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# Critical Review of Pharmaceutical, Analytical and **Toxicity Characterization of** *Pittala Bhasma*

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# ABSTRACT

India has long utilized Brass, also known as Pittala, as a remedy for a range of ailments. The two elementary steps in the preparation of Pittala Bhasma (PB) are Shodhana (detoxification) and Marana (controlled incineration). The current study aims to gather and evaluate all pertinent and standard work that has been done on PB preparation, as well as standardize it concerning its safety, analytical, and pharmaceutical parameters. It is necessary to detect and quantify these drugs because they can accumulate contaminants during multiple stages of manufacturing, transportation, and storage, which can make them dangerous to use. In this regard, analytical instruments and methods are crucial. Advanced analytical techniques such as energy-dispersive X-ray, Fourier-transform infrared, scanning electron microscopy, transmission electron microscope, and X-ray diffraction may expand our comprehension of drugs' overall effects on the body, including their structure, behavior, and response. The preparation of PB involved a thorough search of relevant ancient Indian literature on ayurvedic pharmaceuticals as well as modern research databases like Scopus and PubMed and other relevant online content. This research may shed illumination on its possible application in characterization and therapeutics, eventually enhancing human life.

Key words: Pittala, Pittala Bhasma, Brass

# **INTRODUCTION**

Since the seventh century, the Indian subcontinent has been using Bhasmas, nanosized medications, to cure an array of diseases. They are also encompassed to potency of traditional Ayurvedic increase the

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polyherbal medicines.<sup>[1]</sup> *Pittala Bhasma* (PB) is advisable in the regimen for extensive ailments like Pandu (Anemia), Krimi (Worm infestation), Raktapitta (Bleeding Disorder), Kushtha (Skin diseases), Jwara (Fever), etc.<sup>[2]</sup> In combination with other medicine in a regime, it is used in a dose of ½ Gunja to 1 Gunja (62.5mg to 125mg).<sup>[3]</sup> For all metals and minerals to attain their most potent dosage form, known as Bhasma, they have to undergo the two essential phases of Shodhana and Marana. Shodhana (purification) is the process of eradicating *Doshas* from the Lohadi Dhatus by administering them through procedures like Peshana, Mardana (trituration), Bhavana (levigation), etc. with an Aushadha medication that has been previously prescribed. After this procedure, the Marana process is performed. Marana is described as the process by which metals and minerals are grounded with liquids (Svarasa etc.)

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and when dry reduced to *Bhasma* by heat. For proper achievement of *Paka* of *Rasadi Dhatus*, a quantum heat (*Agni*) in the form of *Puta* is required which should be neither less nor more.<sup>[2]</sup> If *Bhasma* is not prepared properly, it can cause multiple ailments such as skin diseases, fever, delusion, etc. There are various processes mentioned for the preparation of *Bhasma* that may create confusion regarding the standardization related to its quality, safety and efficacy.

The pharmaceutical, analytical, toxicological, pharmacological, and therapeutic aspects of *Shodhana* and *Marana*'s formulations are significantly influenced by the methodology opted for. A couple of studies on *Pittala* (PT, Brass) have been conducted in the areas of chemical characterization & pharmaceutical validation. To choose a better option in the future for an improved outcome, the majority of the research works that are currently available on PT have been compiled in this study along with brief critical information about its pharmaceutical & analytical data.

# **MATERIALS AND METHODS**

A thorough assessment of online search engines Google Scholar, Pubmed, DHARA, and AYUSH research portal as well as other literary sources were screened. Keywords *Pittala Bhasma*, *Pittala*, *Marana*, Crystal Size, XRD, XRF, SEM, TEM, FTIR, NTA, ICP-MS, AAS, and Nanomedicine were searched.

