Intranasal Polyherbal Formulation for Migraine Treatment

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ABSTRACT

Migraine is characterized by attacks of unilateral, throbbing head pain, with sensitivity to movement, visual, auditory, and other afferent inputs. The study outlines the systematic development, evaluation, and outcome of an herbal nasal drop formulation to treat or reduce migraine symptoms. Herbal nasal drops are especially beneficial for migraine patients experiencing nausea or vomiting, where oral routes are less effective. It was planned to utilize the medicinal plants *Xanthium strumarium* and *Portulaca oleracea*, which are recognized for their anti-inflammatory and neuroprotective properties. The formulation process involved the incorporation of appropriate excipients to ensure isotonicity, stability, and patient-friendly viscosity. The nasal drops were evaluated for physicochemical parameters, including pH, particle size, drug content, and impurity levels, ensuring compliance with pharmacopoeial standards. The outcome demonstrated that the herbal nasal drop formulation was successfully developed, met all quality parameters, and showed promising potential for nose-to-brain delivery of anti-migraine agents. This research supports the integration of traditional herbal medicine with modern drug delivery systems to improve the management of neurological disorders like migraine.

The pH distribution across three measurement groups is shown using a boxplot and swarm plot. The boxplot summarizes the data, while the swarm plot highlights individual data points. Minimal variation is observed between groups, supported by ANOVA ($F(2, 9) = 0.063$, $p = 0.94$), indicating no significant difference in mean pH values. This confirms the reproducibility of the pH measurement process across batches.

Keywords: *Xanthium strumarium*, *Portulaca oleracea*, migraine management, intranasal delivery, nose-to-brain transport, nasal pH.

INTRODUCTION

Migraine is a common, disabling brain disorder ranked by the WHO as the most disabling neurological condition and sixth overall [33]. Affecting 15–18% of the global population annually, it occurs three times more often in women and often strikes during peak productive years. Symptoms include unilateral, throbbing pain with sensitivity to light, sound, and movement. Many also experience pre- and post-attack symptoms like fatigue and poor concentration, and about one-third have aura, neurological disturbances that precede or accompany the headache [33]. Traditional medicine offers holistic migraine management through various approaches. Acupuncture may reduce migraine frequency and severity, while herbs like feverfew and butterbur show potential but carry

risks such as liver toxicity. Ayurvedic practices—including herbal remedies, detox therapies, and nasal treatments—are promising but need more scientific support. Other methods like homeopathy, aromatherapy, yoga, meditation, cupping, and dietary changes may help relieve symptoms. Combined with modern care, these therapies can improve quality of life, though effectiveness varies [32]. Biotechnology has enabled the development of numerous protein and peptide drugs, but their oral use is limited due to degradation in the gastrointestinal tract and liver metabolism. Parenteral delivery, though effective, is inconvenient for long-term use. Consequently, intranasal administration has emerged as a viable and promising alternative for delivering these drugs [2]. Nasal drug administration has been used for centuries, mainly for local treatments like rhinitis and respiratory infections. In the late 20th century, it gained recognition for systemic therapies, including cardiovascular conditions.

Migraine is a neurological disorder marked by recurrent moderate to severe headaches, often accompanied by nausea, vomiting, and sensory sensitivity. The neuropeptide CGRP plays a key role by activating receptors in the central and peripheral nervous systems [1].

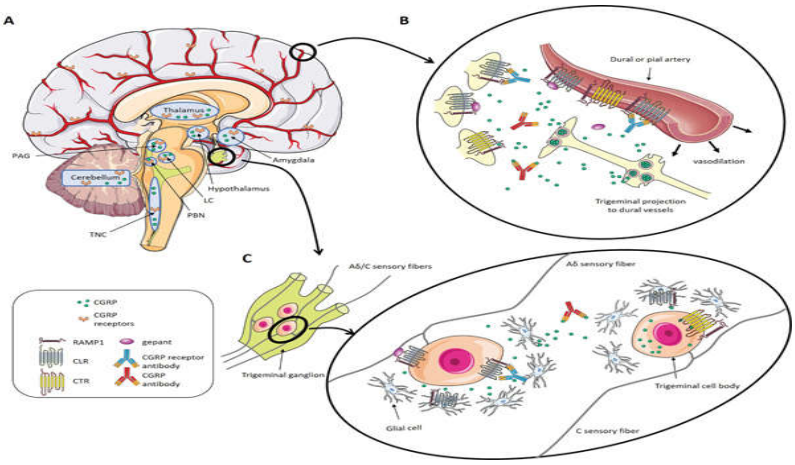

Figure No.1 CGRP and CGRP receptor distribution in the peripheral and central nervous system.

