

FORMULATION AND EVALUATION OF HERBAL NASAL DROPS FOR MIGRAINE

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ABSTRACT

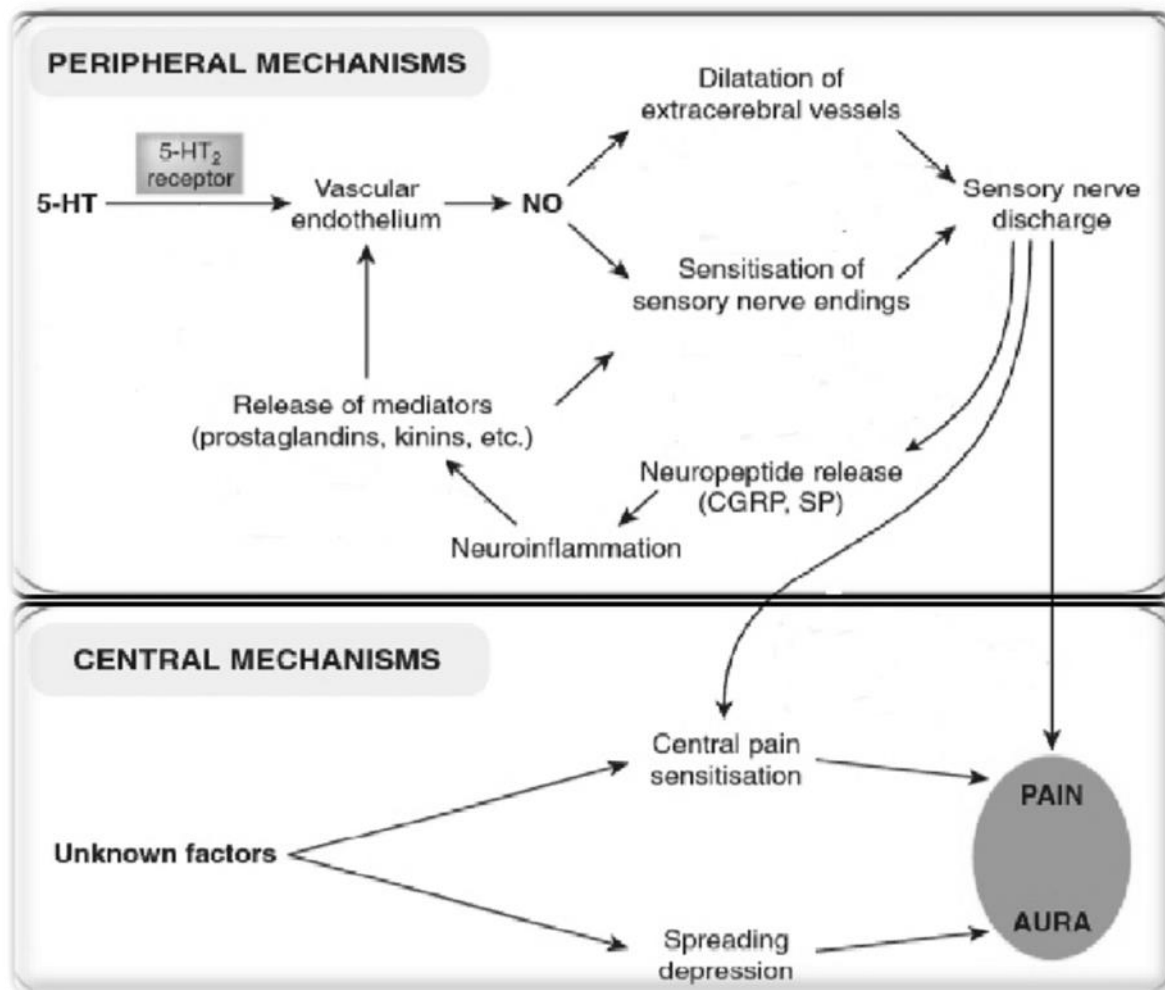
A migraine headache is a complex Neurological disorder, where a person experiences a throbbing sensation in the head on the unilateral side. "World Health Organization has grades migraine as 6th among disability causing diseases". Getting rid of it perpetually can be challenging with conventional medicines. Synthetic drugs for Migraine are often associated with side effects, due to which patients are hesitant to take these medications and prefer herbal remedies. A specific protein called calcitonin gene-related peptide (CGRP) associated with inflammation and pain is involved in migraine. Small c-fibers on the trigeminal nerve, when triggered, release CGRP protein and causes Migraine. Many herbs can block pain signals to the brain by inactivating the chemical messenger CGRP. Nasal Drops are can be efficacious in treatment of Migraine. A drug that is delivered through the nasal mucosa is rapidly absorbed into the bloodstream because of a thin mucosa and a rich blood supply. Moreover, a nasally route is an alternative to people with migraine experiencing nausea and/or vomiting. Many herbs expected to be useful in treatment of migraine like Ginger, Butterbur, Caffiene, Black jeera, Turmeric, Ashwaganda and Menthol has anti-inflammatory, abortive and prophylactic activity for migraine are chosen. Thus, in this study a poly herbal nasal drops is formulated and further evaluated.

