14th century, describes the method of Amritikarana (making nectar-like) of Tamra. Additionally, the Rasa Chintamani outlines special methods for preparing whitecolored Tamra Bhasma (Ra. Chi. 10/26-32). Furthermore, the Rasa Paddhati details the preparation method of Tamra Bhasma without mercury and its therapeutic utility (R.P. 24/28). Texts from the 17th century onwards in the field of Rasa Shastra continue to provide detailed information about Tamra Bhasmas (R.P.S. 5/77) enriching our understanding of its preparation, properties, and applications in traditional Indian medicine.

III. SYNONYMS OF COPPER IN ANCIENT TIMES

Copper has many synonyms and few of them are describing its mythological relations and few are related to its appearance and physical properties [2, 3]. Table 1 mentions the synonyms of *Tamra*.

Ambakam	Kaniyasam	Rakta Dhatu	Tapaneshtam
Anuvindum	Kamodam	Rakta Loham	Tamrakam
Araktaka	Lohitayasam	Raktam	Trilochanam
Arvindam	Mlechchham	Raktapriyam	Tryambakam
Arkam	Nagasya mardanam	Ravipriyam	Udumbara
Bhaskaram	Nepaleeyam	Shulbam	Ushnam
Brahma Vardhanam	Neelavatam	Surya Lauham	Varishthanam
Brahma Varchasam	Rajivam	Surya Sthanam	Vantikam
Hemagarbham			Visanashana

Table 1: List of Synonyms of Copper Available in Different Texts.

Ancient Types of Copper

The ancient varieties of copper along with their descriptions and qualities have been mentioned in Table 2 [3].

Table 2: The Ancient Varieties of Copper Along with their Descriptions and Qualities as Described in
Ancient Texts of <i>Rasashastra</i> .

Variety of Tamra	Description	Quality	Usage
Nepalaka	Very smooth and ductile with heaviness	Best quality	As a Medicine in the form
	and also free from defects.		of its Bhasma.
Mlechchha	White or blackish in appearance with	Inferior	Not useful as a medicinal.
	highly emetic property.		
Rakta Tamra	Red in color	Best quality	Medicinal use
Krishna Tamra	Black in color	Inferior compared to Rakta Tamra	Not specified.

IV. PHYSICAL PROPERTIES OF TWO ANCIENT VARIETIES

Nepalaka Variety of Copper:

It is esteemed for its superior quality, boasts several distinguishing characteristics outlined in *Rasashastra* texts. It is described as slimy to the touch (*Susnigdham*), soft in

nature (*Mridu*), and exhibits a striking copper-red color (*Shonam* or *Japakusuma Varna*). Notably, it possesses the unique property of being malleable enough to be fashioned into sheets without breaking (*Ghanaaghatakshama*). Additionally, it is characterized by its heaviness (*Guru*) and purity, being free from impurities (*Nirvikara* or *Vikara rahita*) [4,5].

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➤ Mlechchha Variety of Copper:

It is characterized by its inferior quality, presents several distinctive traits delineated in *Rasashastra* texts. It exhibits various colors such as white (*Sita*), black (*Krishna*), and reddish (*Aruna Varna*) due to its propensity to tarnish. Notably, its consumption can induce severe vomiting (*Ativami*). Moreover, *Mlechchha Tamra* is described as hard in nature (*Kathora*) and contains impurities such as iron and lead (*Lohanagayuktam*). It is brittle and tends to break upon impact with a hard object (*Ghanaasaham*). Additionally, despite proper washing, it retains its black color (*Kshalita cha punah Krishna*) [4, 5].

Ancient Sources of Copper (Tamra): [6-13]

Tamra, or copper, is available from mineral sources like *Tuttha* (copper sulphate) and *Swarna Makshika* (chalcopyrite), mentioned in texts like *Rasa Prakasha Sudhakara* and *Rasatarangini*. Additionally, animal sources such as *Mayura Puchchha* (peacock feathers) and *Bhunaga* (earthworms) are described in *Rasatarangini* for obtaining *Tamra* as Sattva.

V. ANCIENT METHOD OF PREPARATION OF COPPER NANOPARTICLES IN THE FORM OF TAMRA BHASMA

Shodhana of Tamra is essential during pharmaceutical procedures to eliminate impurities and potential toxins. Tamra, if not purified properly, can cause adverse effects such as changes in complexion, vomiting, emaciation, purgation, and sedation. Shodhana ensures the safety of Tamra-based formulations, mitigating health risks and enhancing therapeutic efficacy.