### Classical method of preparation of Pittala Bhasma

Synonyms of Pittala: Riri, Sulohaka, Brahmi, Ragyi, Kapila, Brahmriti, Shudrasuvarna, Sinhlaka, Pingal, Pitalak, Lohitak, Bhaarkutta, Pingal Loha, Peetak, Peetloha, Vartloha, Triloha, Aara, Aarkuta, Rajriti, Ragyi, Riti.<sup>[2]</sup>

### Grahya Swaroopa (desirable characters)

In almost all the classical texts of *Rasa Shastra* acceptable quality of *Pittala* is said to be: *Guru* (Heavy), *Mridu* (Soft), *Peetabh* (Yellow), *Tadanshama* (Can resist hammering), *Snigdha* (Smooth) and *Mrisana* (soft).<sup>[4]</sup>

Varieties: The classical text mentioned two varieties of *Pittala - Rajritika* and *Kaktundi*.<sup>[5]</sup>

# Authentication of Raw Pittala

For the preparation of *Pittala Bhasma*, Along with *Grahya Lakshana*, the purity should be checked by Scanning Electron Microscope/Energy Dispersive X-ray spectroscopy analysis. *Pittala* must then be processed through *Shodhana* and *Marana* to prepare *Pittala Bhasma*.

#### **Pharmaceutical Process**

Two primary processes for the processing of *Pittala Bhasma* involve detoxification in addition to purification with desired therapeutic properties, namely, *Shodhana* and *Marana*. Numerous *Acharyas* mentioned different media and methods for the *Shodhana* and *Marana* for the preparation of *Pittala Bhasma*. *Shodhana* incorporates numerous techniques such as *Swedana* (boiling), *Bharjana* (baking), *Nirvapa* (heating up and quenching in particular media), and *Bhavana/Mardana* (grinding). *Marana* (incineration) is a system of heating in which a specific quantum of heat (*Puta*) is provided for a specific duration.

The preparation of *Pittala Bhasma* follows the main and basic steps, i.e., *Shodhana* and *Marana*. The *Shodhana* involves two steps, *Samanaya* and *Vishesha Shodhana*.

- Samanya Shodhana is a series of processes in which five fluids are used as quenching media viz, *Taila* (Sesame oil), *Takra* (Buttermilk), *Gomutra* (Cow's urine), *Kajika* (Sour Gruel), *Kultha Kwatha* (decoction of Horse gram). *Pittala* is heated and quenched 7 consecutive times in each media, in successive order.<sup>[2]</sup>
- Vishesh Shodhana After Samanya Shodhana it is necessary to subject it to Vishesh Shodhana to reduce toxicity and enhance its potency. (Table 1)
- 3. *Marana* To render *Pittala* suitable for internal applications, it must undergo the *Marana* process after the *Shodhana* process. *Pittala* must undergo the *Marana* process after the *Shodhana* process to be fit for internal use. The method known as *Marana* transforms metal, mineral, or *Dravyas* into a form that can be readily and effectively absorbed by the body. *Mardana* & *Bhavana* (Trituration & Levigation), *Chakrika Nirmana* (Pellet Formation),

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Sharava Samputa, and Putapaka are the four fundamental steps of the Marana process. There are several techniques available that are categorized depending on the Bhavana Dravya (media) that are implemented in the Marana procedure. (Table 2)

# Table 1: Vishesha Shodhana of Pittala as mentionedin different classical texts

Type of media	Name of the drug	Name of the process	Time/ Number of Puta	Textual Reference
Herbal	Haridra Churna (Powder of Curcuma Ionga) Mixed Nirgundi Swarasa (Vitex negundo)	Quenchin g	5 to 7	Rasa Tarangini, <sup>[6]</sup> Rasa Ratan Samuchchay a, <sup>[4]</sup> Rasendra Chuda Mani, <sup>[7]</sup> Rasa Jala Nidhi, <sup>[8]</sup> Rasamritam, <sup>[10]</sup> Pi Rasa Darpan, <sup>[10]</sup> Rasendra Sambhav, <sup>[11]</sup>
	Nirgundi Swarasa (Vitex negundo)	Quenchin g	5	Rasa Prakash Sudhakara <sup>[12]</sup>
	Nishoth (Operculina turpenthu m) mixed Nirgundi Swarasa (Vitex negundo)	Quenchin g	5	Ayurveda Prakash[13]
Mineral	Three Kshara (Tankana, Sarjikshara & Yavakshara ) and Panch- Lavan (five salts)	Puta	Not mentioned	Rasa Jala Nidhi, <sup>[8]</sup> Anand Kanda, <sup>[14]</sup> Rasendra Mangalam, <sup>[15</sup> <sup>]</sup> Brihad Rasa Raj Sunder, [ <sup>16]</sup> Rasa Ratnakara <sup>[17]</sup>

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Animal	Gomutra	Boiling	4 Yama	Rasa
	(Cow's		(12 hour)	Tarangni <sup>[6]</sup>
	Urine)		(12 11001)	

