RESEARCH PAPER

MICRODOSING IN AYURVEDA: A CONCEPTUAL REVIEW

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ABSTRACT

Microdosing is a contemporary practice involving the administration of very low doses of classical psychedelic substances, principally lysergic acid diethylamide (LSD) and psilocybin, with the intention of producing subtle effects without a conventional psychedelic experience. Although the term microdosing and its contemporary pharmacological context are modern, the broader therapeutic principle of administering small, individualized and appropriately processed doses is represented in several Ayurvedic concepts. The present narrative conceptual review examines classical Ayurvedic literature, *Rasashastra* texts and contemporary scientific publications to identify and critically evaluate principles that may be considered conceptual analogues of low-dose therapeutics. Particular attention is given to *Matra* (dose), *Alpamatra* (small dose), *Alpamatropayogitvat* (therapeutic effectiveness in small doses), individualized dose selection according to *Agni*, *Bala*, *Prakriti*, age and disease status, fractionated administration (*Muhur-Muhur Aushadha Sevana*), route-specific administration such as *Pratimarsha Nasya* and *Matra Basti*, and the use of potent *Rasaushadhis* in relatively small quantities. Pharmaceutical procedures such as *Shodhana*, *Marana*, *Bhavana* and *Kupipakva* processing may alter the physicochemical characteristics, stability and biological behaviour of pharmaceutical preparations and therefore provide a potential basis for dose optimization. Modern characterization studies indicate that some *Bhasma* preparations contain nanoscale crystallites or particles together with larger aggregates, although particle size is formulation- and method-dependent. Experimental evidence also indicates that dose-response relationships may be non-linear, although these findings cannot be directly extrapolated to human therapeutic dosing. Contemporary evidence concerning psychedelic microdosing remains inconclusive, with recent meta-analytic evidence failing to demonstrate overall cognitive enhancement. The evidence therefore supports conceptual comparison rather than historical or pharmacological equivalence between the two approaches. Ayurveda may provide a valuable framework for investigating individualized low-dose therapeutics, cumulative exposure, pharmaceutical processing and route optimization, but these hypotheses require rigorous pharmacokinetic, toxicological and clinical validation.

Keywords: Microdosing, Matra, Alpamatra, *Alpamatropayogitvat*, *Bhasma*, *Pratimarsha Nasya*, *Matra Basti*, low-dose therapeutics.

How to cite this article: Devraj J Saroj, Amit Mishra, Pooja Upadhyay, Bhumika Dewangan,. MICRODOSING IN AYURVEDA: A CONCEPTUAL REVIEW. Int J Drug Deliv Technol. 2026;16(78s):1452-1457. DOI: 10.25258/ijddt.16.78s.196

.INTRODUCTION

Microdosing has emerged as a distinctive contemporary practice involving the administration of very low doses of classical psychedelic substances, particularly LSD and psilocybin, with the intention of producing subtle effects without prominent psychedelic or perceptual disturbance. There is no universally accepted pharmacological definition of microdosing; however, research commonly investigates doses substantially below those producing a conventional psychedelic experience, approximately 6.5–20 µg of LSD and low doses of psilocybin or psilocybin-containing mushroom material. Recent systematic reviews emphasize substantial heterogeneity in dose, schedule, population and outcome assessment [1-4].

The popularity of psychedelic microdosing has largely arisen from reports of enhanced mood, creativity, productivity, concentration and psychological well-being. However, the scientific evidence remains uncertain. A 2024 systematic review reported potentially positive associations with mental well-being but emphasized limitations related to small samples, observational designs, expectancy effects and the limited number of controlled studies [2]. A rapid review of placebo-controlled studies identified 19 controlled microdosing studies and concluded that the evidence was insufficient to determine whether observed effects were predominantly placebo-related [3]. More recently, a preregistered systematic review and meta-analysis of 14 studies involving 1,614 participants found no overall cognitive benefit and identified a small but significant reduction in cognitive control [1]. A 2025 systematic review of adverse effects identified predominantly mild and short-lived effects but also reported dose-related increases in blood pressure, anxiety and cognitive impairment, emphasizing the need for standardized safety assessment [4].