KEYWORDS: Migraine, CGRP, Nasal drug delivery system, Herbal, formulation and evaluation.**INTRODUCTION**

Migraine is a neurological disease characterized by recurrent moderate to severe headaches often in association with a numerous symptoms of autonomic nervous system. A migraine headaches can cause concentrated throbbing or a pulsing sensation in one area of the head and is normally accompanied by nausea, vomiting and intense sensitivity to light and sound, smells, feeling sick, painful headaches and disturbed vision.^[1] The neuropeptide calcitonin gene related peptide (CGRP) play an important role in the pathophysiology of migraine.^[2]

CGRP

CGRP as the prominent neurotransmitter. It binds 2 major receptors like calcitonin receptor and receptor activity modifying protein. CGRP receptors are found at all of the known central and peripheral sites involved in migraine pathogenesis.^[3]

Pathogenesis^[4]**Anti-migraine drugs**

Treatment of migraine with anti-migraine drugs can cause adverse effects that range from mild to severe on human health. When anti-migraine drugs are continuously used, this will cause coronary vasoconstriction, dysrhythmias, contract uterus and may damage fetus, weight gain, sedation, nausea, vomiting.^[4] The development of monoclonal antibodies directed against CGRP or its receptor (like eptinezumab, fremanezumab and galcanezumab) or its receptor (erenumab) has been a major advancement in the treatment of migraine. Unfortunately, not all migraine patients can be considered responders to this type of medication.^[2]

Nasal drug delivery system

Nowadays, using nasal medicines is considered to treat headache because it may be easier and more effective than other known treatment methods. Therefore, patients who have nausea may prefer non-oral formulation due to reduction in the risk of vomiting and its efficacious nature. Why we choose nasal drug delivery system because it is a potential administration route to achieve faster and higher level of drug absorption because it is permeable to more compounds than the gastrointestinal

tract due to lack of pancreatic and gastric enzymatic activity, neutral PH of the nasal mucus and less dilution by gastrointestinal contents and also bypasses first pass metabolism.^[5] If uses of antimigraine drugs, they will have poor oral absorption and bioavailability and some drugs do not cross blood brain barrier (sumatriptan) and if changes the route of administration of antimigraine drugs, have been show delayed response (sumatriptan).^[2]

Herbal nasal drops

Herbal nasal drops 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, minerals are one of the benefits of herbal medicines. Herbal remedies are manufactured with natural substances that do not have impact on health.

Some potent herbs used in treatment of migraine

1. Black jeera (Nigella sativa): The seeds of *Nigella sativa*, commonly known as black seed or black cumin. Black seed is recommended for to treat a wide variety of diseases such as fever, headache, migraine, inflammation, etc. Black seed has also used

externally for nasal ulcers, orchitis, eczema, and swollen joints.^[6]

2. **Menthol (Mentha piperita):** Menthol is a commonly used, affordable herbal medicine. It has consist different pharmacological properties like analgesic, anti inflammatory, anti pyretic, anti oxidant, anti viral, anti microbial activity etc. Consider sterile inflammation theory for the pathogenesis of migraine, menthol whose anti inflammatory action via suppression of prostaglandin E₂, leukotriene B₄ and interleukin-1beta.^[7]
3. **Ginger (Zingiber officinale):** Ginger as an effective home remedy for the acute treatment of migraine, relieving both headache and the acute treatment of migraine, relieving both headache and the associated nausea.^[8]
4. **Ashwagandha (Withania somnifera):** Ashwagandha is use in traditional medicine in india. It is used for conditions such as asthma, anxiety, anti stress, anti inflammatory and neurological disorders.^[9]
5. **Lavender (Lavandula angustifolia):** It has been used for the treatment of stress, anxiety, headaches, migraines etc. some reports shows lavender has a spasmolytic, sedative, anti fungal properties.^[10]
6. **Caffeine (Coffea Arabica):** Caffeine is used for migraine headaches for many years. It is a wide range of physiologic effects that are unrelated to the direct treatment of headache pain but may influence improvement in headache symptoms.^[11]