# Table 2: Marana of Pittala as mentioned in Classics

SN	<i>Marana</i> Drugs	<i>Bhavana</i> drugs	<i>Puta</i> frequency	Textual reference
1.	Shudha Manashila (As <sub>2</sub> S <sub>2</sub> ) Shudha Gandhaka (S)	Ghrita Kumari (Aloe vera)	3	Rasa Tarangini <sup>[18]</sup>
2.	Shudha Gandhaka (S)	Arka Ksheera (Milk of Calotropis procera)	3	
3.	Shudha Hingula (Cinnabar) Shudha Haratala (As <sub>2</sub> S <sub>3</sub> )	Ghrita Kumari (Aloe vera)	3	Rasa Tarangini <sup>[18]</sup> and Rasendra Sambhava <sup>[11]</sup>
4.	Shudha Manashila (As <sub>2</sub> S <sub>2</sub> ) Shudha Gandhaka (S)	Nimbu Swarasa (Citrus limon)	8	Rasa Ratna Samuchaya, <sup>[4]</sup> Rasendra Chudamani, <sup>[7]</sup> Rasa Jala Nidhi <sup>[8]</sup>
5.	Shudha Manashila (As <sub>2</sub> S <sub>2</sub> ) Shudha Gandhaka (S)	Nimbu Swarasa (Citrus limon)	3	Rasamritam, <sup>[9]</sup> Rasa Darpana <sup>[10]</sup>
6.	Shudha Gandhaka (S)	Arka Ksheera (Milk of Calotropis procera)	2	Bhava Prakash Nighantu, <sup>[19]</sup> Ayurveda Prakasha, <sup>[13]</sup> Sharangdhara Samhita <sup>[20]</sup>

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7.	Shudha Gandhaka (S)	Aja Ksheer (Goat Milk) Nirgundi Swarasa (Vitex Negundo)	2	Sharangdhara Samhita <sup>[20]</sup>
8.	Shudha Manashila (As2S2) Shudha Gandhaka (S) Sendhava Lavana (Rock Salt)	Nimbu Swarasa (Citrus limon)	8	Rasa Prakasha Sudhakara <sup>[12]</sup>

# The Necessity for the standardization of *Pittala Bhasma*

In today's era, a wide range of research, be it Pharmaceutical, Analytical, and Pre-clinical (in vivo, in vitro) and clinical has been done on Shudha and Puti Loha, thus increasing its wide use for safe therapeutic purposes. However, the therapeutic efficacy of Mishra Loha still needs to be explored. Indian history dates back thousands of years when PB was recognized for its ability to treat bleeding and skin conditions. As per the description available in Rasa Granthas, Pittala consists of Tamra (Copper) and Yashada (Zinc) in a 2:1 proportion.<sup>[21]</sup> Pittala, formed through the amalgamation of Tamra and Yashada, inherits the distinctive properties of each constituent. As it is made by the combination of Tamra and Yashada, it has properties of both. The classics contain a variety of Shodhana and Marana procedures and methodologies, and it is also stated that Tamra Bhasma's techniques can be used in Pittala Bhasma's Shodhana and Marana process.<sup>[4]</sup> Acharya Sadanand Sharma, claims that Tamra Bhasma and Pittala Bhasma can be consumed in the same way.<sup>[21]</sup> Although Pittala has been mentioned since the 7-8<sup>th</sup> centuries, little or no research work is reported. The research work on Pittala regarding its therapeutic efficacy needs to be explored. Bhasmas responds with its concerns about safety and quality because it lacks appropriate standardization procedures.

# Pharmaceutical Validation

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To explain the thermodynamics of *Puta*, several types of laws can be applied. Heat flow in *Puta* can be explained by using the mechanism of conduction. A temperature gradient occurs when heat moves from a hot surface to a cold surface. The conduction of heat through the pellet can be explained by Fourier's law. The area and gradient of temperature are directly proportional to the heat transfer rate through a homogeneous material. Consequently, pellet shape is crucial. To allow for the easy passage of heat, it must have a flat shape and a uniform thickness. The exchange of heat between the *puta* and the pellets inside the *Sarava Samputa* can be explained by Hess's law of thermodynamics.<sup>[22]</sup>

Different *Putas* are described based on the quantity of fuel and type of raw material to be burned, including *Mahaputa*, *Gajaputa*, *Varahputa*, and *Kukkutaputa*, *Bhandaputa* and so on. Depending on the type of raw material, each puta has a unique dimensional measurement for heat resistance, duration, temperature mode, and specific intensity.<sup>[23]</sup> As technology progressed, the utilization of electrical muffle furnaces (Vertical and horizontal) has increased.

