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FORMULATION OF HERBAL NASAL FORMULATION USING EXTRACTS OF *ADINA CORDIFOLIA* LEAVES *AND SIDA SPINOSA* LEAVES

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ABSTRACT

Nasal formulations represent a vital avenue for drug delivery, offering the potential for targeted and efficient delivery of therapeutic compounds. This study explores the development and formulation of a novel herbal nasal formulation utilizing extracts derived from Adina cordifolia leaves and Sida spinosa leaves, known for their remarkable medicinal properties. The objective of this research is to harness the therapeutic potential of these herbal extracts for various nasal applications, such as alleviating nasal congestion, managing allergic rhinitis, or treating sinusitis. The resulting herbal nasal formulation is subjected to rigorous quality control measures, including stability testing and microbiological evaluation, to ensure safety, efficacy, and compliance with regulatory standards. This research aims to contribute to the growing body of knowledge on herbal-based nasal formulations and their potential benefits in enhancing drug delivery and therapeutic outcomes. As the study bridges traditional herbal wisdom with modern pharmaceutical science, it underscores the significance of nature-derived therapies in addressing common nasal ailments. The findings from this investigation have the potential to pave the way for innovative herbal nasal products, offering a safe and natural approach to nasal health and wellness. Further clinical trials and evaluations may be warranted to validate the efficacy and safety of this herbal nasal formulation for specific nasal conditions.

Keywords: Nasal, Microbiological, Herbal, Formulation, Herbal, Medicinal

INTRODUCTION

The respiratory system, of which the nose is a part, receives air mostly via the nasal cavity. The scent receptors are located on the periphery of the nose. The lower two-thirds of the nasal mucosa make up the respiratory region, whereas the superior third makes up the olfactory area and houses the peripheral organ of smell (Martini, 2004; Moore and Dalley, 2006).

Because of the abundant vascularity of the nasal membrane and the simplicity of intranasal administration, the nasal route of administration is a practical and reliable approach for both the local and systemic delivery of medications. In recent times, the nasal mucosa has been studied as a potential route of administration for improved speed and safety of medication absorption. The nasal route of administration is desirable for many medications, including proteins and peptides, due to the nasal membrane's rich vascular environment and high drug

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permeability. Here in addition, medication absorption in the olfactive area of the nose allows a pharmaceutical molecule to reach the brain. Nasal administration of vaccinations is an additional very contentious usage regarding efficacy and patient acceptability. Historically, people have been interested in using the nasal route as a means of administering medication. The Ayurvedic school of Indian medicine recognises nasal therapy, also known as "Nasaya Karma," as a valid kind of treatment.

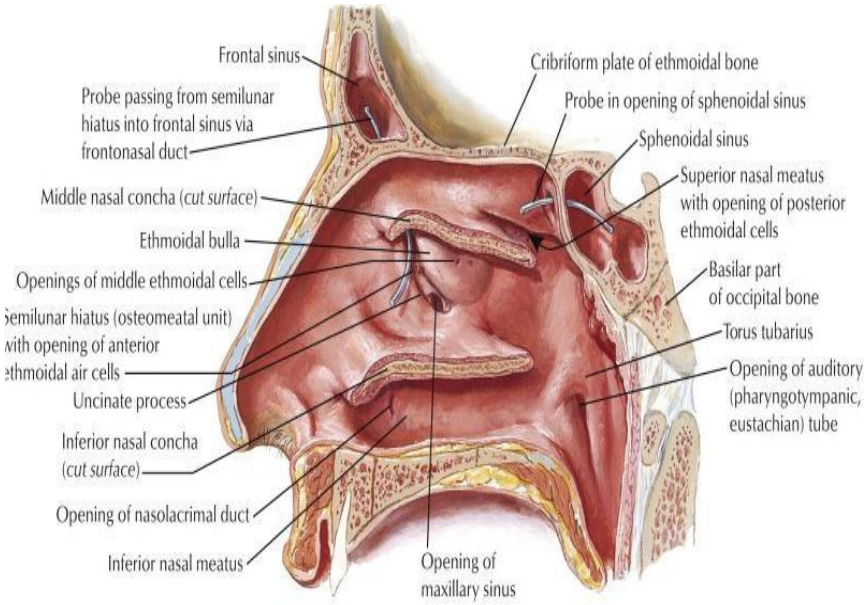

Figure 1.1 The nasal cavity (Netter, 2003)