These observations make the scientific study of low-dose pharmacotherapy particularly relevant. Importantly, the contemporary concept of psychedelic microdosing should not be retrospectively imposed

upon traditional medical systems. Ayurveda does not describe "microdosing" as a unified therapeutic doctrine. Nevertheless, its pharmaceutical and therapeutic literature contains multiple principles concerned with the selection of an appropriate dose, use of minimum effective quantities, repeated administration of small quantities, route-specific delivery, pharmaceutical processing and individualized treatment.

The concept of *Matra* occupies a central position in Ayurvedic therapeutics. Dose is not considered to be an immutable quantity applicable equally to all patients. Rather, therapeutic administration is influenced by characteristics of the patient, medicine, disease, digestive capacity, strength, age, season, habitat and other contextual factors. This individualized approach differs fundamentally from a simple fixed-fraction dosing model.

Within *Rasashastra*, the concept of *Alpamatropayogitvat* is particularly relevant. *Rasaushadhis* are traditionally described as preparations capable of producing therapeutic effects in relatively small quantities, together with rapid action and acceptable palatability [5-7]. Such statements provide a conceptual basis for examining low-dose therapeutics in Ayurveda without claiming that the classical authors were referring to the modern practice of psychedelic microdosing.

Other examples further illustrate the multidimensional character of Ayurvedic dose optimization. *Pratimarsha Nasya* involves the administration of a small quantity of *Sneha* through the nasal route, commonly described as two drops in each nostril [8]. *Matra Basti* is specifically characterized as a small-volume *Sneha Basti*, traditionally described as approximately one and a half *Pala*, or approximately 72 mL, with contemporary practice commonly using approximately 60–70 mL [9]. *Muhur-Muhur Aushadha Sevana* represents repeated administration at short intervals, allowing dose exposure to be distributed over time. Certain potent *Rasaushadhis* are also traditionally administered in milligram quantities.

The present review addresses the question: Can the Ayurvedic literature be understood as containing a broader framework of low-dose therapeutics that is conceptually comparable to selected principles of contemporary microdosing, while remaining pharmacologically and historically distinct from it?

AIM AND OBJECTIVES

Aim: To critically examine the concept of low-dose therapeutics in Ayurveda and evaluate its conceptual relationship with contemporary psychedelic microdosing and its potential relevance to modern pharmacological research.

Objectives

To critically examine Ayurvedic low-dose therapeutics—encompassing dose concepts (*Matra*, *Alpamatra*, *Alpamatropayogitvat*), clinical applications (*Rasaushadhis*, *Bhasmas*, *Pratimarsha Nasya*, *Matra Basti*, *Muhur-Muhur Aushadha Sevana*), pharmaceutical processing (*Shodhana*, *Marana*, *Bhavana*, *Kupipakva*), modern experimental evidence and nano-scale characteristics—and to compare this framework with contemporary psychedelic microdosing while identifying translational research priorities for validation and clinical application.

MATERIALS AND METHODS

This narrative conceptual review integrated classical Ayurvedic literature (*Brihat Trayi*, *Sharngadhara Samhita*, *Kashyapa Samhita*, *Rasashastra* texts) with contemporary evidence from PubMed/MEDLINE, Scopus, Web of Science, Google Scholar and AYUSH Portal using relevant search terms. Priority was given to systematic reviews, meta-analyses and controlled studies. Thematic synthesis was performed under six domains: dose minimization; individualized selection; fractionated administration; route-specific delivery; pharmaceutical transformation; and cumulative exposure and safety. No quantitative meta-analysis was undertaken.

CONCEPTUAL FRAMEWORK OF AYURVEDIC LOW-DOSE THERAPEUTICS

Matra (Dose as an Individualized Therapeutic Variable): *Matra* denotes the quantity or measure of a medicinal substance administered for therapeutic purposes. The classical approach recognizes that the same medicine may require different quantities in different individuals. Factors such as *Agni* (digestive and metabolic capacity), *Bala* (strength), *Prakriti* (constitutional characteristics), *Vaya* (age), *Desha* (habitat), *Kala* (time and season), *Roga Avastha* (stage and severity of disease), *Sattva*, *Koshtha* and the properties of the *Dravya* influence therapeutic decision-making. These considerations are consistent with the broader Ayurvedic principle of *Yukti*, or rational therapeutic planning.