These furnaces have a maximum temperature of 1100°C- 1200°C. Even though the working principle of the *Puta* and electric furnace can be co-related but it is the necessity of the hour to standardize this quantum of heat. Standardization and regulation of heat is a tedious task in *Bhasma Pariksha*. This article focuses on providing a standard temperature pattern that needs to be followed in the preparation of *Pittala Bhasma*.

In one study, PB was prepared using a muffle furnace at a temperature of up to 1100°C and was kept for 3 hours along with the traditional method of *Bhasma* preparation. The process was repeated for 7 times. It was observed that the *Bhasma* prepared by *Putas* had more loss (25 gm) than the muffle furnace method (30.5 gm). No changes in Ayurvedic parameters of both the samples of PB were noticed.<sup>[24]</sup>

A thesis entitled, Pharmaceutico-Analytical and Antimicrobial Study of *Pittala Bhasma* used only traditional method to prepare the PB. It was observed that while

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processing the PT using the *Gajaputa* (35kg of Cowdung), the pellets fused as the temperature provided was around 900-910°C. To overcome this problem, a new method was adopted in which 3 times the weight of the *Sarava Samputa*, cow dung was taken, i.e., 12 kgs. The purpose of using this 3 times of cow dung was to make the material (PT) *Agnisahaya* first. A total of 15 *Putas* were subjected for the preparation of the PB. 10 *Puta* were given in 12 kgs of cow dung, while in the last 5 *puta*, the quantity of cow dung was gradually increased. Out of 5, 3 *Varahaputa* (22 kg) were given and in the last 2 (14<sup>th</sup> and 15<sup>th</sup>), 2 *Gajaputa* were given.<sup>[25]</sup>

The method of preparation mentioned by the *Acharyas* (table 2) stated the use of only 8 *Putas*, but on real ground, the number of *Putas* is more. Thus, a need to standardize the preparation method, the number of *Putas* and the temperature pattern in PB is essential.

Similarly, the methods described in *Rasa Ratna Samuchhaya* (a classical textbook of *Ayurveda*) were followed to perform the *Shodhana* (detoxification) process. The *Shodhana* of PT was carried out in 3 batches (500 gm) each by quenching 7 times in *Taila* (Sesame oil), *Takra* (Buttermilk), *Gomutra* (Cow's urine), *Kanjika* (Sour Gruel), *Kultha Kwatha* (decoction of Horse gram) and *Haridra Churna* (Powder of *Curcuma longa*) Mixed *Nirgundi Swarasa* (*Vitex negundo*). The method concludes that an average of 470 gm of *Shodhit* PT from 500 gm of PT was obtained.<sup>[25]</sup>

### **Analytical Validation**

Metals and minerals have been used for thousands of years as therapeutic medicines attributable to the learning of ancient pharmaceutical techniques. It is also necessary to define the physical and chemical properties of raw materials and final products. An important part of drug standardization is analytical analysis. The implementation of conventional drug development techniques is hindered by the absence of uniform quality control profiles. Drug consistency, or the composition of ingredients in the final product, affects both efficacy and safety. To ensure quality management parameters for *Bhasma* according to the *Rasa Shastra* (ancient Indian classical text for the preparation of *Bhasmas* for therapeutical use) book, classic tests such as *Nischandratva* (loss of metallic luster), *Varitara* (after sprinkling float on the surface of the water), *Rekha-Purnatva* (particle should be tiny that it can get into the finger pores), etc. were used.<sup>[26]</sup>

Along with these, various analytical parameters like SEM, XRD, FTIR and AAS are widely used nowadays for the analysis of various Bhasma preparations. Pittal Bhasma's XRD reveals the presence of CuO, as well as its granular texture and polycrystalline structure. The EDAX analysis reveals the incorporation of several nutrient elements. The SEM displays particles whose morphology has changed. The EMF-prepared Bhasma has smaller size than those prepared using the traditional heating method. FTIR for the traditional method shows major peaks for C-H, C=C, and Cu-O bonds. 60% of the particles in Pittala Bhasma prepared using the conventional heating method are in the 300-750 nm range, whereas 65% of the particles in Pittala Bhasma prepared using an electric muffle furnace are in the 250-750 nm range. The bimodal particle distribution is seen in both situations.<sup>[24]</sup>