[A: Central Nervous System Structures Involved in Migraine, B: Trigeminal Nerve and Dural Blood Vessels, C: Trigeminal Ganglion and Sensory Fibers]

Nasal drug delivery system

Nasal drug delivery is increasingly considered for headache treatment due to its ease of use and potential effectiveness, especially for patients with nausea who may prefer non-oral options to avoid vomiting. This route enables faster and more efficient drug absorption, owing to the nasal cavity's high permeability, neutral pH, absence of digestive enzymes, reduced content dilution, and bypass

of first-pass metabolism. Many antimigraine drugs, such as Sumatriptan, have poor oral bioavailability or limited ability to cross the blood-brain barrier. Switching to nasal administration can improve therapeutic response by overcoming these limitations.

What makes herbal nasal drops a better choice than synthetic ones?

Herbal nasal drop medications are based on naturally occurring substances found in nature. In other words, natural plants, extracts, and herbs are used in herbal formulations. Fewer side effects of natural herbs, plants, and minerals are one of the benefits of herbal medicines. Herbal remedies are manufactured with natural substances that do not have an impact on health.

Few known plants for their anti-migraine activity are as follows,

Rough cocklebur (*Xanthium strumarium*): Cocklebur is a medicinal plant traditionally used in various systems of medicine. It possesses anti-inflammatory and analgesic properties, making it beneficial in managing migraine symptoms. Extracts from the plant are thought to relieve headache and sinus-related discomfort, often linked to migraines [7].

Pursley (*Portulaca oleracea*): Purslane is a nutrient-rich plant with antioxidant, anti-inflammatory, and neuroprotective properties. Traditionally used in herbal medicine, it may help alleviate migraine symptoms by reducing oxidative stress and inflammation. Its high omega-3 fatty acid content also supports brain health [6].

NASAL DROP

Nasal drops are one of the simplest and most user-friendly methods for nasal drug delivery, gaining popularity due to ease of self-administration. However, their main drawback is poor dose precision, which may limit their suitability for prescription medications. Unlike most nasal sprays, which tend to deposit drugs mainly in the anterior nasal cavity, nasal drops can reach deeper areas. Studies suggest that human serum albumin is more effectively deposited using nasal drops than spray.

Advantages:

Nasal drug delivery is fast, non-invasive, and easy to use. It offers high bioavailability, lowersoverdose risk, minimizes side effects, and enables direct access to the CNS and systemic circulation.

Figure No.2 Nasal Drop Container[3]

Characteristic parameters:

a) Isotonicity: It is a critical factor that must be carefully maintained in nasal drug delivery systems.

b) pH: The pH of nasal formulations, ideally between 5.5 and 6.5 to match that of the nasal cavity, is critical to prevent irritation. It is measured using a pH meter and plays a key role in formulation stability and patient comfort.

c) Drug content: Refers to the actual amount of active pharmaceutical ingredient (API) present in a unit dose or total formulation of a nasal drop product. Accurate measurement is essential to ensure therapeutic efficacy and patient safety.

d) Impurities: An established acceptance criterion for individual and total impurities must exist. As per ICH guidelines, any relevant impurity present at 0.1% or above must be reported.

e) Particle size: Droplet size in nasal sprays, typically between 30–120 µm, is influenced by device design, actuation, and formulation. Droplets >120 µm deposit in the anterior nasal cavity, while those <10 µm risk pulmonary inhalation. Thus, controlled droplet size distribution is essential and should be measured under standardized conditions [1].