Alpamatra (The Principle of Small Dose**):** *Alpamatra* denotes administration in a relatively small quantity. In Ayurvedic therapeutics, small doses may be selected because of the potency of a preparation, the susceptibility of the patient, the route of administration or the intended therapeutic objective. The concept is particularly relevant to *Rasaushadhis*, which are often administered in quantities considerably smaller than many crude herbal preparations. Modern psychedelic microdosing is generally defined in relation to a fraction of a conventional psychedelic dose, whereas Ayurvedic *Alpamatra* is embedded within individualized pharmacotherapy and cannot be reduced to a fixed fraction.

Alpamatropayogitvat (Therapeutic Effectiveness at Low Dose): The concept of *Alpamatropayogitvat* is particularly prominent in the description of *Rasaushadhis*. Classical *Rasashastra* literature associates these preparations with therapeutic effectiveness at relatively small doses, rapid action and acceptable palatability [5-7]. This concept provides one of the closest conceptual parallels to the dose-minimization aspect of contemporary microdosing. However, in *Rasashastra*, low-dose administration is linked to the potency and pharmaceutical characteristics of the preparation and is integrated into disease-specific

and patient-specific therapeutic reasoning, rather than being defined by avoiding a psychedelic experience.

Yukti (Individualized Dose Selection): *Yukti* represents rational therapeutic planning based on multiple interacting factors. The same dose may produce different outcomes depending upon *Agni*, *Bala*, *Prakriti*, age, disease stage, concomitant treatment and route. Consequently, the Ayurvedic concept of dose is inherently contextual and potentially relevant to contemporary precision medicine, though the comparison should remain conceptual.

Kala*, *Anupana* and *Marga (Timing, Vehicle and Route): Ayurvedic pharmacotherapy considers the timing of medicine administration (*Aushadha Sevana Kala*), which can influence absorption, metabolism and therapeutic response. *Anupana* refers to the vehicle or accompanying substance administered with a medicine, which may influence dissolution, absorption and systemic exposure through various mechanisms. *Marga* (route of administration) is another important determinant of effective dose, with Ayurvedic therapeutics employing multiple routes including oral, nasal, rectal and, in selected historical preparations, parenteral administration. Route selection may allow therapeutic effects to be achieved with smaller administered quantities, as particularly evident in *Pratimarsha Nasya*, *Matra Basti* and the historical description of *Suchikabharana Rasa*.

CLASSICAL EXAMPLES OF LOW-DOSE THERAPEUTICS

***Rasaushadhis* and *Bhasma* Preparations:** *Rasaushadhis* represent a major category of potent Ayurvedic preparations involving processed metals, minerals and/or mineral-derived substances, often combined with herbal ingredients. Classical *Rasashastra* literature emphasizes their potency, rapid action and administration in relatively small quantities. Examples include *Rasasindura*, *Makardhvaja*, *Vatagadankusha Rasa* and other formulations.

Bhasmas are traditionally prepared through sequential pharmaceutical procedures including *Shodhana*, *Bhavana* and *Marana*. They are generally administered in quantities considerably smaller than many crude herbal preparations. Examples include *Swarna Bhasma*, *Abhraka Bhasma*, *Lauha Bhasma* and *Yashada Bhasma*. The low-dose principle in *Bhasma* therapy should be understood at three levels: single-dose exposure, course exposure, and cumulative exposure over the entire period of administration.

Suchikabharana Rasa: *Suchikabharana Rasa* provides a historically distinctive example of an extremely small-dose, route-specific preparation in *Rasashastra*. Classical descriptions associate needle-related administration with potent substances and emergency therapeutic contexts. The significance lies primarily in the principle of dose minimization combined with route optimization [12].

