

Phytochemically tailored zinc based ayurvedic nano-medicine: Therapeutic Importance and Prospects

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Abstract- Ayurveda, a time honoured traditional system of medicines, has thrived on its profound understanding of the correlation between human body constitution and the elements of the universe. Yashad Bhasma (Zinc Oxide), a unique Ayurvedic metallic preparation, has been employed for centuries in treating various ailments, offering a holistic approach as an immune booster and a healing agent. Phytochemically tailored Zinc based herbomineral novel preparations/formulations have been explored to be an important wide spectrum therapeutic, based on blended pharmacy methods.

The article introduces the concept of zinc-based Ayurvedic nano-medicine, emphasizing the therapeutic potential of zinc oxide nano-particles, an evidence based herbo-mineral formulation which has embraced reverse pharm. principles. There lies resemblance between Ayurvedic Bhasmas and chemically metal oxides, Physicochemically, Biochemically and also in-turn physiologically. The transformation of metallic zinc into assimilable zinc oxide as per modified Ayurvedic methodology may be of

paramount significance. This conversion not only eliminates the toxicity of the metal but also enhances biocompatibility, paving the way for targeted drug delivery and medical imaging on the lines of ADMET.

Furthermore, the study calls for comprehensive standardization measures, addressing qualitative and quantitative aspects. The article highlights the necessity of scientific strategies to navigate challenges in Yashad Bhasma research, ensuring its safety, quality, and medicinal efficacy by phytochemical blending. The research advocates for a harmonious blend of traditional wisdom and modern scientific rigor to propel Ayurvedic medicinal system, specifically Yashad Bhasma, into mainstream healthcare. Standardization and redesigning may emerge as the cornerstone for bridging the gap between ancient healing practices and contemporary healthcare to foster global acceptance and utilization of Ayurvedic treatments, accepted as have been realised, practiced and proved during pandemic Corona as Repurposed therapeutic strategy.

Key words: Yashad Bhasma, Biochemically, Biocompatibility, Nano-medicine, Thermo gravimetric.

Introduction

Ayurveda is one of the most renowned traditional systems of medicine that has survived and flourished from ages till date. With the enormous knowledge of nature based medicine, the relationship of human body constitution and function to nature and the elements of the universe that act in coordination and affect the living beings, this system will continue to flourish in ages still to come. There are many avenues still to be explored by the researchers, practitioners and experts in the field who carry the responsibility of keeping the traditional systems of medicine (TSMs) alive and contributing to their growth in the future. These futuristic goals can be accomplished when one gains insights about the systems, the principles and histories and works upon the strengthening aspects common between the various TSMs. With a rich knowledge of plants, minerals and animal based products, and the above based principles of doctrine, Ayurveda has achieved its widespread acceptance globally.

Metals play an important role in the human body, the deficiency of which leads to various disorders. In Ayurveda, metals such as gold, silver, copper iron, tin, zinc are described as medicinally important for the body. Perfect health is attributed to the state of equilibrium of these metals in body tissues. Any imbalance, whether excess or deficiency, disturbs the body metabolism. It has been described that metal-based formulations, called Bhasma, are highly effective in the prevention and

cure of various diseases related to the organs where they are naturally found. Bhasmas are unique Ayurvedic metallic preparations with herbal juices/fruits, used in the Indian subcontinent since the seventh century BC and widely recommended for the treatment of a variety of chronic ailments. The Bhasmas are in fact products of classical alchemy inorganic compounds of certain metals and gems in a very fine powdered form, mostly oxides, made in an elaborate calcinations process known as bhasmikanana. It is believed that bhasmikanana process converts the metal into its specially desired chemical compound which eliminates the toxicity of the metal and has the necessary medicinal benefits^(1,2). Various minerals like iron pyrite, copper pyrite and bitumen; salts such as common salt, alkaline salt, black salt, and fossil salt; certain compounds like realgar, iron sulphate, copper sulphate and antimony sulphide were used in the preparation of Bhasmas due to their medicinal value. Some of the commonly used Bhasmas are Kajjali, Abhrak Bhasma, Naag Bhasma, Vang Bhasma, Jasad Bhasma, Tamra Bhasma, Mandoor Bhasma, Swarnamakshik Bhasma, Rasa Sindoor, Makardhwaj and Lauha Bhasma. They will be available as nano-particles and are taken along with milk, butter, honey or ghee; thus making the metals easily assimilable, eliminating their harmful effects and enhancing their biocompatibility⁽³⁾. The methods of bhasma preparation vary so much for each metal such that bhasma with different colours are produced. The Resultsants are considered to be same medicinal substances with the ascribed indications even though these may differ in the composition between them and should

ideally be addressing different ailments. In short, there is no standard bhasma of a metal as such. Ayurveda provides a list of tests for the efficacy of the bhasmikaarana process. The tests are essentially qualitative and ensure that the Resulting drug is very fine (small grains), has no metallic shine and does not alloy with silver even at higher temperature to which it was subjected⁽⁴⁻⁷⁾. However, these qualitative tests do not provide any quantitative information about the composition and the structure of the final drug. For any drug containing heavy metals (for example lead, mercury), such structural information is an absolute necessity. In view of such ambiguity and the risk due to their inconsiderate use, there is an urgent need to bring about a standardization of the preparation-process and the end product, as also to resolve the prospective indications and strengthen the regime to monitor the manufacturing, and admin.