- There are two Methods of Shodhana used for Dhatu Shodhana:
- Samanya Shodhana: This refers to general purification methods applicable to all Dhatus. It involves heating and quenching the metal successively in various liquid medias to remove impurities and enhance its therapeutic properties.

Various methods of *Samanya Shodhana* applicable to *Dhatus* in classical texts can also be applied to *Tamra*. Some of these methods include:

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- Heating and quenching the *Dhatus* for 7 times successively in *Tila Taila* (oil), *Takra* (buttermilk), *Gomutra* (cow urine), *Aranala* (fermented gruel), and *Kulattha Kwatha* (horse gram decoction) [14].
- Heating and quenching the *Dhatus* for 7 times successively in *Takra*, *Kanji*, *Gomutra*, *Tila Taila*, and *Kulattha Kwatha* [15].
- Heating and quenching the *Dhatus* for 7 times successively in *Taila*, *Takra*, *Gomutra*, *Kanji*, and *Arkadughdha* (latex of *Calotropis procera* L.) [16].
- Heating and quenching the *Dhatus* for 7 times in *Kadlimoola Swarasa* (banana stem juice) [17].
- Heating and quenching the *Dhatus* for 3 times successively in the order of *Kanji* (sour gruel), *Takra, Kulattha Kwatha, Gomutra,* and *Tila Taila* (sesame oil) [18].
- Heating and quenching the *Dhatus* for 3 times successively in *Tila Taila*, *Takra*, *Kanji*, *Gomutra*, and *Kulattha Kwatha* [19].
- Vishesh Shodhana: This refers to specific purification methods tailored to individual metals based on their characteristics and impurities. It may involve additional steps or specific substances to achieve thorough purification. Many Acharyas in Ayurveda agree that while Samanya Shodhana is essential for metals, it may not be sufficient to completely eliminate all impurities and enhance potency. Therefore, they advocate for Vishesha Shodhana (specific purification) to further refine the metal and maximize its therapeutic benefits.

Ayurveda Prakasha specifically highlights the necessity of Vishesha Shodhana for Tamra, emphasizing that Samanya Shodhana alone may not be adequate to address all the Doshas associated with Tamra. Table 3 likely enumerates various methods of Vishesha Shodhana (specific purification) elucidated in classical texts.

Reference	Drugs used	Procedure	Media
Rasarnava 7/106	Snuhi Ksheera, Arka Ksheera, Lavana,	Nirvapana	Nirgundi Swarasa
	Kshara, Amla Lepa.		
Rasahridaya Tantra 9/13	Lavana, Kshara, Amlavarga,	Nirvapana	Nirgundi Swarasa
	Snuhiksheera, Arka Ksheera – Lepa.		
Rasaratna Samucchaya 5/49	Ksharamla	Nirvapana	Mahisha Takra
		(7 times)	
Rasaratna Samucchaya 5/51	Saindhava Lavana and Nimbu Rasa –	Nirvapana	Nirgundi Swarasa
	Lepa.	-	_
Rasaratna Samucchaya 5/52	Gomutra	Swedana	Gomutra
		(1 Yama period)	
Rasaratna Samucchaya	Gomutra	Swedana	Gomutra
1/280		(1 Yama period)	
Rasaratna Samucchaya	Saindhava Lavana and Arka Dugdha –	Nirvapana	Nirgundi Swarasa
1/279	Lepa	-	-