EXPERIMENTAL WORK

Collection & Authentication of Plant:

This study selected two medicinal plants—*Xanthium strumarium* and *Portulaca oleracea*—previously reported for their pharmacological properties. *X. strumarium*, known for its anti-inflammatory, antimicrobial, and antioxidant effects, was collected while the fruits were still green. *P. oleracea*, noted for its antioxidant, anti-inflammatory, and wound-healing properties, was also collected.

Both plants were gathered during the June–July monsoon season from Village-Vathar, Tarf Vadgaon, Kolhapur, State-Maharashtra, India. The plant materials were washed with distilled water, shade-dried at room temperature (~25 °C) to retain phytochemical content, and authenticated by a taxonomist at the Department of Botany, Kanya Mahavidyalaya, Islampur, State-Maharashtra, India. Voucher specimens were prepared and archived for reference.

1. *Xanthium strumarium*

Xanthium strumarium (also known as *Xanthium indicum*), a member of the Asteraceae family and commonly called rough cocklebur, is valued for its aroma and traditional medicinal uses. It is widely used to treat conditions such as colds, coughs, nasal disorders, fever, headaches, skin itching, ulcers, urticaria, rheumatism, infections, arthritis, and other painful ailments. Green fruits were collected from healthy plants in Vathar Tarf Vadgaon, Kolhapur, State-Maharashtra, India. The fruits were washed, then shade-dried at room temperature (25 °C) for 6–8 days until fully dried [12].

2. Portulaca oleracea

Portulaca oleracea, a member of the Portulacaceae family, has long been used to treat conditions such as hypercholesterolemia, shortness of breath, gastric issues, diabetes, hypertension, intestinal ulcers, sinusitis, spastic paralysis, leprosy, earache, toothache, urticaria, anthrax, boils, and abscesses. Fresh, disease-free leaves were collected from *P. oleracea* in Village-Vathar Tarf, Vadgaon, Kolhapur, State-Maharashtra, India. The leaves were washed and shade-dried at room temperature (25°C) for 6–8 days until fully dried. [15].

Figure No 3:- *Xanthium strumarium* herb

Figure No. 5 :- *Portulaca oleracea* herb

Taxonomical classification [8&6]

Kingdom	Plantae
Class	Equisetopsida
Order	Asterales
Family	Asteraceae
Genus	*Xanthium*
Species	*X. Strumarium*

Kingdom	Plantae
Class	Equisetopsida C. Agardha
Order	Caryophyllales
Family	Portulacaceae
Genus	*Portulaca*
Species	*P. Oleracea*

Biological and pharmacological properties of *Xanthium strumarium* & *Portulaca oleracea* [28]

Xanthium strumarium	*Portulaca oleracea*
1. Anti-AR Effect 2. Analgesic & Anti-inflammatory 3. Anti-Tumor Effect 4. Insecticide and Antiparasitic Effects 5. Antioxidant Effect 6. Antibacterial and Antifungal Effects 7. Antidiabetic Effect 8. Antilipidemic Effect 9. Antiviral Activity[9]	1. Neuroprotective Activity 2. Antidiabetic Activity 3. Anti-Inflammatory Activity 4. Antioxidant Activity 5. Anticancer Activity 6. Antimicrobial 7. Antiulcerogenic Activity 8. Hepatoprotective Activity[5]

MATERIALS AND METHODS

Procedure

Extraction procedure for *Xanthium strumarium*

Fresh green fruits of *X. strumarium* L. were cleaned with purified water and air-dried at room temperature. Once dried, the fruits were ground into a coarse powder using a stainless-steel grinder. Forty grams of the powder were then extracted with 350 ml of 70% ethanol using a Soxhlet apparatus at 78°C for 16 hours. The resulting ethanolic extract was placed in a petri dish and allowed to dry for one week. After drying, the extract was collected, weighed, and stored [16].

