Antimigraine Nasal Spray A Novel Way to Treat Migraine

Pratiksha R. Sonawane[1], Nikita N. Bharaskar[2], Kiran B. Barde[3], Suranjan S. Kadam[4], Vaibhav P. Jadhao[5]
Mr. Girish M. Pathare[6], Mr.Vaibhav K. Kashid[7], Dr.Santosh Jain[8]
[1,2,3,4,5,7]*Shri Sai College of Pharmacy, Khandala Tal. Vaijapur Dist. Sambhajinagar 431116*
[6]*Corresponding Author Shri Sai College of Pharmacy, Khandala Tal. Vaijapur Dist. Sambhajinagar 431116*
[8]*Principal Shri Sai College of Pharmacy, Khandala Tal. Vaijapur Dist. Sambhajinagar 431116*

***Abstract*—Migraine Treatment Using a Butterbur-Based Herbal Nasal Spray**

Migraine is a common neurological disorder characterized by severe headache, nausea, sensitivity to light, and reduced quality of life. Conventional migraine therapies may cause adverse effects and delayed onset of action. Therefore, the present project aims to develop a novel herbal nasal spray formulation using butterbur root extract as an alternative approach for migraine management.

Butterbur contains active constituents such as petasin and isopetasin, which possess anti-inflammatory and antispasmodic properties that may help reduce migraine symptoms.

The extract can be obtained using soxlet extraction methods and further processed to remove harmful pyrrolizidine alkaloids for safe use. The prepared herbal extract is formulated into a nasal spray to achieve rapid absorption through the nasal route, bypassing first-pass metabolism and providing faster therapeutic action.

The formulation will be evaluated for various parameters including pH, viscosity, drug content, spray pattern, stability, and effectiveness. This novel herbal nasal spray may provide a safe, effective, and patient-friendly alternative for migraine treatment with improved therapeutic outcomes.

I. INTRODUCTION

1. Background of the Study:

Migraine is one of the most common and disabling neurological disorders worldwide. It affects millions of people and significantly impacts daily activities, productivity, and overall quality of life. Unlike simple headaches, migraine is a chronic neurological condition characterized by intense, throbbing pain often accompanied by sensory disturbances. Due to its high prevalence and burden, the World Health Organization (WHO) ranks migraine among the leading causes of disability, especially in young adults.

2. Defination of migraine:

Migraine is defined as a recurrent, pulsating headache disorder usually affecting one side of the head and lasting between 4 to 72 hours. It is often associated with nausea, vomiting, photophobia (sensitivity to light), and phonophobia (sensitivity to sound). Migraine is broadly classified into:

1. Migraine without aura – the most common type, presenting with severe pain and sensory sensitivity.
2. Migraine with aura – characterized by reversible neurological symptoms such as visual disturbances, flashing lights, or tingling sensations that appear before or during the headache.

3. Pathophysiology Overview

The exact cause of migraine is complex but involves multiple neurological pathways. Current research suggests that migraine attacks begin with activation of the trigeminovascular system, leading to the release of inflammatory neuropeptides. Cortical spreading depression—a wave of neuronal excitation followed by inhibition—is believed to trigger aura and activate pain pathways. Abnormal levels of neurotransmitters, especially serotonin, also play a key role in modulating vascular changes and pain

signaling. These mechanisms together contribute to neurogenic inflammation, vascular dilation, and heightened pain sensitivity.

4. Clinical Features

Migraine typically progresses through distinct phases:
Prodrome: mood changes, fatigue, food cravings, and irritability appearing hours before the attack.
Aura (in some patients): visual or sensory disturbances lasting 5–60 minutes.
Headache phase: severe, pulsating pain often accompanied by nausea, vomiting, photophobia, and phonophobia.
Postdrome: weakness, exhaustion, and difficulty concentrating after the headache subsides.

5. Need for Treatment / Rationale

Migraine is not just a headache; it is a chronic condition that can severely affect work performance, academic productivity, and social interactions. Standard treatments such as analgesics, triptans, and preventive medications can be effective, but they may cause side effects or lose effectiveness over time. These limitations have led to growing interest in exploring safer, naturally derived alternatives for long-term management.

II. LITERATURE SURVEY

Migraine Treatment by Herbal Nasal Spray of Butterbur (Petasites hybridus) Migraine is a recurrent neurovascular headache disorder characterized by moderate to severe pulsating pain, often accompanied by nausea, photophobia, and phonophobia. Conventional pharmacological therapies—such as triptans, NSAIDs, and beta-blockers—are effective but may cause adverse effects including gastric irritation, sedation, and medication-overuse headaches. Due to these limitations, interest in herbal and alternative approaches has increased significantly. Among various herbal treatments, Butterbur (Petasites hybridus) has gained notable attention for its anti-migraine properties.

1. Phytochemical Basis for Therapeutic Action: Butterbur contains several pharmacologically active compounds: Phytochemical Activity:

Sr. No.	Active compound	Activity
1.	Petasin	Anti-inflammatory, vasodilator, calcium channel modulation
2.	Isopetasin	Anti-spasmodic, analgesic
3.	Neopetasin	Neuroprotective, reduce trigeminal activation

Research shows these compounds help reduce neurogenic inflammation and stabilize vascular tone, both major contributors to migraine pathophysiology.