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Rasendra Chudamani 14/45	Kshaaratraya and Nimburasa Lepa	Melt in <i>Moosha</i> and add <i>Gairika. Nirvapana</i> (7 times)	Mahishi Takra mixed with Gomaya.
Rasendra Chudamani 14/47	Saindhava Lavana and Nimburasa – Lepa	Nirvapana (8 times)	Nirgundi Swarasa
Rasendra Chudamani 14/46	Saindhava Lavana and Nimburasa – Lepa	<i>Nirvapana</i> (8 times)	Kanji
Rasendra Chudamani 14/48- 50	Ksheera and Tintidi Phala Kalka, Lavana, Nimbu Rasa.	Swedana (1 Yama period) Nirvapana (7 times)	Nirgundi Swarasa
Bhavaprakash 3/118	Snuhi Ksheera, Arka Ksheera, Saindhava Lavana.	<i>Nirvapana</i> (3 times)	Nirgundi Swarasa
Rasa Kamdhenu 3/2	Amla – Kshara, Snuhi Ksheera, Dhatura, Chitraka, Triphala Kwatha, Gomutra.	Nirvapana (7 times)	Triphala Kwatha, Gomutra.
Rasamritam 3/39	Lavana and Arka Dugdha Lepa	Nirvapana	Nirgundi Swarasa
Rasamritam 3/39	Gomutra	Swedana (1 yama period)	Gomutra
Rasapradip 3/11	Taila, Takra	Nirvapana	Tila Taila, Takra
Rasapradip 3/14	Snuhi – Arka Dughdha	Nirvapana	Arka ksheera
Rasapradip 3/15	Chincha, Saindhava, Gomutra	Swedana (1 yama period)	Gomutra
Rasatarangini 17/12	Changeri Patra Swarasa	Nirvapana (21 times)	Changeri patra Swarasa
Rasatarangini 17/13	Nirgundi Swarasa	Swedana (1 day)	Nirgundu Swarasa
Rasatarangini 17/14	Saindhava Lavana, Kanji	Swedana (1 day)	Kanji
Rasatarangini 17/15	Arka – Snuhi Dugdha and Saindhava Lavana - Lepa	Nirvapana (7 times)	Nirgundi Swarasa
Rasatarangini 17/17	Saindhava Lavana1/8 th part and Gomutra	Pachana (2 Yama)	Gomutra
Rasatarangini 17/18	Trikshara and Kanji – Lepa	Nirvapana (7 times)	Nirgundi Swarasa

Tamra Marana (incineration of copper):

After the *Shodhana* process, *Tamra* (copper) undergoes *Marana* (incineration) to prepare it for internal use in Ayurvedic medicine. *Marana* categorizes the process based on different media used to prepare *Bhasma* (copper nanoparticles). This enhances the metal bioacceptability, palatability, and reduces particle size. The resulting material becomes homogeneous, making it easily digestible, absorbable, and assimilated by the body, transforming it from a heterogeneous to a homogeneous form. Total 53 methods of *Marana* processes have been described in ancient texts of Ayurveda.

Amritikarana of Tamra Bhasma

After the *Marana* process, possible impurities may still remain in *Tamra Bhasma*. To remove these impurities, a specialized procedure known as *Amritikarana* is recommended. While this procedure is advised for all *Bhasmas*, it's particularly crucial for *Tamra Bhasma* to eliminate its *Utklesha*, *Vanti*, and *Bhranti Doshas*, ensuring the purity and safety of the final product [20].

Reference	Drug used	Method of preparation
Rasa Tarangini	 a. Tamra Bhasma 1 part b. Shuddha Gandhaka ¹/₂ part c. Pancamrita a. Tamra Bhasma 1 part b. Shuddha Gandhaka ¹/₂ part c. Nimbu Swarasa 	By mixing a and b together. Performing <i>mardana</i> along with c. Subjecting the mixture to <i>Gajaputa</i> , which is then repeated three times. By mixing a and b together. Performing <i>mardana</i> along with c. <i>Golaka</i> is kept inside <i>Surana Kanda</i> . After <i>Kapadmitti</i> , <i>Gajaputa</i> is given.
	a. <i>Tamra Bhasma</i> 1 part b. <i>Kumari Swarasa</i>	By giving <i>bhavana</i> of substance b to substance a. Subjecting the mixture to <i>Varaha Puta</i> after drying. Repeating the entire process seven times.

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Rasamritam	a. h	Tamra Bhasma 1 part Nimbu Swarasa	By giving <i>bhavana</i> of substance b to substance a. Keeping the mixture in <i>Surana Kanda</i> . Subjecting the mixture to <i>Gaja Puta</i> .	
	υ.	Tumbu Swarasa	Repeating the entire process seven times.	
Rasayanasara	a. <i>Tamra E</i> b. <i>Panchar</i>	Tamra Bhasma 1 part	Giving <i>bhavana</i> of substance b to substance a.	
		Panchamrita	Performing <i>Sharava Samputa</i> . Subjecting the mixture to <i>Gaja Puta</i> after drying.	
		1 инстиптии	Repeating the entire process three times.	

➤ Ancient Sources of Copper (Tamra):⁶⁻¹³

According to different texts of *Rasa Shastra*, the range of dose of *Tamra Bhasma* for internal administration is

between $1/8^{\text{th}} Ratti - 1 Masha$ (15 mg-1g). However, it is used in clinical practices with a dose of $\frac{1}{2} Ratti - 1 Ratti$ (60-120 mg), depending on the status of the patient [21].