7. **Hydroxypropyl methylcellulose, Methyl paraben, Sodium sulfite:** These three are used as excipients in nasal drop preparations. HPMC is used as thickening agent, viscosity increasing agent and suspending agent. Methyl paraben is used as preservatives. Sodium sulfite is used as anti oxidant, preservatives, bleaching agent and solubilizing agent.^[12,13,14]

MATERIALS AND METHODS

Preparation of aqueous extarctions

The extraction procedure involves soaking the crude drug, in the form of a powder, for a specified period of time. During the soaking time to this add small amount of solvents (such as chloroform, petroleum ether etc) with water. After soaking, filtrate the solution using whatsmann filter paper and keep it this solution in a hot air oven to evaporate the solvent. Finally, once again filter the solution and get a aqueous extraction.




Preparation of nasal drops

For the preparation of nasal drops, calculate the required quantity of ingredients and weight it accordingly to the calculated quantity and add it to the beaker, now heat 7ml of purified water up to 70°C and add it to the hPMC with stirring. After this, allow the mixture to cool at room temperature followed by adding the remaining ingredients to it with constant stirring it will be uniformly distributed, add the sufficient amount of the purified water to it, for making final volume of the nasal drops.

Formulation of herbal nasal drops for migraine

Sl.no	Drugs	Biological source	Uses	Quantity
01	Black cumin liquid extract	It is obtained from dried ripe seeds of Nigella sativa F: Ranunculaceae	Chronic headache, migraine, bronchitis, asthma	1ml
02	Pudina liquid extract	It is a dried leaves of Mentha spicata F: Lamiaceae	Analgesic Anti inflammatory	0.5ml
03	Ginger liquid extract	It is a rhizomes of Zingiber officinale F: Zingiberaceae	Exert abortive and prophylactic effects in migraine	0.2 ml
04	Ashwagandha liquid extract	It is a dried root of Withania somnifera F: solanaceae	Anti inflammatory	0.2ml
05	Lavendar liquid extract	It is a flowers of Lavandula angustifolia F: Lamiaceae	Anti fungal	0.1ml
06	Caffeine	It is obtained from dried ripe seeds of Coffea Arabica F: Rubiaceae	Anti inflammatory	0.05 g
07	Hydroxypropyl methylcellulose	-----	Viscosity enhancer	0.1 g
08	Methyl paraben	-----	Solubilizer or stabilizer	0.03 g
09	Sodium sulfite	-----	Anti-oxidant/anti-microbial, preservative	0.05 g
10	Purified water	-----	Vehicle	Q.S.

Evaluation parameters^[15]

Sl. No.	Evaluation parameters	Outcome	Result
01	Visual appearance and color		Clear and pale yellow
02	pH	-----	07
03	Stability		Stable for 2 months
04	Sterility		Sterile and free from contamination of microorganism

RESULT AND DISCUSSION

This invention relates to an improved herbal based migraine nasal drops which includes known constituents in specific ratios. They work to very quickly relief the migraine. The preservatives, anti inflammatory, anti fungal, excipient (e.g., hpmc, sodium sulfite) are used in this formulation. The finished product, herbal nasal drops was clear and pale yellow. The pH of nasal drops is 7.2 (neutral). This herbal formulation stable upto 2 months. It is free from contamination of microorganism.

CONCLUSION

After conducting research and analysis, it can be concluded that the preparation of a new herbal nasal drops holds a potential benefits for individuals suffering from migraine. The use of herbal nasal drops offers several advantages. The development of drugs for directly target the brain in order to attain a good therapeutic effects in CNS with reduced systemic side effects. The finding of his study indicated that herbal nasal drops preparations for the migraine treatment are effective and safe.

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