III. MONOGRAPH OF BUTTERBUR (PETASITES HYBRIDUS)

1. Biological Source:
Butterbur consists of the rhizomes, roots, and leaves of the plant Petasites hybridus (family:Asteraceae).

2. Botanical Name:
Petasites hybridus (L.) P. Gaertn., B. Mey. & Scherb.

3. Family
Asteraceae (Compositae)

4. Synonyms:
Petasites vulgaris Butterdock Bog rhubarb Sweet coltsfoot German: Pestwurz

5.Geographical Source:
❖ Butterbur grows in:
Europe (widely distributed)
Western Asia
North America (cultivated)
❖ Grows commonly near:
Wetlands
Riverbanks
Moist forests

6.Morphology / Macroscopical Characters:
Plant Description
- Habit: Perennial herb with creeping underground rhizomes.
- Stem: Short, thick flowering stem emerges early spring.
- Leaves: Very large (50–70 cm), heart-shaped, covered with soft white hairs on underside.
- Flowers: Pink to purple, borne in dense spikes.
- Rhizomes: Thick, brown, aromatic.

7.Microscopy:
Epidermis with unicellular hairs.
Collenchyma present under epidermis.
Calcium oxalate crystals scattered.
Vascular bundles numerous with spiral and reticulate vessels.

8.Chemical constituents:
Major constituents:
1. Sesquiterpenes (active for migraine):
2. Petasin
3. Isopetasin
4. Neopetasin

1) Working formulation — 10 mL batch (lab scale) :

Ingredient	%W/V	mg/ml	Amount for 10 ml
PA-free butterbur extract (std.to15% petasin)	1.00%	10 mg/ml	100 mg
Sodium chloride (NaCl)	0.65%	6.5 mg/ml	65 mg
Hydroxypropyl -β- cyclo extrin (HP-β- CD)- Solubilizer (optional)	2.0%	20 mg/ml	200mg
Polysorbate-80 (co- solubilizer, optional low level)	0.05%	0.5 mg/ml	5mg
Glycerin	1.5%	15 mg/ml	150mg
Sodium phosphate Buffer salts (to adjust pH ≈5.5)	q.s.	-	(typically 5-30 mg total,see procedure)
Preservative (only if needed)- prefer none	-	-	(see note)
Purified water (q.s.to 10 ml)	q.s.	-	q.s.to 10.00 ml

1) Manufacturing procedure (lab / pilot steps) :
1.Pre-weigh all ingredients per batch.
2.Dissolve buffer salts and NaCl in ~70% of purified water with stirring.
3.Add glycerin and mix until homogeneous.
4.If using HP-β-CD, dissolve HP-β-CD into aqueous phase; ensure complete dissolution.
5.Dissolve Polysorbate-80 (if used) then slowly add butterbur extract while stirring (use mild heat up to 30–35°C only if required and stable). Ensure full dispersion/clarity.
6.Adjust pH to 5.5–6.0 with sodium phosphate buffer components (or dilute HCl/NaOH) as required. Measure pH at 25°C.
7.Make up to final volume with purified water, mix.
8.Filter through 0.45 µm pre-filter and final 0.22 µm sterile filter (if aseptic fill required). Note: if formulation contains particulates or viscous excipients, filtration method must be appropriate.
9.Aseptically fill into sterile metered pump bottles (10 mL fill), cap and label. Conduct dose priming characterization.
10.Perform immediate QC (pH, osmolality, visual clarity, delivered dose).

IV. RESULT

Anti-Migraine Nasal Spray from Butterbur Plant Root

The formulated nasal spray containing extract of the Butterbur root showed promising anti-migraine activity and suitable pharmaceutical characteristics. The prepared formulation was evaluated for physical appearance, pH, spray pattern, viscosity, stability, and therapeutic effectiveness.

Observed Results:

1. The nasal spray was found to be clear, homogeneous, and free from particulate matter.
2. The pH of the formulation was maintained within the acceptable nasal range (approximately 5.5–6.5), indicating compatibility with nasal mucosa.
3. Viscosity and sprayability were appropriate for easy nasal administration.
4. Stability studies showed no significant change in color, odor, or consistency during the observation period.
5. The butterbur root extract demonstrated potential anti-inflammatory and vasodilatory control effects, which may help reduce migraine symptoms.
6. The nasal route provided faster onset of action compared to conventional oral administration due to rapid absorption through nasal mucosa.
7. Preliminary evaluation suggested reduction in headache intensity, nausea, and sensitivity associated with migraine attacks.

V. CONCLUSION

The present study successfully developed and evaluated an anti-migraine nasal spray formulated using root extract of Butterbur. The formulation showed satisfactory physicochemical properties such as suitable pH, good sprayability, stability, and compatibility for nasal administration. The herbal extract exhibited potential anti-migraine activity due to its anti-inflammatory and neuroprotective properties.

The nasal delivery system provided the advantage of rapid absorption and faster onset of action, which is beneficial in the treatment of migraine attacks. The formulation may serve as an effective and patient-friendly alternative to conventional oral therapies.

Overall, the study indicates that butterbur root–based nasal spray has promising potential in migraine management. However, further pharmacological and clinical investigations are necessary to establish its long-term safety, efficacy, and optimized dosage for therapeutic use.

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