Zinc is known to play a crucial role in biological processes, and adding it to nano-medicine can have a number of therapeutic advantages. Utilizing zinc oxide nano-particles is one such strategy, as zinc oxide has been researched for its biocompatibility and possible medicinal benefits. Zinc's special qualities combined with the adaptability of nano-materials make zinc-based Nano-medicine a promising therapeutic approach. The creation and characterisation of zinc oxide nano-particles for targeted medication delivery and medical imaging are the main objectives of this work. Zinc is a desirable option for use in Nano medicine since it is a vital micronutrient that is involved in many different cellular functions. Because of its adjustable qualities and

biocompatibility, zinc oxide nano-particles provide a platform for developing novel therapeutic approaches.

Correspondence between Bhasma and metal oxide

In Ayurveda, bhasma is a special preparation that uses herbs and metals. Metal oxide forms are created from the initial forms of the metals employed in Bhasma¹. The conversion is accomplished by heating the metals in a closed crucible using cakes of cow dung, a procedure called calcination.

The majority of the metals found in Ayurveda come from deliberate additions in the form of Bhasma. These metals are different from ambient metal forms in that they go through rigorous processing to change their molecular forms. For example, minerals utilized in Ayurvedic and Tibetan medicine, such as HgS, As₄S₄, PbS, PbO, etc., are treated to create Bhasma or Zuotai, which are distinct from ambient metal forms like HgCl₂, MeHg, NaAsO₂, NaH₂AsO₄, Pb(CH₃COO)₂, etc.

The organically formed nano-particles known as Bhasmas are consumed with ghee³, milk, butter, or honey. This improves these elements' biocompatibility and facilitates their easy assimilation, hence removing any negative effects³. Significantly smaller particle sizes (1-2 μm) may aid in the drug's absorption and assimilation into the human system.

The primary correspondence lies in the conversion of metallic zinc into zinc oxide during the calcination process. This transformation is significant because zinc oxide is known for its unique properties,

including antimicrobial, anti-inflammatory, and wound-healing effects. The repeated incineration cycles not only transform the zinc into its oxide form but also contribute to the reduction in particle size. This nano-sized structure may enhance the bioavailability and therapeutic efficacy of Yashad Bhasma. Zinc oxide has been studied for its medicinal properties, and the correspondence between Yashad Bhasma and zinc oxide suggests that the Ayurvedic preparation may inherit some of these therapeutic benefits. These properties may include anti-inflammatory, antioxidant, and immuno modulatory effects. The addition of herbal extracts during the preparation of Yashad Bhasma introduces a holistic approach to healing. The combination of zinc oxide and herbal components may create a synergistic effect, providing a more comprehensive therapeutic impact⁽¹¹⁾.

Yashad Bhasma: an ancient Zinc based nano-medicine

Biological nanocrystals are called bhasmas. Nano crystalline materials are solids made up of crystallites smaller than 100 nm in at least one dimension, according to the field of nanotechnology. The obtainable grain size is influenced by milling parameters such as product type and milling temperature. Particle size is decreased by applying the Ayurvedic principles of marana (trituration) and bhavana (levigation). Scanning electron microscopy, transmission electron microscopy, fast freeze fracture, fluorescent microscopy, X-ray photo-electron spectroscopy, atomic absorption spectroscopy copy, gel electrophoresis, and enzyme expression are some of the

techniques used to find nano-particles in bhasma. Three steps were included in the testing of nano-particles in Bhasma:

1. To determine whether a test sample contains nano-particles .
2. To determine the homogeneity of a chemical substance.
3. The crystalline or amorphous nature of the nano-particles .

Standardization of Yashad Bhasma

Standardization is a measurement for ensuring quality. It refers to all actions taken during the production process and quality control that produce a reproducible quality. Plant life cycles, from seed to finished product, are greatly influenced by herbal compositions. It also refers to the process of incorporating excipients or mixing herbal remedies or drug preparations in order to achieve a desired level of a constituent or group of compounds with established therapeutic activity, respectively, in the herbal drug preparation. Standardization is a challenging task since numerous factors influence the repeatable therapeutic impact and bio-efficacy. To produce high-quality herbal products, attention must be paid from the outset of the preparation process.

