

FORMULATION AND EVALUATION OF HERBAL NASAL ROLL-ON

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ABSTRACT

Objective: To determine Anti nasal inhaler activity of an oily formulation containing camphor, menthol and thymol as ingredients in topical apply. **Methods:-** Acute toxicity studies were done as per OECD 423 guidelines. No signs of toxicity were observed up to runny nose. Based on this, a formulation was designed. Inhaler activity was performed in camphor, menthol and thymol oil spray forms. **Results:** The formulation at a produced a dose dependent significant inhaler effect. Inhale as often as needed for adults. Inhaler relief nasal inhaler through a nostril while holding the nostril closed. Inhaler deeply for clear breathing. **Conclusion:** In the above investigations OFCMT (oily formulation of camphor, menthol and thymol) has shown tremendous protection from inhaler & relief nasal inhaler in experimental above pharmacological effects may be due to the presence of monoterpenoids in the formulation.

KEYWORDS: OFCMT, Anti-inhaler activity.

INTRODUCTION

Herbal medicine has been used since ancient era for many centuries. In today's life there is need for efficacious therapy for inhaler. In the search for new therapeutic options, novel biomolecules of natural sources are to be investigated. Purpose of this study was to evaluate the inhaler effects of OFCMT (Oily formulation of camphor, menthol and thymol).

The common cold is an acute, self-limiting viral infection of the upper respiratory tract

involving the nose, sinuses, pharynx and larynx. The virus is spread by hand contact with secretions from an infected person (direct or indirect) or aerosol of the secretions and virus.^[1] The incubation period varies but is just under two days for rhinovirus.^[2] Symptoms, which generally relate to the infected mucosa, typically peak at 1-3 days and last 7-10 days, although they occasionally persist for three weeks.^[1,3-5] They include sore throat, rhinitis, rhinorrhea, cough and malaise.^[1,4] The severity and type of symptoms will vary among individuals and with different infective agents. For example, fever is common in children but rare and mild in adults.¹ The incidence of the common cold declines with age.^[5-7] Children under two years have about six infections a year, adults two to three and older people about one per year.^[5-9] Stress^[10] and poor sleep^[11] may increase the risk of the common cold among adults, whereas attendance at a daycare center^[12] increases the risk among preschool children.

Rhinovirus accounts for 24%-52% of clinical cases or 52%-76% of infections with an identified pathogen.^[6-8,13] No pathogen is identified in 31%-57% of upper respiratory tract infections,^[8,13] likely because of a host of reasons, including poor collection technique, low pathogen count due to sampling late in the illness, or previously unidentified agents.¹ Only about 5% of clinically diagnosed cases were found to have bacterial infection (with or without viral co-infection).^[13]

Although self-limiting, the common cold is highly prevalent and may be debilitating. It causes declines in function and productivity at work^[14,15] and may affect other activities such as driving.^[16] Its impact on society and health care is large. Of individuals with an upper respiratory tract infection, 7%-17% of adults and 33% of children visit a physician.

Upper respiratory tract infections result in an estimated increase of 12.5% in patient visits per month during cold and flu season.^[19] In the United States, direct medical costs related to the common cold (physician visits, secondary infections and medications) were an estimated \$17 billion a year in 1997.¹⁷ Indirect costs owing to missed work because of illness or caring for an ill child were an estimated \$25 billion a year.^[17]

We review the evidence underpinning preventive and treatment interventions for the common cold. We do not explore the proposed biologic mechanisms for the different products, because most are not substantiated and generally represent more supposition than science. The quality of the evidence was frequently poor, with a moderate to high risk of bias. Although preventive interventions have somewhat discrete outcomes (presence of an upper respiratory

tract infection), interpretation of the evidence for treatment of the common cold is challenged by the complexity of outcome reporting.