The significance of particle size in Bhasma (Ayurvedic metallic preparations) lies in its profound impact on the efficacy and safety of the formulation. Finely powdered particles ensure enhanced bioavailability and assimilation of the active constituents, facilitating optimal therapeutic outcomes. Additionally, controlled particle size contributes to the uniform distribution of medicinal properties, promoting consistent potency across doses. Moreover, smaller particle sizes are often associated with improved solubility and absorption, facilitating better penetration and utilization within the body. Conversely, larger particle sizes may impede absorption and increase the risk of adverse effects or incomplete therapeutic response. Hence, meticulous attention to particle size during the preparation of Bhasma is imperative to maximize its therapeutic benefits while ensuring safety and efficacy.

# **Safety Validation**

Pittala being an alloy of *Tamra* (Copper) and *Yashada* (Tin) has the properties of both. Although a wide range

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of toxicity studies has been done on Tamra and Yashada and has proven them to be non-toxic, a toxicity study of Pittala Bhasma remains an area of research. One research examined the acute and subchronic toxicity of Tamra Bhasma (TB), the findings revealed that, at the therapeutic dose level (5.5 mg/kg) and therapeutic equivalent dose (TED) × 5 (27.5 mg/kg), neither of the TB samples exhibited any signs or symptoms of toxicity. However, after repeated administration of TB for 28 days in rats at a higher dose of TED × 10 (55 mg/kg), TB exhibited mild toxicity in the liver, kidney, heart, and thymus.<sup>[27]</sup> Yashada Bhasma does not appear to have any significant negative effects on the body's overall functions. The moderately intense alterations in kidney function are probably reversible, and the epithelial proliferation may be a sign of androgenic activity rather than pathological changes. By encouraging the production of anti-stress proteins, encouraging the turnover of epithelial tissues in various organs, and preventing lipid peroxidation and DNA fragmentation in target tissues, it has a moderately cytoprotective effect.<sup>[28]</sup>

### **Limitations and Future Perspective**

Although quality control parameters were more advanced in the past relative to their time, they now have certain limitations. The standardization of Bhasmas might benefit from the modern era's use of sophisticated tools. Such protocols for analyzing Bhasmas based on particle mass, range, and chemical and physical stability are outlined in most ancient texts. However, the chemistry of these phases is not covered in detail by these experiments, which are merely observational. These days, we may continue to incorporate advanced analytical methods for collecting data and creating structural maps. Following Bhasma Pariksha's classical control parameters for judgment, these techniques - which include TEM, infrared spectroscopy, X-ray fluorescence, particle-induced Xray emission, matrix-assisted laser desorption / ionization, atomic force microscopy, electron spectroscopy for chemical analysis, nuclear magnetic resonance, EDAX, and electron probe micro-analyzer become crucial tools for standardizing intermediate and final products. These analytical techniques offer a

comprehensive understanding of the drug's subatomic, geometrical and cellular functions. Several academics have expressed concerns about the safety and toxicity of medications based on metals or minerals.<sup>[29,30]</sup> Consequently, to evaluate the safety of *Bhasmas*, toxicity studies on global standards should be conducted. These procedures can also be used to access permissible levels. The generation of fingerprints and the establishment of standard operating procedures and manufacturing procedures for *Bhasma* preparations can be facilitated by these methods in conjunction with other complementary procedures from the foundational laboratory sciences.

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# **CONCLUSION**

In the Classical texts, *Pittala*, an alloy containing copper and zinc, has been used to treat an array of ailments. However, in the contemporary age, standardization is imperative due to the proper accessibility of genuine samples. It becomes crucial to characterize pharmaceuticals in terms of validation, safety assessment, and analytical standardization. To create a standardized protocol for analysis and gain a deeper comprehension of drug behavior through the use of modern analytical tools, sophisticated data analysis is required for the standardization of *Ayurvedic* drugs. The work done on *Pittala* standard operating procedures and various advanced / sophisticated analytical techniques may be better understood with the aid of this article.

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