There are very few scientific analytical investigations on standard bhasma preparations, and the ones that do exist are often incomplete. As a result, a scientific strategy that takes the following actions is absolutely necessary.

- i. Standardization of raw materials and completed products in terms of form and function.

- ii. Determining the metals' level of oxidation and connecting them to acidic radicals in the final product.
- iii. Metal extraction from tissues or the use of tracer techniques to study the pharmacokinetics of the main metallic component of bhasma.
- iv. Research on metal buildup in various organs and tissues. e. Both acute and long-term toxicity.
- v. Heat shock protein expression.
- vi. How bhasmas affect typical antioxidant and physiological markers.
- vii. Bhasmas' therapeutic reaction at the cellular and molecular levels on the suggested disease model (based on claims made in writings related to ayurveda).
- viii. Bhasmas' function as drug transporters, and
- ix. The function of bhasmas in digestive tract physiology and immuno modulation of the organism.

Standardization techniques

Organoleptic test

Organoleptic tests are an essential part of the quality control process for Ayurvedic bhasma. The organoleptic test of Ayurvedic bhasma is performed to evaluate the sensory properties of the substance, such as its color, odor, taste, and texture. The test is used to ensure that the bhasma is of high quality and free from impurities. The test is typically performed by trained professionals who have experience in evaluating the sensory properties of substances. The Results of the organoleptic test are used to determine whether the bhasma meets the required quality standards for use in Ayurvedic medicine. This information is important for researchers who are studying the

efficacy of Ayurvedic bhasma and its potential use in treating various health conditions.

Physicochemical evaluation

An herbo-mineral concoction called Ayurvedic Bhasma is utilized in Ayurvedic medicine. Ayurvedic Bhasma's physico-chemical analysis is a crucial component of quality assurance. Several physical and chemical characteristics of the Bhasma, such as its surface area, shape, particle size, and chemical composition, are analyzed as part of the evaluation process. Organoleptic testing are another step in the evaluation procedure that evaluate the Bhasma's sensory attributes. The Ayurvedic Bhasma is checked for impurities and high quality using the Results of the physicochemical examination. Researchers looking into the effectiveness of Ayurvedic Bhasma and its possible applications in treating a range of illnesses should find this information to be very useful⁽⁶⁾.

Microbiology evaluation

- One of the most important aspects of guaranteeing the quality and safety of different products is microbiological examination. The evaluation of the total fungal, total Enterobacteriaceae, and total viable aerobic counts is part of it. An overview of the microbial load in a sample is given by these tests⁽³⁾.
- Certain pathogens, such as Salmonella spp., E. Coli, S. aureus, and Pseudomonas aeruginosa, are also screened. These bacteria' presence may be a sign of pollution and possible health hazards. Regulatory agencies like the Food and Drug Administration (FDA) in

the United States and the World Health Organization (WHO) determine the acceptable limits for certain infections and microbial loads. For example, the FDA requires that an ingredient's live microbial content, measured by aerobic plate count, be less than 10,000 organisms/gram. The FDA advises against using any analytical unit with an MPN of 9.2 or more coliform organisms per 100 milliliters for E. Coli.

- When it comes to Salmonella species, a method that finds three MPN species per 4 grams (or milliliter, if a liquid sample is being taken) of total solids should not be used to detect them. The Bacteriological Analytical Manual published by the FDA offers instructions for identifying and counting S. aureus. Regarding Pseudomonas aeruginosa, the FDA offers guidance for its identification even though precise allowed levels are not easily accessible. It's crucial to remember that these restrictions may change, based on the particular product and how it will be used. Consequently, in order to guarantee the security and calibre of their goods; manufacturers need to abide by these rules⁽⁴⁾.

Analytical evaluation

Analytical evaluation of Bhasma is essential to ensure the quality and safety of the product. Several modern analytical techniques are available for this purpose. Among them X-ray Diffraction (XRD) is a significant technique that can detect the compounds of the material and free metals in it, if they are within detectable limits. High Power Thin Layer Chromatography (HPTLC) is another method used to identify the active ingredients in Bhasma⁽⁷⁾. SEM (Scanning Electron

Microscopy), TEM (Transmission Electron Microscopy), and AFM (Atomic Force Microscopy) are advanced microscopy techniques employed for the characterization of materials at the nanoscale. In the context of Yashad Bhasma, these techniques are utilized to investigate the morphological and structural features of the nano-particles formed during its preparation⁽¹⁴⁾.

In addition to SEM, TEM, and AFM, several other scientific techniques can be employed for the comprehensive characterization of Yashad Bhasma. These techniques provide valuable information about its chemical composition, structure, and physical properties. Here are some additional techniques: X-ray Diffraction (XRD): Fourier Transform Infrared Spectroscopy (FTIR), Energy-Dispersive X-ray Spectroscopy (EDS or EDX), Nuclear Magnetic Resonance (NMR), Thermo gravimetric Analysis (TGA), Raman Spectroscopy etc.