Pseudostratified columnar epithelial tissue (the typical metabolic process epithelial tissue lining 80-90% of the nasal cavity) is found posteriorly, where basal, columnar, and mucus-secreting glands are located. The vestibules (those receptive the face through the nostrils) are lined with skin (keratinized, dynamical to non-keratinized, stratified squamous epithelium), where Although they are not ciliated at the front end, many columnar cells develop cilia thereafter and these microvilli help to expand the body cavity. The nasal secretions that lining the airways are produced by liquid body substance and mucoserous submucosal glands, as well as goblet cells. The first inborn psychoanalytic mechanism is called mucociliary clearance (MC), and its primary components are mucous secretion and cilia. Due to its large surface area, the nasal cavity is an ideal site for drug delivery through the nasal route. However, the front half of the cavity (the vestibule) is keratinized with oleaginous glands, making it a poor site for drug porosity, especially in the vicinity of the nostrils. Still, mc is involved in the regular metastasis of epithelial tissue, whereby the secretory lining is pushed downward by beating cilia, along with any deposited material, into the tubular cavity, where it may be encased or expectorated. This leads to insufficient bioavailability and/or efficacy as a result of insufficient contact (residence) time for the medication at the absorption web site (for generally delivered pharmaceuticals) or the area of action (for regionally acting drugs).

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Factors affecting nasal formulation design

a) Formulation pH

pH of a nasal formulation is fundamental for the following motive:

- Keep away from infection of the nasal mucosa;
- Allow die drug to be in unionized form for absorption;
- Avoid the boom of pathogenic microorganism in die nasal passage;
- Maintain the functionality of excipients inclusive of preservatives; and
- Maintain everyday physiological ciliary motion.

Nasal discharge contains lysozyme, which, when exposed to bacteria at a low enough pH, may kill them. When exposed to an alkaline environment, lysozyme is rendered ineffective, leaving nasal tissue vulnerable to microbial infection. Therefore, it is very advantageous to adopt the formulation at a pH of 4.5 to 6.5, taking into account the drug's physicochemical qualities as tablets are enveloped in the un-ionized state.

B) Buffer Capacity:

Nasal formulations are often given in 100 pL doses, with the normal range being 25–200 pL. As a result, the pH of the administered dosage may be influenced by nasal secretions. This may affect how much of the un-ionized medication is available for absorption. As a result, keeping the pH stable may need a formula with sufficient buffering capacity.

Osmolality:

Tonicity of nasal formulation should allow for drug absorption. In response to hypertonic solutions, epithelial cell contraction has been reported. Ciliary movement is also slowed or halted by hypertonic saline solutions. A hypertonic solution mimics the effects of low pH.

C) Gelling/Viscofying Agents or Gel-Forming Carriers:

A method that might extend the curative impact of the nasal environment may be suggested by the growing reaction on viscosity. Evidence shown indicated a drug carrier along with hydroxypropyl cellulose improved the absorption of low molecular weight capsules but had no effect on the absorption of high molecular weight peptides. From a protective (nasal irritancy) standpoint, it is recommended that you employ a mixture.

D) Solubilizers:

The medication's poor aqueous solubility remains an issue for nasal drug administration. Glycols, alcohol in tiny amounts, Transcutol (diethylene glycol monoethyl ether), medium-chain glycerides, and Labrasol (saturated polyglycolyzed C8- Cio glyceride) are all examples

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of conventional solvents or co-solvents that might be employed to improve the solubility of pharmaceuticals. Surfactants and cyclodextrins like HP-B-Cyclodextrin, which act as a biocompatible solubilizer and stabiliser when combined with lipophilic absorption enhancers, are two of the former options. Their effect on nasal irritability must be evaluated under these conditions.