One of the important and effective parts of herbal plants is essential oil and substances present in different parts of plants. Essential oils are components which are oil soluble that have effective smell and aroma and are separated by use of water and steam distillation and prepared by extraction with solvents and enzymatic hydrolysis.^[20] The solvent system chosen was able to solubilize the drug at the desired concentration and an environment was provided where the drug has sufficient chemical stability. Likewise, OFCMT of oily nature is the combination of the three active ingredients (camphor, menthol and thymol), which was emulsified using excipients. The excipients used to solubilize drugs in oral and injectable dosage forms include pH modifiers, organic solvents, surfactants, water-insoluble organic solvents, triglycerides and phospholipids. Each active individual ingredient of OFCMT has its own medicinal value. Camphor, a natural product derived from the wood of the tree *Cinnamomum camphora*, has a long history of use as antiseptic, analgesic, antipruritic, counter irritant and rubefacient.^[21] Menthol is a natural compound of plant origin known to produce cool sensation. Menthol, the cooling natural product of peppermint, is widely used preparations for pain relief in sports injuries, arthritis, and other painful conditions. cymene, isomeric with carvacrol, found in oil of thyme, and extracted crystalline substance of a pleasant aromatic.^[22]

However, limited information is available on the pharmacological properties of the above individual ingredients and mixture of the above in the form of formulation. There is no scientific report on the Anti inhaler effects of the above formulation to best of our knowledge. Based on the above claims, the present study is undertaken to evaluate anti nasal inhaler effect of the formulation.

MECHANISM OF ACTION

Anatomy and Physiology of Nasal Cavity

Researchers became interested in the nasal route for the systemic delivery of medication due to a high degree of vascularization and permeability of the nasal mucosa.^[30] In humans and other animal species the major functions of the nasal cavity are breathing and olfaction. However, it also affords an important protective activity once it filters, heat and humidity the inhaled air before reaching the lowest airways. Passage of the nasal cavity which runs from nasal vestibule to nasopharynx has a depth of approximately 12-14cm. The total surface area

of the nasal cavity in human adult is about 150 cm² and total volume is about 15 ml.^[31] Each of two nasal cavities can be subdivided into different regions: nasal vestibule, inferior turbinate, middle turbinate, superior turbinate, olfactory region, frontal sinus, sphenoidal sinus, and cribriform plate of ethmoid bone. The nasal cavity also contains the nasal associated lymphoid tissue (NALT), which is mainly situated in the nasopharynx. Nasal cavity is lined with mucus layer and hairs which are involved in those functions are trapping inhaled particles and pathogens. Moreover, mucociliary clearance, immunological activities and metabolism of endogenous substances are also essential functions of nasal structures.^[32] The nasal cavity is covered with a mucous membrane which can be divided into two areas; nonolfactory and olfactory epithelium, in this non-olfactory area includes the nasal vestibule which is covered with skin-like stratified squamous epithelium cells, whereas respiratory region, which has a typical airways epithelium covered with numerous microvilli, resulting in a large surface area available for drug absorption and transport.^[33] Nasal cavity is divided by middle septum into two symmetrical halves, each one opening at the face through nostrils and extending posterior to the nasopharynx. Both symmetrical halves consist of four areas (nasal vestibule, atrium, respiratory region and olfactory region) that are distinguished according to their anatomic and histological characteristics.

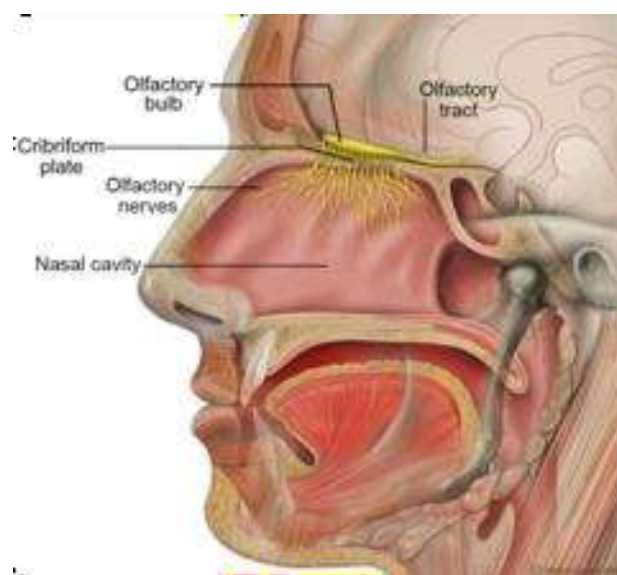


Fig. Human Nose.