VI. PHARMACOLOGICAL ACTIONS OF TAMRA BHASMA AND COPPER

Tamra Bhasma has many pharmacological actions and they have depicted in Fig.1.



Fig 1: Pharmacological Actions of Tamra Bhasma.

[•] *Vital Roles of Copper in the Human Body:* Copper plays a vital role in human physiology [22]. All the functions of the copper have been depicted in Fig. 2.



Fig 2: Role of Copper in Human Physiology

VII. TOXICOLOGICAL HAZARDS OF TAMRA BHASMA AND COPPER AND THEIR MANAGEMENT

Tamra Bhasma if not prepared well or compromised pharmaceutical processing leads to many noxious events [23, 24] as mentioned in Table 4.

Table 5: List of all Doshas of Improperly Prepared Tamra Bhasma.				
S.N.	Doshas	Modern Terminology		
1.	Aadhmana	Distension due to flatus		
2.	Aruchi	Anorexia		
3.	Ayuraghnam	Reduce life longevity		
4.	Balapahatva	Loss of physical strength		
5.	Bhrama	Dizziness		
6.	Bhranti	Vertigo		
7.	Chittasantap	Perplexed mind		
8.	Chittatapa	Perplexed mind		
9.	Daha	Burning sensation		
10.	Dhatushosha	Debility		
11.	Gatratapa	Warmness in the body		
12.	Kantighnatva	Reduced skin texture		
13.	Kledanam	Moistened body		
14.	Krimi	Worm infestation		
15.	Kushtham	Skin diseases		
16.	Madah	Intoxication		
17.	Moha	Disoriented mind and body		

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18.	Murchcha	Fainting
19.	Shoola	Pain
20.	Shosha	Cachexia
21.	Sweda	Sweating
22.	Udara	Ascitis
23.	Utkleda	Nausea, Vomiting
24.	Utklesha	Nausea
25.	Vami	Vomiting
26.	Vireka	Purgation
27.	Viryapahatva	Reduce strength or semen

Classical Antidote to Manage Copper Poisoning [25]

- Juice of *Munivrihi* mixed with *Sita*
- Juice or infusion of Dhanyaka mixed with Sita
- Use of *Mukta Bhasma*

VIII. COPPER POISONING

Copper is a reddish heavy metal that is generally nontoxic in its pure form. However, when alloyed and converted into fine powder, it can become poisonous if ingested or inhaled. Common copper salts include copper sulfate (blue vitriol) and copper acetate (verdigris or zangal), both of which can be toxic in certain forms and concentrations. While copper is essential in small amounts for human health, excessive exposure to its compounds can lead to various health issues [26].

> Acute Poisoning:

Copper sulfate, also known as blue vitriol or tuttha (CuSO4.5H2O), is used medicinally in small doses as an astringent or emetic. However, in larger amounts, it can become an irritant poison.

Acute poisoning from copper salts typically begins within 15-30 minutes of ingestion. Symptoms include a metallic taste, increased salivation, and a burning pain in the mouth, nausea, vomiting with blue or green vomitus, thirst, diarrhoea, oliguria, haematuria, albuminuria, uraemia, jaundice, cramps or spasms, convulsions, frontal headache, circulatory collapse, limbs paralysis, drowsiness, insensibility, and coma leading to death [26, 27].

> Fatal Period:

The usual fatal period is 1-3 days, but it can be prolonged for several days [26, 27].

> Management:

In cases of copper sulfate poisoning, vomiting typically occurs within 5-10 minutes after ingestion. Therefore, emetics are not required. Instead, a gastric wash should be administered using a 1% potassium ferrocyanide solution, which forms insoluble cupric ferrocyanide. White bulk of egg or cold milk that contain albumin will form

insoluble copper albuminate and act as an antidote. Intramuscular injection of B.A.L. (British Anti-Lewisite) is advised at a dose of 2.5 mg/kg/body weight. Castor oil can also remove the poison from the intestine. Symptomatic treatment includes administering morphine hydrochloride to relieve pain and maintaining electrolyte and fluid balance [26, 27].

> Chronic Poisoning:

Chronic poisoning from copper typically occurs among workers in copper factories or individuals exposed to copper dust over time. This exposure can happen through inhalation of copper dust in the workplace or using dirty copper vessels for food preparation. Dust can be absorbed through the alimentary canal, lungs, and partly through the skin during the handling of Cu metal and related salts [26, 27].