E) Preservatives:

Nasal preparations often use aqueous bases and need preservatives to stop the development of bacteria. Common preservatives in nasal formulations include parabens, benzalkonium chloride, phenyl ethyl alcohol, ethylenediaminetetraacetic acid, and benzoyl alcohol.

F) Antioxidants:

Sodium metabisulfite, sodium bisulfite, butylated hydroxytoluene, and tocopherol are some of the most often utilised antioxidants to prevent medication oxidation to an acceptable level. Antioxidants often do not affect medication absorption or cause nasal discomfort. The components upgrade programmes need to think about the chemical/physical interactions between antioxidants and preservatives in tablets, excipients, production equipment, and packaging additives.

G) Humectants:

Mucous membrane crusting and air exposure has been linked several times to a wide variety of allergy and chronic illnesses. several excipients, including several preservatives and antioxidants, may cause nasal irritation, particularly when used in larger doses. Maintaining an acceptable level of intranasal moisture is critical for reversing dehydration. As a result, humectants may be utilised everywhere a gel is needed, even in nasal solutions. Common sugar alcohols include glycerine, sorbitol, and mannitol.

H) Role of Absorption Enhancers:

When it becomes challenging for a nasal medication to achieve the desired absorption profile, absorption enhancers are recommended. The choice of absorption enhancers relies heavily on the influence of authoritarian corporations on the physiological functioning of the nasal passages. Drugs that lack lipophilicity, have a large molecular size, and are difficult for enzymes like amino-peptidases to break down may benefit from absorption enhancers.

I) Effect of Pathological Condition

Nasal absorption and the mucociliary release mechanism may be affected by intranasal diseases such as allergic rhinitis, infections, or previous nasal surgery. The effectiveness of an intranasal therapy is often diminished during the typical bloodless. When diabetes has been established, there is a decrease in nasal clearance. Drug absorption may also be affected by nasal pathology, which can normalise mucosal pH.

MATERIALS AND METHODS

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Table 1: Effect of hydro-alcoholic extract of *Adina cordifolia leaves and Sida spinosa leaves* (burm fruit) on BP in sub acute toxicity.

Weeks	**Control (1%CMC)**		***Adina cordifolia leaves and Sida spinosa leaves*(burm fruit)**			
	SBP	**DBP**	**1 SBP**	**DBP**	**2 SBP**	**DBP**
Male 0	448.11 ± 1.84	89.10± 1.80	414.14 ± 1.17	87.71± 1.14	414.4 ± 1.94	91.7± 1.14
1	419.74 ± 4.18	87.84± 4.44	416.18 ± 6.71	79.11± 4.48	416.7 ± 1.18	94.7± 1.34
2	436.73 ± 3.84	407.74± 3.76	448.76 ± 8.94	96.87± 6.48	436.9 ± 4.48	89.4± 3.64
3	436.84 ± 4.89	97.93± 9.87	436.84 ± 3.78	96.84± 3.84	438.6 ± 3.34	96.3± 4.37
4	438.84 ± 3.38	436.44± 3.86	434.70 ± 4.43	404.74± 4.37	438.4 ± 4.34	403.4± 6.44
Female 0	434.33 ± 3.44	94.80± 3.94	430.46 ± 3.39	86.84± 4.84	430.8 ± 3.44	84.38± 4.94
1	430.83 ± 4.74	86.84± 4.44	479.74 ± 3.79	86.43± 3.78	444.4 ± 4.37	83.43± 4.64
2	446.84 ± 6.34	90.40± 3.44	434.63 ± 4.44	86.46± 8.44	407.7 ± 6.07	73.84± 3.94
3	408.70 ± 4.34	84.40± 4.34	44.44 ± 4.64	7.44± 6.44	440.8 ± 4.44	74.33± 4.38

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4	404.40 ± 6.34	73.43± 6.49	403.34 ± 4.67	74.37± 3.97	404.3 ± 4.34	83.63± 4.37

Data are expressed as mean S.E.M. $n = 5$, no statistical difference between control and *test doses* SBP: systolic blood pressure and DBP: diastolic blood pressure.