***Swarna Bhasma* and Non-Linear Dose-Response:** Modern experimental research has investigated the biological effects and physicochemical characteristics of *Swarna Bhasma*. Some studies demonstrate nanoscale crystallites or particles together with larger aggregates. One characterization study reported mean particle diameters of approximately 669–717 nm by dynamic light scattering, while X-ray diffraction estimated gold crystallite size at approximately 28 nm [10]. Other research has described *Swarna Bhasma* as consisting of larger aggregates containing smaller nanoparticles [11]. Studies reporting concentration-dependent effects at 2.5, 5 and 10 µg/mL demonstrate the principle that biological responses may be non-linear and concentration-dependent, though these findings cannot be directly translated into human therapeutic dosing.

Pratimarsha Nasya*, *Matra Basti* and *Muhur-Muhur Aushadha Sevana: *Pratimarsha Nasya* is a low-volume form of nasal administration involving *Sneha* administered through the nostrils, commonly described as two drops in each nostril [8]. *Matra Basti* is explicitly characterized by a smaller quantity of *Sneha* than conventional *Basti* procedures, approximately one and a half *Pala* (approximately 72 mL) [9]. *Muhur-Muhur Aushadha Sevana* refers to repeated administration of medicine at relatively short intervals, distributing total exposure into multiple administrations to avoid excessive peak concentration, maintain therapeutic exposure, and potentially improve tolerability.

PHARMACEUTICAL BASIS OF DOSE OPTIMIZATION

***Shodhana*, *Marana*, *Bhavana* and *Kupipakva* Processing:** *Shodhana* constitutes a group of classical pharmaceutical procedures used for the processing and purification of selected raw materials. *Marana* involves repeated processing and incineration to produce *Bhasma*, which can alter crystallinity, oxidation state, particle morphology and elemental associations. Importantly, *Marana* should not be described as universally producing particles of a fixed nanoscale range; particle size differs according to the substance, manufacturing process and analytical technique [10,11]. *Bhavana* involves wet trituration or levigation of a pharmaceutical material with a prescribed liquid medium, potentially influencing particle size, surface area and drug–matrix interactions. The *Kupipakva* method involves specialized pharmaceutical processing of selected *Rasaushadhis*, with formulations often administered in relatively small quantities.

Particle Size, Bioavailability and the Nano-Scale Hypothesis: Modern studies have demonstrated that some *Bhasma* preparations contain nanoscale crystallites or particles. However, "nano" should not be used as a universal descriptor for every *Bhasma*; a preparation may contain nanoparticles, microscale aggregates and other particulate structures simultaneously. Particle size can influence surface area, dissolution, cellular interaction, aggregation and biological distribution, but particle size alone cannot establish therapeutic superiority or safety. The concept of Ayurvedic *Bhasma* as "ancient nanomedicine" should be regarded as a hypothesis requiring formulation-specific scientific validation.

Cumulative Dose: An Understudied Dimension: A major conceptual contribution of Ayurvedic dose theory is the importance of considering not only the quantity administered at one time but also the pattern and duration of administration. For a repeated-dose regimen, cumulative dose equals the sum of all administered doses during the treatment period. A small individual dose cannot automatically be considered safe if repeated administration results in substantial cumulative exposure. This is particularly important for mineral- and metal-containing preparations and highly relevant to modern pharmacovigilance and toxicology.

AYURVEDIC LOW-DOSE THERAPEUTICS VERSUS CONTEMPORARY PSYCHEDELIC MICRODOSING

The comparison between the two systems should be conceptual rather than historical. Contemporary psychedelic microdosing is a relatively specific practice centred primarily on LSD and psilocybin. Ayurvedic low-dose therapeutics, in contrast, is a broad pharmacotherapeutic concept involving different classes of medicines, routes, pharmaceutical processes and individualized dosing principles.

