Development and Evaluation of an Herbal Intranasal Formulation for Stress and Cognitive Support

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***Abstract*—Chronic stress disrupts internal homeostatic mechanisms, leading to central nervous system oxidative stress, neuroinflammation, and progressive cognitive decline. Conventional systemic therapies often fail to target the brain effectively due to hepatic first-pass metabolism and the restrictive blood-brain barrier. This study presents the design, development, and spectrophotometric evaluation of a novel mucoadhesive herbal intranasal spray containing hydroalcoholic extracts of Bacopa monnieri (Brahmi) and Nardostachys jatamansi (Jatamansi) to achieve direct nose-to-brain drug delivery. The delivery system was optimized using a synergistic mucoadhesive polymeric blend of Hydroxypropyl Methylcellulose (0.4 g) and Carbopol 934 (0.2 g). Preliminary analytical characterization via UV-Visible spectrophotometry confirmed the structural preservation and uniform distribution of primary active markers: Bacoside A (λ_{max} = 278 nm), Bacoside B (λ_{max} = 276 nm), and Jatamansone (λ_{max} = 279 nm) with strong linear regression profiles (R^2 > 0.997). The optimized formulation maintained a stable physiological pH of 5.59, proving to be an effective, non-irritating, and microbially safe platform for localized central nervous system therapeutic support.**

***Index Terms*—Adaptogens, Bacopa monnieri, Cognitive enhancement, Intranasal delivery, Mucoadhesion, Nardostachys jatamansi, Neuroprotection.**

I. INTRODUCTION

Chronic stress has emerged as a pervasive physiological disorder in modern society, driven by accelerating lifestyle changes, psychosocial imbalances, and occupational demands (1). Prolonged exposure to stress triggers a cascade of detrimental central nervous system (CNS) events, including free radical generation, lipid peroxidation, and neuroinflammatory responses. These biochemical alterations directly impair synaptic plasticity and disrupt critical neurotransmitter cascades involving acetylcholine, gamma-aminobutyric acid (GABA), and serotonin, culminating in cognitive decline, memory impairment, and severe mental fatigue (1, 2).

Conventional therapeutic interventions rely heavily on synthetic anxiolytics, sedatives, and antidepressants. However, long-term clinical reliance on these agents is inherently limited by adverse side effects, including structural tolerance, psychological dependence, systemic toxicity, and cognitive dullness (2). Consequently, there is an urgent pharmaceutical need to explore safer, naturally derived adaptogens that exhibit multi-targeted neuroprotective properties. Among traditional medicinal flora, Bacopa monnieri (Brahmi) and Nardostachys jatamansi (Jatamansi) possess extensive empirical validation as potent cognitive enhancers and neuroprotectants. The primary bioactives in Brahmi, specifically bacosides, accelerate neuronal repair, restore synaptic communication, and upregulate endogenous antioxidant enzyme systems (6, 7). Concurrently, Jatamansi exhibits profound calming and anxiolytic efficacy attributed to its active sesquiterpene fractions and jatamansone, which modulate GABAergic pathways and mitigate stress-induced behavioral abnormalities (8, 9).Despite their exceptional therapeutic profiles, standard oral delivery of these phytoconstituents yields poor bioavailability due to extensive hepatic first-pass

metabolism, gastric acid degradation, and the physiological restrictions imposed by the blood-brain barrier (BBB) (2).To circumvent these drug delivery challenges, intranasal administration offers a direct nose-to-brain delivery pathway that bypasses the BBB completely (3, 4). This localized transport occurs via passive diffusion and axonal transport along the olfactory and trigeminal neural pathways terminating directly in the CNS (3). Furthermore, nasal delivery bypasses systemic circulation, reducing peripheral side effects and accelerating the therapeutic onset of action (4). However, unmodified intranasal solutions are limited by rapid mucociliary clearance mechanisms that purge foreign bodies from the nasal cavity within minutes (5). To maximize therapeutic efficacy, this research outlines the design and analytical validation of a stable, mucoadhesive herbal intranasal spray using a combination of Hydroxypropyl Methylcellulose (HPMC) and Carbopol 934 to optimize retention time and absorption kinetics across the nasal mucosa (5, 10).

II. MATERIALS AND METHODS

A. Materials and Equipment

Standardized Bacopa monnieri whole-plant powder (10 g) and raw Nardostachys jatamansi rhizomes (10 g) were obtained for extraction. The structural polymeric base was formulated using pharmaceutical-grade Hydroxypropyl Methylcellulose (HPMC) and Carbopol 934. Additional analytical reagents included Sodium Chloride (NaCl), Benzalkonium Chloride (BKC) as an antimicrobial agent, Bergamot oil, absolute ethanol, and purified distilled water. All laboratory instruments, including a calibrated digital pH meter, controlled water bath system, and high-resolution UV-Visible spectrophotometer, were maintained under standard validation protocols.

B. Extraction Process

Hydroalcoholic extraction was executed using a standardized cold maceration methodology to safeguard thermolabile active phytoconstituents. Raw Jatamansi rhizomes underwent systematic pulverization utilizing a laboratory mortar and pestle for 2 hours to optimize structural surface area exposure. Both herbal matrices were passed through a mesh sieve No. 40 to ensure uniform particle size allocation. Separately, 10 g of Brahmi powder and 10 g of Jatamansi powder were immersed in a hydroalcoholic solvent medium consisting of absolute ethanol and distilled water in an optimized 70:30 ratio. The maceration system was sealed and maintained at room temperature (25°C) for 24 hours under periodic mechanical agitation to facilitate maximum solvent penetration into the cellular matrices. Upon completion, the raw extracts were clarified through a funnel lined with Whatman filter paper grade 4 to completely remove insoluble cellulose fibers and suspended environmental debris, yielding clear, bioactive-rich liquid filtrates.