Clinical Presentation:

In chronic Cu poisoning, symptoms look like those of lead poisoning. Common signs include gums with a green or purple line, a persistent coppery taste in the mouth, headache, nausea & vomiting, giddiness, dyspepsia, diarrhoea, colicky pain, laryngitis & bronchitis, renal damage, anaemia, peripheral neuritis, muscle atrophy, jaundice, and greenish urine, perspiration and hairs. Eyes may experience inflammation of the conjunctiva and ulceration of the cornea due to copper dust exposure. Direct skin contact with copper may lead to dermatitis or eczematous lesions. Chronic copper poisoning can also result in a symptom complex known by various names such as hemochromatosis, bronzed diabetes, and pigment cirrhosis, as described by Mallory [26, 27, 28].

➤ Management:

First step is to find out the cause and remove it as soon as possible. Do massage and take a bath with warm water. The patient should be rehabilitated in fresh air. Attend to his diet and dyspepsia [27, 28].

➢ Safety Studies on Tamra Bhasma

Different types of in vitro and in vivo toxicity study reports of *Tamra Bhasma* have been summarized in Table 5.

Table 6: Toxicity Studies on Tamra Bhasma.

1. **Chronic toxicity study:** *Tamra Bhasma* to albino Wistar rats. TED of 5.5 mg/kg, $5 \times$ TED, and $10 \times$ TED. Significant decreases in body weight in $5 \times$ TED, and $10 \times$ TED. The TED showed non-toxic effects. However, $5 \times$ TED, and $10 \times$ TED

		were found to have a toxic effect [29].
4	2.	Genotoxicity study: TB, prepared with and without Amritikaran to Swiss albino mice at 7.8 mg/kg body weight for 14
		days. All treated groups showed significant body weight gain compared to the cyclophosphamide (CP) group. No
		structural deformities compared to the CP group [30].
~	3.	TB made from shodhita and ashodhita Tamra, examined for toxicity study in albino rats at 5.5, 27.5, and 55 mg/kg for 45
		days. Histopathological results indicated that TB prepared from shodhita Tamra was safe even at 5× TED. However, TB
		prepared from ashodhit Tamra showed toxicity even at TED [31].
4	4.	In a chronic toxicity study in albino Wistar rats, at dose levels of 2.25 mg/200 gm and 4.5 mg/200 gm rat (2×TED) for 90
		days. The study found no toxicity [32].
4	5.	TB prepared with and without Amritikaran administered for 28 days at 5.5, 27.5, and 55.5 mg/kg in albino Wistar rats to
		evaluate acute and subacute toxicity. Mild toxicity affecting the liver, kidney, heart, and thymus observed at the 55.5
		mg/kg dose level only. The sample prepared without Amritikarana exhibited a greater extent of toxicity [33].
(6.	In a toxicity study of TB in Albino rats (Charles Foster strain), the calculated LD ₅₀ dose was found to be 480 mg/100 gm
		in rats. Dose levels of 1000 mg/kg (3 days), 2 mg/kg (30 days), and 5 mg/kg (90 days) did not result in toxicity.
		However, at 100 mg/kg for 15 days, slight increases in all these enzymes observed [34].

Pharmacological Activities of Tamra Bhasma

Different types of pharmacological activities of Tamra Bhasma have been summarized in Table 6.

Table 7: Studies on Tamra Bhasma for Validation by Pharmacological Activities.

1.	Antioxidant study- Lipid Peroxidation (LPO) and reduced Glutathione (RGSH) levels were evaluated for antioxidant study.
	Both the activities showed statistically significant decrease in TB at 5 x TED and 10 x TED dose as compared to control
	group. Significant decreased CK-MB activity, LDH activity and ALP level were seen at 5 x TED and 10 x TED doses.
	Significant increase in ASE and ALT activities was seen in TED, TED x 5 and TED x 10 dose levels [29].
2.	Comparative anti-hyperlipidaemic activity: Shuddha Tamra Bhasma (STB) demonstrated significant anti-hyperlipidemic
	activity, while Ashuddha Tamra Bhasma (ATB) lacked such effect [35].
3.	Anti hyperlipidaemic activity: Study concludes that lipid lowering capacity of TB was more in TB prepared using Mulika
	and followed by Kajjali. TB prepared using sulphur was not effective [36].
4.	Anti-oxidant potential: Findings suggested that <i>Tamra Bhasma</i> is a potent antioxidant medication and can be considered for
	managing lipid peroxidation without any detactable adverse effects [37].
5.	Tamra Bhasma and Somnathi Tamra Bhasma subjected to albino Wistar rats. Insignificant changes were seen in BSL, serum
	cholesterol, triglycerides as well as in all other biochemical parameters when compared to control group. This reveals the
	safety of these formulations [38].
6.	The antioxidant activity of Tamra Bhasma was studied in albino rats across three parameters: Lipid Peroxidation: Normal
	at doses up to 7.5 mg/kg, but increased at higher doses. Aerial Oxidation of GSH: Maintained at 5 mg/kg, but rapidly
	increased at higher doses. SOD Activity: Initially decreased at doses up to 5 mg/kg, then gradually increased at higher doses,
	accompanied by increased lipid peroxidation and rapid GSH oxidation. In summary, Tamra Bhasma showed antioxidant
	effects at lower doses but induced oxidative stress at higher doses, with a complex impact on antioxidant enzyme activity
	[34].

