A Proposal

Discovering the Mode of Action of Mahakashaya Mentioned in Charaka Samhita Using Analytical Methods and In-Silico Technology: A Proposal

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ABSTRACT

Background: The *Charaka Samhita*, a cornerstone of Ayurvedic medicine, describes *Mahakashayas* (great categories of herbal formulations) with well-documented therapeutic applications. However, the molecular mechanisms underlying their efficacy remain largely unexplored in contemporary scientific terms. Employing analytical methods and in-silico technology offers an innovative approach to bridge this knowledge gap. **Objectives:** This proposal outlines a multidisciplinary strategy to investigate the mode of action of selected *Mahakashayas* using advanced analytical techniques and computational tools. The aim is to identify their bioactive compounds, predict molecular targets, and establish a scientific basis for their therapeutic claims. **Proposed Methods**: A comprehensive review of *Charaka Samhita* to shortlist *Mahakashayas* based on therapeutic relevance and feasibility for experimental investigation. Phytochemical Profiling (Employ chromatographic and spectroscopic techniques (e.g., HPLC, GC-MS, LC-MS/MS) to identify bioactive compounds in selected *Mahakashayas)*. In-Silico Analysis: Utilize molecular docking, virtual screening, and ADMET (absorption, distribution, metabolism, excretion, and toxicity) predictions to evaluate compound interactions with potential biological targets and use network pharmacology to explore the multi-target and multi-pathway effects of the compounds. Validation Studies: Design in vitro assays (e.g., enzymatic and cell-based studies) to validate predicted molecular interactions and their biological effects. Correlate in silico findings with phytochemical and experimental data to develop a mechanistic understanding of *Mahakashayas*. **Expected Outcomes**: Identify key bioactive compounds in *Mahakashayas* and their molecular targets. Provide evidence for their mechanisms of action in terms of modern pharmacology. Demonstrate the utility of combining traditional knowledge with contemporary scientific tools. **Significance**: The study aims to establish a scientific foundation for the therapeutic efficacy of *Mahakashayas*, thereby facilitating their integration into evidence-based medicine. It also aims to highlight the potential of Ayurveda in drug discovery and holistic healthcare.

Keywords: *Mahakashaya*, in-silico technology, molecular docking, network pharmacology

1. INTRODUCTION

Ayurveda, the ancient science of life, encompasses a comprehensive system of healthcare that has been practiced in India for millennia. The *Charaka Samhita*, one of Ayurveda's principal texts, introduces the concept of *Mahakashaya*, a unique classification of medicinal plants into fifty groups, each consisting of ten herbs with specific therapeutic properties [1]. These groups are meticulously categorized based on their pharmacological actions, such as *Deepaniya* (digestive stimulants), *Shonitasthapana* (hemostatic agents), and *Balya* (strength-enhancing herbs) [2].

Despite their historical and clinical significance, the molecular mechanisms underlying the therapeutic efficacy of *Mahakashaya* remain poorly understood. Traditional Ayurvedic formulations are often met with skepticism in modern biomedical contexts due to a lack of rigorous scientific validation [3]. This gap underscores the need for a systematic exploration of these herb groups using contemporary analytical and computational methodologies.

The integration of analytical techniques and in-silico tools offers a promising pathway to unravel the complex phyto-chemistry and biological mechanisms of *Mahakashaya*. Analytical methods such as High-performance liquid chromatography (HPLC) and Nuclear magnetic resonance (NMR) spectroscopy enable the identification and quantification of bioactive compounds [4], while in-silico technologies such as molecular docking and pharmacophore modelling facilitate the prediction of their interactions with specific biological targets [5].

This study proposes an integrative approach to decode the mode of action of *Mahakashaya*, aiming to bridge the traditional knowledge of Ayurveda with evidence-based scientific research. By elucidating the molecular basis of these herb groups' therapeutic actions, this research endeavours to validate Ayurvedic formulations and enhance their global acceptance.