Table 2Effect of hydro-alcoholic extract of *Adina cordifolia leaves andSida spinosa leaves* on BP in sub-acute toxicity

	Female			**Male**		
	Control	***Adina cordifolia leaves and Sida spinosa leaves* (g/kg)**		**Control**	***Adina cordifolia leaves and Sida spinosa leaves* (g/kg)**	
	(1% CMC)	**1**	**2**	**(1% CMC)**	**1**	**2**
Hb[a]	44.00 ± 0.40	44.40 ± 0.47	44.60 ± 0.39	44.04 ± 4.04	47.47 ± 0.94	47.70±0.47
Ht[b]	47.40 ± 4.74	49.74 ± 4.97	47.73 ± 4.37	46.46 ± 3.46	43.66 ± 4.64	46.46±3.44
RBC[c]	06.63 ± 0.63	09.46 ± 0.46	06.90 ± 0.60	06.60 ± 0.36	09.36 ± 0.44	9.94±4.03
WBC[d]	04.63 ± 4.96	03.96 ± 0.44	06.46 ± 3.46	06.34 ± 4.44	06.40 ± 3.33	6.40±0.99
Lymp.[e]	63.60 ± 4.64	66.00 ± 4.06	73.00 ± 3.67	79.70 ± 4.44	76.74 ± 3.43	76.74±4.74
Eosino.[f]	00.60 ± 0.20	02.00 ± 0.22	03.00 ± 0.72	00.70 ± 0.37	02.72 ± 2.03	0.32±0.32
Monoc.[g]	03.20 ± 2.27	02.32 ± 0.32	03.32 ± 2.03	02.00 ± 2.37	03.32 ± 2.33	3.00±0.72
PLT.[h]	943.70 ± 96.37	4343.00 ± 63.74	4007.34 ± 93.40	906.37 ± 404.33	934.36 ± 404.74	4077.37±37.37
MCV[i]	44.60 ± 3.66	44.40 ± 0.77	63.40 ± 3.37	44.30 ± 4.34	47.00 ± 3.37	44.00±4.33
MCH[j]	47.36 ± 0.97	46.47 ± 0.34	49.37 ± 4.33	46.74 ± 0.47	47.47 ± 0.43	47.40±0.97
MCHC[k]	34.03 ± 0.30	30.33 ± 0.37	30.74 ± 0.40	30.43 ± 0.37	30.03 ± 0.33	37.67±0.63
Seg.[l]	43.70 ± 0.73	43.00 ± 0.73	44.00 ± 3.43	43.30 ± 6.49	47.34 ± 3.66	34.40±4.47

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Data are expressed as mean ± S.E.M., $n = 5$. No statistical difference between controland *Adina cordifolia leaves and Sida spinosa leaves* ($P > 0.05$).

CONCLUSION

Herbal remedies complement conventional medical treatment for a wide range of conditions. Therefore, in light of the existing medical system, these natural medications need in-depth investigation. Herbal medicines have a place in treatment alongside manmade pharmaceuticals. The availability of synthetic antioxidants is limited owing to their harmful side effects, hence there has been a surge of interest in identifying natural compounds (i.e. antioxidants) contained in foods or medicinal plants to replace them. Humans are beginning to recognise the value of natural antioxidants owing to their ability to reduce oxidative stress and prevent macromolecular oxidation, hence lowering the risk of cardiovascular and degenerative illnesses. Because they include many plant medicines with different pharmacological effects, herbal formulation theories contain the synergistic, potentiative substances themselves. To achieve optimal treatment effectiveness with minimal adverse effects, pharmacological activities are performed in a coordinated fashion. The leaves of Adina cordifolia and Sida spinosa were chosen as possible plants on the basis of the aforementioned assumptions. For this research, we chose two herbal medications made from the leaves of two different plants: Adina cordifolia and Sida spinosa. Ayurvedic texts provide them for the sake of health enhancement. Adina cordifolia leaves have anti-inflammatory and antioxidant properties, whereas Sida spinosa leaves have anti-bacterial and anti-microbial properties. Hepatoprotective, anti-inflammatory, antibacterial, and hypoglycemic actions are only some of the purported biological effects of these plants.