Table 1. Conceptual Comparison of Contemporary Psychedelic Microdosing and Ayurvedic Low-Dose Therapeutics

Parameter	**Contemporary psychedelic microdosing**	**Ayurvedic low-dose therapeutics**
Historical context	Modern pharmacological practice	Embedded within classical pharmacology
Primary substances	Mainly LSD and psilocybin	Herbal, mineral, metal-containing preparations
Dose determination	Often substance-specific	Individualized according to *Matra*, *Agni*, *Bala*, *Prakriti*
Main objective	Subtle psychological/cognitive effects	Therapeutic, preventive and restorative objectives
Administration	Frequently oral	Oral, nasal, rectal and other routes
Pharmaceutical processing	Usually limited	Extensive processing may be central
Evidence base	Increasing controlled research but inconsistent	Classical textual evidence plus emerging experimental/clinical evidence
Historical equivalence	Not established	Should not be described as psychedelic microdosing

DISCUSSION

The present review indicates that Ayurveda contains a multidimensional framework of low-dose therapeutics, but this framework should not be retroactively labelled as "microdosing" in the contemporary psychedelic sense. The strongest conceptual correspondence is provided by *Alpamatra* and *Alpamatropayogitvat*, which recognize that a relatively small quantity of a potent preparation may be therapeutically effective. However, the Ayurvedic framework extends substantially beyond dose reduction.

First, Ayurvedic dose selection is individualized, considering patient characteristics and disease conditions rather than simply being defined as a fixed fraction of a standard dose. Second, dose is connected to pharmaceutical processing; the therapeutic characteristics of *Rasaushadhis* are understood in relation to procedures such as *Shodhana*, *Bhavana* and *Marana*. Third, route optimization is explicitly represented through *Pratimarsha Nasya* and *Matra Basti*. Fourth, fractionated administration represented by *Muhur-Muhur Aushadha Sevana* introduces the concept of distributing drug exposure over time. Fifth, the concept of cumulative exposure deserves particular attention, especially for preparations containing metals or minerals [13, 14, 15].

Comparison with the Contemporary Microdosing Literature: The contemporary microdosing literature remains methodologically heterogeneous. Recent quantitative syntheses found no overall cognitive enhancement and reported a small reduction in cognitive control [1], with adverse effects including increased blood pressure, anxiety and cognitive impairment [4]. Therefore, contemporary microdosing itself should not be presented as an established effective therapy. The scientific value of comparing it with Ayurvedic low-dose therapeutics lies primarily in identifying common research questions concerning dose-response relationships, route optimization, bioavailability, cumulative exposure and individualized dosing.

Dose Is Not the Same as Exposure: A central finding is that dose and exposure are related but distinct variables. A single low dose may produce a low peak concentration, but repeated administration may produce substantial cumulative exposure. A more comprehensive model of therapeutic exposure may be represented as: Therapeutic response = f (dose × bioavailability × route × frequency × duration × patient factors × pharmaceutical characteristics).

Pharmaceutical Processing as a Determinant of Dose: The Ayurvedic emphasis on pharmaceutical processing provides an important translational research opportunity. Rather than assuming that a raw material and its processed product are pharmacologically equivalent, modern research should determine how processing changes elemental composition, oxidation

state, crystallinity, particle size, surface chemistry, solubility, dissolution, pharmacokinetics and toxicity.

Individualized Dose and Precision Medicine: The Ayurvedic concept of individualized dose [16] selection has potential relevance to precision pharmacotherapy. However, Ayurvedic constitutional categories should not automatically be equated with genomic phenotypes. A useful translational model would involve: Ayurvedic phenotype → measurable biological variables → pharmacokinetic characteristics → dose-response relationship → individualized dose.

SAFETY CONSIDERATIONS

The concept of low-dose therapy should never be interpreted as synonymous with "safe therapy." Safety depends upon identity and quality of the medicine, pharmaceutical processing, chemical composition, contamination/adulteration, dose, frequency, duration, cumulative exposure, route, patient characteristics, and interactions with other medicines. This is especially relevant to *Rasaushadhis* and *Bhasma*. The contemporary psychedelic microdosing literature similarly demonstrates that low dose does not eliminate adverse effects. Thus, dose minimization should be studied as a strategy for optimizing therapeutic exposure, not as an assumption of safety.