2. OBJECTIVES

The primary objectives of this research are as follows:

1. **Phytochemical Profiling:** To identify and quantify the bioactive compounds present in selected *Mahakashaya* groups using advanced analytical techniques [6].
2. **Structural Elucidation:** To determine the molecular structures

of these compounds through NMR spectroscopy [7].

3. **In-Silico Analysis:** To predict the biological activities and therapeutic targets of the identified compounds using molecular docking and pharmacokinetic modelling [8].
4. **Validation of Therapeutic Claims:** To correlate the traditional therapeutic applications of *Mahakashaya* with scientifically validated mechanisms of action [9].
5. **Development of Novel Therapeutics:** To explore the potential of *Mahakashaya*-derived compounds as templates for the development of new drugs [10].

3. LITERATURE REVIEW

The concept of *Mahakashaya* in Ayurveda reflects a sophisticated understanding of pharmacology and therapeutics. These herb groups are extensively documented in the *Charaka Samhita*, with detailed descriptions of their properties, indications, and formulations [11]. Recent studies have highlighted the pharmacological potential of individual herbs from *Mahakashaya* groups, but comprehensive investigations into their collective mechanisms remain sparse [12]. For instance, the *Shonitasthapana Mahakashaya*, known for its hemostatic properties, includes herbs such as *Lodhra* (*Symplocos racemosa*) and *Shatavari* (*Asparagus racemosus*). These herbs have demonstrated significant bioactivity in preclinical studies, including anti-inflammatory, antioxidant, and wound-healing effects [13]. However, the synergistic interactions within the group and their molecular basis warrant further investigation [14].

In recent years, advances in analytical chemistry and computational biology have facilitated the exploration of complex herbal formulations. Techniques such as HPLC and Gas chromatography–mass spectrometry (GC-MS) have been employed to analyse phytoconstituents, while molecular docking studies have provided insights into the interactions between herbal compounds and protein targets [15]. These methodologies offer a robust framework for studying *Mahakashaya* groups, enabling the validation of their traditional uses through scientific evidence [16].

The integration of in-silico methods has gained prominence for predicting drug-likeness and therapeutic potential. Several studies have utilized pharmacokinetic modelling to assess the ADME

(absorption, distribution, metabolism, excretion, and toxicity) properties of herbal constituents [17]. For instance, the bioactive compound berberine, derived from *Daruharidra* (*Berberis aristata*), has been extensively studied for its pharmacokinetics and molecular interactions with diabetic targets. Such approaches pave the way for a deeper understanding of *Mahakashaya* groups, offering a scientific basis for their clinical applications [18].

4. MATERIALS AND METHODS

4.1 Selection of *Mahakashaya* Groups

Based on their therapeutic relevance and prevalence in classical texts, specific *Mahakashaya* groups will be selected for this study. Criteria for selection include:

1. Documentation in the *Charaka Samhita* [19].
2. Therapeutic applications with contemporary relevance (e.g., anti-inflammatory, immunomodulatory, and anti-diabetic properties) [20].
3. Availability of constituent herbs for research purposes [21].

4.2 Phytochemical Analysis

4.2.1 Sample Preparation

Herbs will be procured from authenticated sources and subjected to quality control measures, including macroscopic and microscopic examination. Extracts will be prepared using solvents of varying polarities, such as ethanol, methanol, and water, to ensure comprehensive phytochemical profiling [22].

4.2.2 Chromatographic Techniques

HPLC and GC-MS will be employed to identify and quantify bioactive compounds. These techniques enable the separation, detection, and characterization of phytoconstituents based on their physicochemical properties [23].

4.3 Structural Elucidation

Isolated compounds will be subjected to NMR spectroscopy for structural elucidation. One-dimensional (1H and 13C) and two-dimensional (COSY, HSQC, and HMBC) NMR experiments will be conducted to obtain detailed structural information [24].

4.4 In-Silico Analysis

4.4.1 Molecular Docking

Molecular docking studies will be performed to predict the interactions between phytoconstituents and biological targets. Tools such as AutoDock Vina and

Schrödinger Suite will be used to evaluate binding affinities and interaction patterns [25].