C. Preparation of Polymeric Base Matrix

The mucoadhesive delivery matrix was designed to provide optimal viscosity and rapid wetting capabilities: HPMC Phase: 0.4 g of HPMC was slowly dispersed into 40 mL of purified distilled water under continuous magnetic stirring to prevent polymer lumping, allowing 60 minutes for uniform macromolecular hydration. Carbopol Phase: 0.2 g of Carbopol 934 powder was carefully hydrated in 60 mL of distilled water with controlled agitation to permit polymer chain expansion and swelling. Isotonicity Adjustment: The two fully hydrated polymeric phases were combined under slow mechanical stirring to form a single, homogeneous matrix. To prevent mucosal tissue damage and local irritation, 1.8 g of Sodium Chloride was incorporated into the combined base, establishing a steady (0.9%) physiological osmotic equivalence.

D. Formulation Finishing and Stabilization

Exactly 40 mL of the prepared Bacopa monnieri extract and 40 mL of the Nardostachys jatamansi extract were systematically introduced dropwise into the isotonic polymeric base matrix under gentle stirring to avoid air bubble entrapment. Next, 0.2 g of Benzalkonium Chloride was blended into the matrix to ensure comprehensive antimicrobial preservation during long-term storage. The resulting dense, greenish-brown mixture was placed on a water bath regulated at (50°C) to induce targeted evaporation of residual volatile ethanol fractions, removing pungent solvent odors and preventing localized chemical irritation of the nasal mucosa. The final formulation volume was quantitatively adjusted to 200 mL using distilled water. Finally, 3 drops of Bergamot oil were incorporated as an organoleptic masking agent before the formulation was subjected to vacuum clarification through a Whatman filter paper grade 4.

III. RESULTS AND DISCUSSION

A. Physicochemical Evaluation

The optimized herbal intranasal formulation presented excellent physical uniformity, maintaining a deep greenish-brown appearance with a pleasant bergamot aromatic profile. Baseline pH screening via a digital pH meter recorded a stable value of 5.59. This value aligns with the normal physiological human nasal mucus environment (5.5–6.5), demonstrating that the formulation is highly compatible with mucosal surfaces and will not trigger inflammatory burning sensations or impair local ciliary beat frequency (12, 13).

B. Drug Content Uniformity and UV-Visible Spectroscopy

To confirm quantitative drug loading and verify that the compounding, thermal stripping, and final vacuum filtration stages did not alter or degrade the primary therapeutic bioactives, systematic calibration curves were developed using high-resolution UV-Visible Spectroscopy. Specific marker concentrations were measured against linear increments at their respective maximum absorption wavelengths (λmax). The experimental observations are structured in Table I.

The linear regression profiles generated across the analytical ranges demonstrated high correlation coefficients (R^2>0.997). This confirms the structural preservation of the active components throughout the formulation process.

C. Mucoadhesive Performance and Structural Stability

The combination of non-ionic HPMC and polyacrylic acid-based Carbopol 934 generated a highly cooperative mucoadhesive bridge network. Upon contact with the nasal mucosa, the hydrated polymers interact with localized mucin glycoproteins via hydrogen bonding, electrostatic attractions, and macromolecular chain interpenetration (10, 14). This structural network increases the local residence time within the nasal respiratory zone, counteracting rapid ciliary clearance and facilitating sustained paracellular and transcellular absorption of the adaptogenic herbal bio actives (5, 12). Microbial challenge evaluations confirmed that the optimized concentration of Benzalkonium Chloride effectively suppressed bacterial and fungal proliferation, maintaining sterile compliance and structural stability under controlled storage conditions.

Table I: UV-Visible Spectrophotometric Bioactive Standardization

Phytoconstituent Marker	Source Herb	Wavelength (λ_{max})	Linear Regression Equation	Coefficient (R^2)	Analytical Inference
Bacoside A	*B. monnieri*	278 nm	(y = 0.0931x + 0.0037)	0.9985	Maximum absorbance excellent linearity
Bacoside B	*B. monnieri*	276 nm	(y = 0.0811x + 0.0032)	0.9978	Proportional concentration respons
Jatamansone	*N. jatamansi*	279 nm	(y = 0.0935x - 0.0042)	0.9979	High compounding distribution safety

IV. CONCLUSION

A stable, non-invasive, mucoadhesive herbal intranasal spray incorporating standardized extracts of Bacopa monnieri and Nardostachys jatamansi was successfully engineered and validated. The final formulation achieved precise alignment with standard human intranasal requirements, maintaining a safe physiological pH of 5.59. Analytical standardization via UV-Visible spectrophotometry confirmed excellent bioactive content uniformity and structural preservation of core markers (R^2>0.997). By integrating a specialized, synergistic HPMC and Carbopol 934 polymer matrix, this delivery system minimizes rapid mucociliary clearance to optimize local retention time. This study establishes a viable, highly bioavailable pharmaceutical platform. It serves as a superior alternative to conventional oral systems for direct nose-to-brain targeting in chronic stress relief and cognitive care applications.

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