Extraction procedure for *Portulaca oleracea*

Fresh *P. oleracea* leaves were washed with distilled water to remove impurities and then air-dried at room temperature. Once dried, the leaves were ground into a coarse powder using a stainless-steel grinder. Thirty grams of the coarse powder were then extracted using 350 ml of 75% ethanol in a Soxhlet apparatus at 75°C for 14 hours, until discoloration occurred. After a week of drying, the ethanolic extract was collected, weighed, and stored as a powdered extract[17].

Preparation of Nasal Drops

A modified method for the formulation of nasal drops was developed with reference to the procedure described by Suraj M. et.al To prepare the herbal nasal drop formulation, the ingredients—*Xanthium strumarium* extract, *Portulaca oleracea* extract, 0.2 g Hydroxypropyl Methylcellulose (HPMC), 0.06 g Methylparaben, and 0.1 g Chlorobutol were weighed accurately. In a beaker, 14 ml of purified water was heated to 70°C, and HPMC was added under constant stirring to dissolve completely. After cooling to room temperature, the extracts, Methylparaben, and Chlorobutol were added and mixed. The volume was adjusted to 20 ml with purified water, and the mixture was stirred continuously. The solution was filtered through Whatman No. 1 paper, and the clear formulation was transferred to sterile nasal dropper bottles for storage in a cool, dry place [35]. The final formulation was evaluated for its physicochemical properties to ensure suitability for nasal use. Chlorobutol acts as a preservative, preventing microbial contamination and extending shelf life [1&21].

Table 1. Formulation of nasal drop[35]

Sr. No.	Ingredient	Formulation						Role
		F1		F2		F3		
		ml	%	ml	%	ml	%	
1.	*Xanthium strumarium* extract	0.5	2.5	1	5	2	10	Analgesic
2.	*Portulaca oleracea* extract	0.25	1.25	0.5	2.5	1	5	Anti-inflammatory
3.	Hydroxypropyl Methylcellulose	0.2	1	0.2	0.1	0.2	0.1	Viscosity enhancer
4.	Methyl paraben	0.06	0.3	0.06	0.3	0.06	0.3	Solubilizer
5.	Chlorobutol	0.1	0.5	0.1	0.5	0.1	0.5	Preservative
6.	Purified water	q.s.	q.s	q.s	q.s	q.s	q.s	Vehicle

EVALUATION PARAMETER

By comparing product with marketed Nasal drop is typically translucent and has a clear appearance. It does not contain artificial dyes or colorants but prepared nasal drop colour is Pale yellow or Dark amber. It depended on its Active pharmaceutical ingredient (API).

The local pH of the nasal cavity directly affects drug absorption, with an optimal pH range for nasal sprays between 4.5 and 6.5 [4].

Measurement of pH

Statistical analysis:

Illustrates the distribution of pH values across three measurement groups using a combination of boxplot and swarm plot. The boxplot provides a summary of the data through median, quartiles, and overall range, while the swarm plot overlays individual data points to show the actual distribution within each group.

Visual inspection reveals minimal variation between the groups, which is supported by the ANOVA analysis ($F(2, 9) = 0.063$, $p = 0.94$), indicating no statistically significant difference in mean pH values among them. This consistency confirms the reproducibility of the pH measurement process across the sample batches [32].

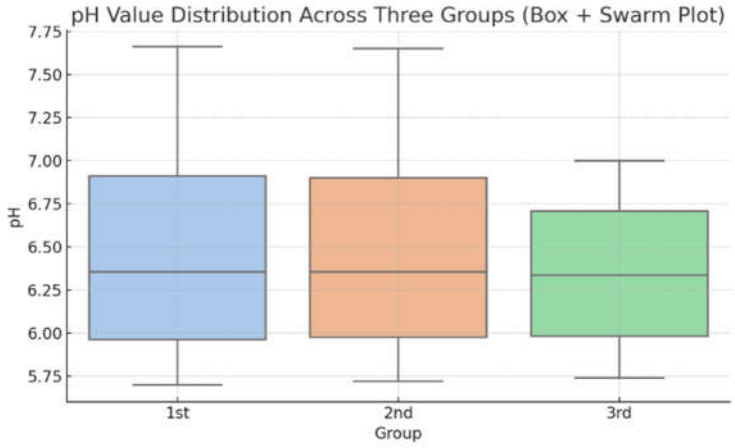

Figure No.8: Distribution of pH values across three sample groups

Table 2. Measurement of pH

Sr. No.	Batch	pH		
		1st	2nd	3rd
1.	F1	6.66	6.65	6.61
2.	F2	6.05	6.06	6.06
3.	F3	5.70	5.72	5.74
4.	Base	7.66	7.65	7.00