4.4.2 Pharmacokinetic Modelling

Pharmacokinetic properties, including absorption, distribution, metabolism, and excretion (ADME), will be predicted using in-silico tools. This analysis will provide insights into the bioavailability and safety profiles of the compounds [26].

4.5 Validation Studies

The findings from analytical and in-silico studies will be validated through in-vitro and in-vivo experiments, where feasible. These studies will assess the biological activities and therapeutic potential of the identified compounds [27].

5. EXPECTED OUTCOMES

1. Identification of key bioactive compounds within selected *Mahakashaya* groups [28].
2. Structural elucidation of these compounds using advanced spectroscopic techniques [29].
3. Insights into the molecular interactions and therapeutic targets of the compounds through in-silico studies [30].
4. Correlation of traditional therapeutic claims with scientifically validated mechanisms of action [31].
5. Development of a scientific framework for integrating Ayurvedic formulations into modern medicine [32].

6. DISCUSSION

The integration of traditional knowledge and modern science is essential for advancing healthcare systems. By elucidating the molecular mechanisms of *Mahakashaya*, this study aims to validate the therapeutic potential of Ayurvedic formulations and promote their acceptance in global healthcare [33].

One of the critical challenges in the field is the complexity of Ayurvedic formulations, which often contain multiple herbs working synergistically. The interactions among these compounds may result in enhanced therapeutic efficacy, yet such synergies remain difficult to model and analyse [34]. The lack of standardized methodologies for evaluating these complex mixtures further complicates research efforts. Advanced techniques such as network pharmacology could provide insights into how multiple bioactive compounds interact within the human body [35].

Furthermore, the safety and toxicity profiles of *Mahakashaya* formulations

require thorough investigation. Traditional use often assumes safety based on historical evidence, but modern validation demands rigorous testing under controlled conditions. Employing tools such as high-content screening and animal models could bridge this gap [36].

A significant limitation of current research lies in its narrow focus on isolated compounds rather than the holistic use of the herb groups. While isolating active compounds facilitates understanding of specific mechanisms, it overlooks the broader therapeutic benefits of using whole formulations. Future studies should aim to balance these approaches by considering both reductionist and holistic methodologies [37].

The incorporation of in-silico technologies, including molecular docking and virtual screening, has proven invaluable in hypothesizing the mechanisms of action of bioactive compounds. However, these predictions require validation through experimental studies. For example, docking studies may indicate high binding affinity of a compound to a particular protein target, but such interactions must be confirmed using biophysical techniques like surface plasmon resonance or isothermal titration calorimetry [38].

Another critical aspect is the alignment of traditional claims with modern therapeutic needs. For instance, many *Mahakashaya* groups are described in Ayurveda as immune-modulators (*Balya*), digestive aids (*Deepaniya*), or rejuvenators (*Jeevaniya*). These properties align with contemporary concerns such as managing chronic diseases, enhancing immunity, and combating oxidative stress. Bridging these concepts requires collaborative efforts among Ayurvedic practitioners, pharmacologists, and data scientists [39].

Finally, the global acceptance of *Mahakashaya* formulations depends on their integration into regulatory frameworks. International standards for herbal medicines, such as those set by the World Health Organization (WHO), provide a basis for ensuring quality, safety, and efficacy. Meeting these standards necessitates the development of robust standardization protocols and clinical trials, both of which are currently underdeveloped in the context of Ayurveda [40].

By addressing these challenges, the proposed study design provide a comprehensive understanding of *Mahakashaya* and its potential contributions to modern medicine. This work represents a step toward integrating traditional knowledge with cutting-edge scientific methodologies, fostering a holistic approach to healthcare.

6. CONCLUSION

This research proposal outlines a comprehensive approach to investigating the mode of action of *Mahakashaya* groups mentioned in the *Charaka Samhita*. By integrating analytical techniques with in-silico technologies, this study aims to bridge the gap between ancient Ayurvedic wisdom and contemporary biomedical science, fostering the global acceptance and integration of Ayurvedic formulations into evidence-based medicine [41].

Conflict of Interest

Nil

Funding

Nil

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