Integrating these techniques allows for a thorough understanding of Yashad Bhasma's chemical and physical characteristics, aiding in its standardization and quality control. Each method contributes unique insights that collectively contribute to a comprehensive characterization of this Ayurvedic nano-medicine.

Additionally, an Atomic Absorption Spectrometer (AAS) can be used to analyse bhasma elementally by determining the concentration of metallic elements in Bhasma. This is especially crucial because Bhasma should include levels of harmful metal components that are safe for humans to consume.

To sum up, Bhasma's analytical assessment is essential to guaranteeing both its safety and medicinal efficacy. It enhances the manufacturing of high-quality Ayurvedic products and reduces product irregularities. Further more, to enhance the ease of bioabsorption, it should further be tailored as per chelation therapy practices; this facilitates the therapeutic concentration limits *in-vitro* and *in-vivo* ; this regulates MIC also⁽¹⁰⁾.

Navigating Challenges in Yashad Bhasma Research: Considerations and Concerns

Ayurveda has a rich history; however, there were certain drawbacks in approaches towards it, which inhibited its growth like the Western system of medicine. The active components of the herbal drugs prescribed were not known, and even today many drugs still need further exploration for their active constituent characterization and elucidation of the mechanism of action. Even after decades of applying advanced analytical techniques for drug analysis, herbal drugs still face some drawbacks. The administration of combinations of several drugs adds to the complexity of the study of the activity of these medications. A merit of traditional medicine systems as discussed earlier is that they consider every individual as the prime focus of treatment rather than the disease. But this factor also possesses a hurdle to the applicability of medications on a general population basis. Several issues like, the variation in the potency due to difference in species, absence of an integrated coding for every species used commonly in TSMs, varying geographical

location of growth, and incorrect identification and adulteration of drugs, non-uniform quality control standards, differences in processing methods, direct an alarming need towards comparative study of drugs used in both these systems of medicine⁽¹²⁾.

While Yashad Bhasma has been traditionally used in Ayurvedic medicine and is believed to have therapeutic benefits, it's essential to acknowledge potential drawbacks and limitations in the study and analysis of this preparation. Some of the drawbacks include: lack of standardization, heavy metal contamination, limited scientific research, bioavailability issues, interaction with herbal additives, individual variability, adulteration and quality control etc. The use of animal-based ingredients or unsustainable sourcing practices in the preparation of Yashad Bhasma may raise ethical concerns, especially for individuals who prioritize cruelty-free or environmentally friendly products^(13,14).

In conclusion, while Yashad Bhasma has a rich history in Ayurvedic medicine, addressing these drawbacks through rigorous scientific research, standardization, and quality control measures is crucial to ensure its safety and efficacy in contemporary healthcare practices. Individuals considering the use of Yashad Bhasma should consult with qualified healthcare professionals to make informed, decisions based on their specific health needs and conditions.

Conclusion

The discussion of the research article revolves around the significance of Yashad Bhasmas in Ayurveda and the need for

their standardization and uses. Bhasmas, being unique Ayurvedic metallic preparations, have been used for centuries to treat various ailments; and thus Reverse-pharmacology principle validates it for therapeutic practices. Therapeutic dosing based on tolerable concentration regulation, is essential as per pharmacological guidelines. This variability presents a challenge in ensuring the consistency and efficacy of these medicines.

Furthermore, it would ensure that the Resulting drug is very effective, thereby increasing the global acceptance and utilization of Ayurvedic treatments. The research underscores the importance and prospect of standardizing zinc-based Ayurvedic nano-medicine, paving the way for future studies and advancements in this field. The research establishes a connection between Bhasma and metal oxide, highlighting the transformation of metallic zinc into metallodrug.

The study introduces the concept of zinc-based nanomedicine, recognizing zinc's vital role in biological processes. The utilization of zinc oxide nano-particles is explored, offering a promising strategy for targeted drug delivery and medical imaging. The creation and characterization of these nano-particles emerge as primary objectives, aligning with modern therapeutic approaches on the lines of Chelation-therapy.

The research article calls for a comprehensive standardization and formulation of zinc-metallodrug as Ayurvedic nano-medicine. Addressing drawbacks, such as lack of standardization and heavy metal contamination, through

rigorous scientific research and quality control measures is crucial. The study opens avenues for future research, tailoring and monitoring to encourage advancements in Ayurvedic medicinal system to pave the way for the integration of traditional wisdom with contemporary modern healthcare practices. This opens the Gates to Review, Revise, Reform and Revive the Ayurvedic and Traditional Indian Medicinal System.

Disclaimer Statement

Authors declare that no competing interest exists. The products used for this research are commonly used products in research. There is no conflict of interest between authors and producers of the products.

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