IX. PHARMACOTHERAPEUTICS OF COPPER COMPOUNDS

Copper plays a crucial role in iron absorption from the gastrointestinal tract (GIT) and regulates or activates iron from its storage tissues by its catalytic activities. It helps in the haemoglobin formation, with a requirement of 3 mg/day daily for the hemopoietic purposes. The highest percentage of copper in the blood is found in haemoglobin. A combination of copper with iron results in faster recovery in anaemic children compared to iron alone.

Oral administration of copper sulfate at 1-3 mg/day, along with milk or fruit juice, is found effective for children [39]. Bacteriostatic and bactericidal action of copper is well reported. Historically, copper salts were used to induce vomiting due to their irritant effects on the gastrointestinal tract. However, excessive absorption of copper can lead to toxic symptoms, although prompt vomiting due to copper's irritant properties helps mitigate this risk [40]. B.L. Pandey *et al.* studied on the action of *Tamra Bhasma* on experimental gastric ulcers and secretions, discovering an anti-ulcerogenic effect on experimental animals [41]. They observed a reduction in the content of sugars of mucosa glycoproteins and found that the drug's effect was prolonged and increased gastric mucosal thickening [42]. Researchers suggest that copper powder may have an additional mechanism of action, possibly involving the enhancement of prostaglandin secretion. The role of prostaglandins in cytoprotection of the gastric mucosa and the action of proteolytic enzyme activity by copper have been explored by Moddox J. S *et al.* in 1993 and Menguy R. Masters *et al.* in 1965 [43, 44].

In 1977, Oster G and Salgo *et al.* reported that copper reduces carbonic anhydrase activity [45]. Singh PP and Das PK *et al.* found in 1978 that a single dose of copper inhibits the development of tolerance to certain nervous system effects of cannabis in rats after 7 days [46]. Additionally, in 1982, Sanyal et al. reported the effect of copper in reducing

peptic activity [47]. Furthermore, Leung *et al.* (1992) suggested cupric ions as a potential chemotherapy treatment for human lung tumours [48].

- Scientific Reports Addressing Chemical Identity of Tamra Bhasma
- Wadekar et. Al. (2005) reported that *Tamra Bhasma* is composed of cupric oxide (cuo), and it is present as a crystalline material having a crystallite size of 32.2 nm. The crystallite size of *Tamra Bhasma* was greater than that of lab-prepared cupric oxide nanoparticles (23.6 nm) [49].
- The findings of Singh et. Al. (2019) also report the same findings of Wadekar et. Al. (2005) [50].
- Dr. Lalit Mohan Sah (2005) in his M.D. thesis (submitted to Banaras Hindu University, Varanasi) reported that the *Tamra Bhasma* prepared by using Kajjali has phases of cus and *Tamra Bhasma* prepared with Gandhaka has dominant phases of cus with a few phases of cuo. Whereas, *Tamra Bhasma* prepared with Tilparni swarasa has phases of cuo only [51].
- Reddy et. Al. (2006), Jagtap et. Al. (2012), and Chaudhary et. Al. (2013) reported that *Tamra Bhasma* is copper sulfide as a crystalline material [52-54].

X. CONCLUSION

Copper (*Tamra*) has been used for various purposes since Vedic period. The use of *Tamra Bhasma* to treat different ailments is evidenced in different classical texts of Ayurveda. Copper has many vital functions in the body and plays a crucial role in human physiology. *Tamra Bhasma* is a safe and effective bioavailable form of copper, if prepared and used in a judicious way. It is concluded that copper is used in the form of *Tamra Bhasma* by converting it to a best bioavailable nanomedicine with the help of ancient pharmaceutical techniques. It is well established that *Tamra Bhasma* is a safe and ancient nanomedicine form of copper.

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