Stability

After 2 months of storage at room temperature, the herbal nasal drop formulation showed no significant

changes in key stability parameters. The pH remained within the acceptable intranasal range (4.5–6.5), while the color, odor, and appearance remained stable and unchanged, indicating that the formulation retained its physical and chemical integrity throughout the testing period [4].

Table 3. Evaluation parameter

Sr. No.	Formulations			
	Base	**F1**	**F2**	**F3**
1.Appearance				
2. pH	7.00	6.61	6.06	6.61
3. Colour	Transperant	Pale Yellow	Orange yellow	Yellowish Brown
4. Odour	Odourless	Camphoraceous	Camphoraceous	Camphoraceous

RESULT AND DISCUSSION

This invention presents an improved herbal-based nasal drop formulation aimed at providing rapid relief from migraine symptoms. The formulation incorporates phytoconstituents derived from *Xanthium strumarium* and *Portulaca oleracea s*pecies, known for their anti-inflammatory and analgesic properties. These herbal components are combined in optimized ratios, along with preservatives, antifungal agents, and pharmaceutical excipients such as hydroxypropyl methylcellulose (HPMC) and chlorobutanol[21]. The final formulation appears as a clear, pale-yellow solution with a pH in the range of 4.5 to 6.5, which falls within the physiologically acceptable intranasal range for nasal mucosa. ANOVA statistical analysis of the formulation parameters confirmed significant positive outcomes in terms of stability and efficacy ($p < 0.05$). The formulation remained stable for up to two months under accelerated conditions. Phytochemical screening confirmed the presence of key active constituents responsible for the therapeutic effect. Overall, this herbal-based nasal drop offers a safe, effective, and non-invasive alternative for the management of migraine.[1].

CONCLUSION

Research suggests that a new herbal nasal drop formulation offers notable benefits for migraine sufferers. These drops deliver active ingredients directly to the brain, enabling targeted therapeutic effects in the CNS. This method minimizes the systemic side effects often seen with oral treatments. The formulation provides an effective alternative for migraine relief. The study concludes that herbal nasal drops are both safe and effective. Overall, they offer a promising new approach to migraine treatment.

REFERENCES

[1]. Sikwal DR, Kalhapure RS, Govender T. An emerging class of amphiphilic dendrimers for pharmaceutical and biomedical applications: Janus amphiphilic dendrimers. European Journal of Pharmaceutical Sciences. 2017 Jan 15;97:113-34.

[2]. Chugh Y, Kapoor P, Kapoor AK. Intranasal drug delivery: a novel approach. Indian Journal of Otolaryngology and Head & Neck Surgery. 2009 Apr 25;61(2):90.

[3]. Alagusundaram M, Chengaiah B, Gnanaprakash K, Ramkanth S, Chetty CM, Dhachinamoorthi D. Nasal drug delivery system-an overview. Int J Res Pharm Sci. 2010;1(4):454-65.

[4]. Rahman Z, Xu X, Katragadda U, Krishnaiah YS, Yu L, Khan MA. Quality by design approach for understanding the critical quality attributes of cyclosporine ophthalmic emulsion. Molecular pharmaceutics. 2014 Mar 3;11(3):787-99.

[5]. Zhou YX, Xin HL, Rahman K, Wang SJ, Peng C, Zhang H. Portulaca oleracea L.: a review of phytochemistry and pharmacological effects. BioMed research international. 2015;2015(1):925631.

[6]. Iranshahy M, Javadi B, Iranshahi M, Jahanbakhsh SP, Mahyari S, Hassani FV, Karimi G. A review of traditional uses, phytochemistry and pharmacology of Portulaca oleracea L. Journal of ethnopharmacology. 2017 Jun 9;205:158-72.