RESEARCH GAPS AND FUTURE DIRECTIONS

The present conceptual framework identifies several areas requiring systematic research. Standardized dose-response studies should establish minimum effective concentration, therapeutic window and cumulative exposure for individual Ayurvedic formulations. Pharmacokinetic studies should evaluate conventional versus processed preparations, different doses, *Anupanas*, routes, and single versus repeated administration. For *Bhasma* research, particle-size analysis should be accompanied by SEM/TEM, DLS, XRD, elemental analysis and surface chemistry studies. Future clinical studies should report not only daily dose but also treatment duration, total course dose, cumulative dose and exposure-adjusted outcomes. Prospective research should investigate whether Ayurvedic determinants such as *Prakriti*, *Agni* and *Bala* predict pharmacokinetic or pharmacodynamic differences.

PROPOSED FRAMEWORK: AYURVEDIC LOW-DOSE THERAPEUTICS

Based on the literature reviewed, the authors propose the term Ayurvedic Low-Dose Therapeutics (ALDT) as a modern research framework—not as a classical Sanskrit term. ALDT may be conceptualized as the therapeutic use of an individualized and potentially minimal effective quantity of a medicinal preparation, optimized through pharmaceutical processing, route, vehicle, timing, frequency and duration, while accounting for cumulative exposure and patient-specific factors. The framework consists of five interacting domains: Dose Minimization (*Alpamatra* → *Alpamatropayogitvat*); Individualization (*Prakriti*, *Agni*, *Bala*, *Vaya*, disease status); Pharmaceutical Optimization (*Shodhana*, *Marana*, *Bhavana*, *Kupipakva*); Delivery Optimization (oral, nasal, rectal, other route-specific administration); and Exposure Management (single dose, frequency, duration, cumulative dose).

LIMITATIONS

Several limitations should be acknowledged. The present review is conceptual and narrative rather than systematic. Ayurvedic classical texts were composed in historical contexts that differ substantially from contemporary biomedical pharmacology. Evidence concerning *Bhasma* is heterogeneous, with particle size, elemental composition and biological behaviour varying among preparations. Experimental dose-response findings cannot be directly translated into human therapeutic dosing without appropriate pharmacokinetic and clinical studies. Finally, low-dose administration should not be interpreted as proof of safety or efficacy.

CONCLUSION

Ayurveda does not contain a classical therapeutic doctrine identical to contemporary psychedelic microdosing. Nevertheless, its pharmacological literature contains a sophisticated and multidimensional approach to low-dose therapeutics. The principles of *Alpamatra* and *Alpamatropayogitvat* emphasize therapeutic effectiveness with relatively small quantities. Individualized *Matra* incorporates patient-, drug- and disease-specific determinants. *Muhur-Muhur Aushadha Sevana* provides a model of fractionated administration, while *Pratimarsha Nasya* and *Matra Basti* illustrate route-specific dose optimization. *Rasaushadhis* and *Bhasmas* further demonstrate the relationship between pharmaceutical processing and the administration of relatively small quantities.

Modern research provides preliminary scientific avenues through which these principles can be investigated. Selected *Bhasma* preparations demonstrate nanoscale crystallites or particles together with larger aggregates, suggesting that pharmaceutical processing may generate complex particulate systems. However, such findings are formulation-specific and do not justify the universal characterization of *Bhasma* as nanomedicine. Similarly, contemporary psychedelic microdosing remains an emerging field rather than an established therapeutic modality, with recent meta-analytic evidence not demonstrating overall cognitive enhancement.

The principal translational value of Ayurveda lies not in the claim that it "invented microdosing," but in its broader conceptualization of dose, individualization, pharmaceutical processing, route, timing, fractionation and cumulative exposure. These principles provide a potentially valuable framework for modern investigation of individualized low-dose therapeutics. Future research should prioritize standardized pharmaceutical characterization, pharmacokinetics, dose-response studies, cumulative-exposure assessment, toxicology, route-specific delivery and prospective clinical validation.

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