A 50% hydroalcoholic solution was used to extract the oils from the leaves of Adina cordifolia and Sida spinosa. Adina cordifolia leaf extract had a 58% weight-to-weight yield. Sida spinosa leaves had a 42% w/w yield. Adina cordifolia and Sida spinosa leaf extracts were tested chemically to determine their phytoconstituents using phytochemica;l screening. In this investigation, 3 doses at 1 g/kg/day did not exhibit toxicity consequences, in accordance with the sub acute toxicity guiding concept (OECD, 2001a). Since human research demonstrates the usage of an excessive dosage level according to the guideline (OECD, 2001a), high-dose Adina cordifolia leaf and Sida spinosa leaf extracts combinations were incorporated inside the subacute studies. To evaluate dose-related hazardous effects, a reduced dosage of 1 g/kg-day was employed. Sub acute toxicity tests indicated that the 50% hydroalcoholic extract of neither produced any noticeable changes in male or female mice, as evidenced by the lack of adverse signs and symptoms, no changes in water/food consumption, and no weight gain. No animals died before their planned euthanasia, and no obvious pathological changes were discovered in the internal organs. This research concluded that the hydro-alcoholic extract of the combined plants was non-toxic to experimental animals when tested for both acute and subacute toxicity.

References

1. Ajuogu, P. K., Mgbere, O. O., Bila, D. S., & McFarlane, J. R. (2019). Hormonal changes, semen quality and variance in reproductive activity outcomes of post pubertal rabbits fed Adina cordifolia Lam. leaf powder. Journal of ethnopharmacology, 233, 80-86

2. Amaglo, N. K., Bennett, R. N., Curto, R. B. L., Rosa, E. A., Turco, V. L., Giuffrida, A & Timpo,

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, Nov 2022

G. M. (2010). Profiling selected phytochemicals and nutrients in different tissues of the multipurpose tree Adina cordifolia L., grown in Ghana. Food Chemistry, 122(4), 1047-1054.

3. Annapurna, D., & Rathore, T. S. (2010). Direct adventitious shoot induction and plant regeneration of Sida spinosa leaves Burm F. Plant Cell, Tissue and Organ Culture (PCTOC), 101(3), 269-277.

4. Bachert, C., Krysko, O., Gevaert, P., Berings, M., Perez-Novo, C., & Van Crombruggen, K. (2015). Nasal Immunity, Rhinitis, and Rhinosinusitis. In Mucosal Immunology (pp. 1899-1921). Academic Press.

5. Cáceres A, Saravia A, Rizzo S, Zabala L, De Leon E, Nave F. (1992) Pharmacologie properties of Adina cordifolia. 2: Screening for antispasmodic, antiinflammatory and diuretic activity. Journal of ethnopharmacology. 1;36(3):233-7.

6. Chin, C. Y., Jalil, J., Ng, P. Y., & Ng, S. F. (2018). Development and formulation of Adina cordifolia standardised leaf extract film dressing for wound healing application. Journal of ethnopharmacology, 212, 188-199.

7. D'souza, J., Kulkarni, A.R., (1993). Comparative studies on nutritive values of tender foliage of seedlings and mature plants of Adina cordifolia Lam. Journal of Economic and Taxonomic Botany 17, 479–485.

8. Makkar, H. P. S., & Becker, K. (1997). Nutrients and antiquality factors in different morphological parts of the *Adina cordifolia* tree. *The Journal of Agricultural Science*, *128*(3), 311-322.

9. Menaka M, Pandey VP (2014). Formulation development and evaluation of cinnarizine nasal spray. International Journal of Pharma Researxh and Health Sciences.;2(4):339-46

10. Mitra R (1995) 'Vidanga' (*Sida spinosa leaves*) – an Ayurvedic drug can help family planning. Applied Botany Abstracts, National Botanical Research Institute, Lucknow, India