[7]. Fan W, Fan L, Peng C, Zhang Q, Wang L, Li L, Wang J, Zhang D, Peng W, Wu C. Traditional uses, botany, phytochemistry, pharmacology, pharmacokinetics and toxicology of Xanthium strumarium L.: A review. Molecules. 2019 Jan 19;24(2):359.

[8]. Hoque M, Rahman MM, Uddin MN. A Study of Central Nervous System (CNS) Effect of Xanthium Strumarium in Swiss Albino Mice.

[8]. Sharifi-Rad J, Hoseini-Alfatemi SM, Sharifi-Rad M, Sharifi-Rad M, Iriti M, Sharifi-Rad M, Sharifi-Rad R, Raeisi S. Phytochemical compositions and biological activities of essential oil from Xanthium strumarium L. Molecules. 2015 Apr 17;20(4):7034-47.

[9]. Fatima N, Syed S, Ahmad M, Jabeen M, Jahan N. A comparison of analgesic and anti-inflammatory activities of Portulaca oleraceae leaf and seeds. RADS Journal of Pharmacy and Pharmaceutical Sciences. 2018 Nov 23;6(3):194-9.

[10]. Jalali J, Rahbardar MG. Ameliorative effects of Portulaca oleracea L.(purslane) and its active constituents on nervous system disorders: A review. Iranian Journal of Basic Medical Sciences. 2023 Jan;26(1):2.

[11]. Han T, Li HL, Zhang QY, Han P, Zheng HC, Rahman K, Qin LP. Bioactivity-guided fractionation for anti-inflammatory

and analgesic properties and constituents of Xanthium strumarium L. Phytomedicine. 2007 Dec 4;14(12):825-9.

[12]. Villalón CM, Olesen J. The role of CGRP in the pathophysiology of migraine and efficacy of CGRP receptor antagonists as acute antimigraine drugs. Pharmacology & therapeutics. 2009 Dec 1;124(3):309-23.

[13]. Jiang H, Wang XJ, Yang L, Zhang JX, Hou AJ, Man WJ, Wang S, Yang BY, Chan K, Wang QH, Kuang HX. The fruits of Xanthium sibiricum Patr: A review on phytochemistry, pharmacological activities, and toxicity. World Journal of Traditional Chinese Medicine. 2020 Oct 1;6(4):408-22.

[14]. Tran TT, Bui PH, Thanh NP, Hoang DM, Minh TN. Bioactive Compounds from Portulaca oleracea L. Extract. CET Journal-Chemical Engineering Transactions. 2023 Dec 10;106.

[15]. Tong C, Chen RH, Liu DC, Zeng DS, Liu H. Chemical constituents from the fruits of Xanthium strumarium and their antitumor effects. Natural Product Communications. 2020 Aug;15(8):1934578X20945541.

[16]. Kharat A, Nagar A, Sanap A, Sakhare S, Kheur S, Dubewar A, Bhonde R. Xanthium strumarium seed extract boosts osteogenesis in human dental pulp stem cell model. Journal of Ayurveda and Integrative Medicine. 2023 Nov 1;14(6):100811.

[17]. Khadka J, McAlinden C, Pesudovs K. Quality assessment of ophthalmic questionnaires: review and recommendations. Optometry and Vision Science. 2013 Aug 1;90(8):720-44.

[18]. Jalali J, Rahbardar MG. Ameliorative effects of Portulaca oleracea L.(purslane) and its active constituents on nervous system disorders: A review. Iranian Journal of Basic Medical Sciences. 2023 Jan;26(1):2.

[19]. Islam SU, Shehzad A, Ahmed MB, Lee YS. Intranasal delivery of nanoformulations: a potential way of treatment for neurological disorders. Molecules. 2020 Apr 21;25(8):1929.

[20]. Ehrick JD, Shah SA, Shaw C, Kulkarni VS, Coowanitwong I, De S, Suman JD. Considerations for the development of nasal dosage forms. Sterile Product Development: Formulation, Process, Quality and Regulatory Considerations. 2013:99-144.

[21]. Al-Sultani HA, Ajeena SJ. Identification of some Phenolic Compounds of Purslane Extracts (Portulaca Oleraceae L.) and Evaluation its Content from vit. E and vit. C and its Antioxidant Activity in Iraq. InIOP Conference Series: Earth and Environmental Science 2023 Dec 1 (Vol. 1262, No. 6, p. 062039). IOP Publishing.

[23]. F. Gong, F. Li, L. Zhang, J. Li, Z. Zhang, and G. Wang, "Hypoglycemic effects of crude polysaccharide from Purslane," International Jou.

[24]. J. Behravan, F. Mosafa, N. Soudmand, E. Taghiabadi, B. M. Razavi, and G. Karimi, "Protective effects of aqueous and ethanolic extracts of Portulaca oleracea L. aerial parts on H2O2- induced DNA damage in lymphocytes by comet assay," Journal of Acupuncture and Meridian Studies, vol. 4, no. 3, pp. 193–197, 2011.

[25]. G. Karimi, M. Aghasizadeh, M. Razavi, and E. Taghiabadi, "Protective effects of aqueous and ethanolic extracts of Nigella sativa L. and Portulaca oleracea L. on free radical induced hemolysis of RBCs," DARU, Journal of Pharmaceutical Sciences, vol. 19, no. 4, pp. 295–300, 2011.

[26]. Y. Liu, C. Liu, H. Tan, T. Zhao, J. Cao, and F. Wang, "Sulfation of a polysaccharide obtained from Phellinus ribis and potential biological activities of the sulfated derivatives," Carbohydrate Polymers, vol. 77, no. 2, pp. 370–375, 2009.

[27]. J. Zhu and M.Wu, "Characterization and free radical scavenging activity of rapeseed meal polysaccharides WPS-1 and APS-2," Journal of Agricultural and Food Chemistry, vol. 57, no. 3, pp. 812–819, 2009.

[28]. G. Tommonaro, C. S. Segura Rodr´ıguez, M. Santillana et al., "Chemical composition and biotechnological properties of a polysaccharide from the peels and antioxidative content from the pulp of Passiflora liguralis fruits," Journal of Agricultural and Food Chemistry, vol. 55, no. 18, pp. 7427–7433, 2007.

[29]. X. B. Yang, Y. Zhao, Y. Yang, and Y. Ruan, "Isolation and characterization of immunostimulatory polysaccharide from an herb tea, Gynostemma pentaphyllum makino," Journal of Agricultural and Food Chemistry, vol. 56, no. 16, pp. 6905–6909, 2008.

[30]. Y. G. Chen, Z. J. Shen, and X. P. Chen, "Evaluation of free radicals scavenging and immunity-modulatory activities of Purslane polysaccharides," International Journal of Biological Macromolecules, vol. 45, no. 5, pp. 448–452, 2009.

[31]. T. Chen, J. Wang, Y. Li, J. Shen, T. Zhao, and H. Zhang, "Sulfated modification and cytotoxicity of Portulaca oleracea L. polysaccharides," Glycoconjugate Journal, vol. 27, no. 6, pp. 635–642, 2010.

[32]. Cannady SB, Batra PS, Citardi MJ, Lanza DC. Comparison of delivery of topical medications to the paranasal sinuses via "vertex-to-floor" position and atomizer spray after FESS. Otolaryngology–Head and Neck Surgery. 2005 Nov;133(5):735-40.

[33]. Pineda T, Eckstein C, Diethelm G, Cure J. Neurocysticercosis. Headache: The Journal of Head & Face Pain. 2007 May 1;47(5).

[34]. A. S. Lee, J. S. Kim, Y. J. Lee, D. G. Kang, and H. S. Lee, "AntiTNF-α activity of Portulaca oleracea in vascular endothelial cells," International Journal of Molecular Sciences, vol. 13, no. 12, pp. 5628–5644, 2012.

[35]. M s. Formulation and evaluation of herbal nasal drops for migraine. European journal of pharmaceutical and medical research. 2024 feb 29;(2394-3211).