OBJECTIVE OF STUDY

The present investigation is an effort to study the suitability of active individual ingredient of OFCMT has its own medicinal value. Camphor, a natural product derived from the wood of the tree *Cinnamomum camphora*, has a long history of use as antiseptic, analgesic,

antipruritic, counter irritant and rubefacient.^[21] Menthol is a natural compound of plant origin known to produce cool sensation. Menthol, the cooling natural product of peppermint, is widely used preparations for pain relief in sports injuries, arthritis, and other painful conditions. cymene, isomeric with carvacrol, found in oil of thyme, and extracted crystalline substance of a pleasant aromatic.^[22]

The purpose of this study is to investigate the efficiency of a camphor obtained from *Cinnamomum camphora*, this was used as a for model roll-on.

GENERAL OBJECTIVES

This objective of the project is to evaluate the flow rate of mixer in roll-on formulation.

SPECIFIC OBJECTIVES

- To study the method of isolation & purification of mixer.
- To prepare roll-on their physical properties (bulk density, tapped density, granule flowability, spryflowability).
- To determine properties of the roll-on namely, density, porosity, flow properties and evaporationtime.
- To prepare and flow roll-on of the formation and floe rate in the mixer of roll-on.

REVIEW LITERATURE

- In July and August 2012, a literature search was performed by one of us (G.M.A.) of PubMed, the Cochrane Database of Systematic Reviews, ACP Journal Club and Evidence-Based Medicine. Searchterms included "common cold" and "upper respiratory tract infection." In PubMed, the search was restricted to randomized controlled trials (RCTs), reviews, systematic reviews and meta-analyses. Individual treatments were also searched (e.g., "vitamin C"). A similar search was performed in early 2012 by B.A. for a related project. We conducted a manual search of the bibliographies of included articles. Further details of the literature search are available from the authors upon request.
- We selected the highest level of evidence available for each intervention, focusing on systematic reviews (with or without a meta- analysis) and RCTs. We rated the quality of evidence for each intervention as high, moderate or low risk of bias. For systematic reviews, we considered the authors'assessment of methodologic quality (e.g., blinding) of included trials but also examined the quality of the systematic review itself (e.g., thoroughness of the literature search). For RCTs, we considered traditional validity

criteria (e.g., allocation concealment) as well other limitations (e.g., funding or restricted populations). Lastly, we considered the overall volume (size and number of RCTs) and the consistency of the evidence. We used lower levels of evidence for general information such as epidemiology.

HOW CAN THE COMMON COLD BE DISTINGUISHED FROM OTHER CONDITIONS?

- The symptoms and signs of the common cold overlap with those of other conditions. Allergic rhinitis presents similarly, but it may have a seasonal component or clear allergic aggravation and is unlikely to have an accompanying sore throat. When sore throat is the primary complaint, streptococcal pharyngitis should be considered. Centor criteria are helpful in delineating the need for throat swabs and antibiotics.^[23]
- Sinusitis (acute or subacute) is a clinical diagnosis without reliable clinical scoring criteria to help differentiate it from the common cold. Groups reviewing the evidence for the antibiotic treatment of sinusitis recommend that symptoms be present for 7-10 days and not show signs of improvement before antibiotics are considered.^[24,25]

Ear pain and otitis media commonly accompany or follow the common cold, particularly in children. Findings on physical examination can be helpful in diagnosing otitis media (e.g., a bulging tympanic membrane has a likelihood ratio of 51),^[26] and there are simple rules for prescribing antibiotics or using watchful waiting in children with possible otitis media.^[27]

People with influenza usually are sicker than those with the common cold, the former having fever, chills, headaches, myalgia and malaise. Influenza can be serious in older people and those who are immunocompromised. More serious illness should prompt consideration of meningococcal disease or septicemia.

More details regarding primary conditions whose signs and symptoms overlap with those of the common cold are available in guidelines and review articles on allergic rhinitis, sore throat, sinusitis, otitis media²⁴ and influenza. In addition, the National Institute for Health and Care Excellence (NICE) has released a primary care guide for prescribing antibiotics for upper respiratory tract infections.^[28]

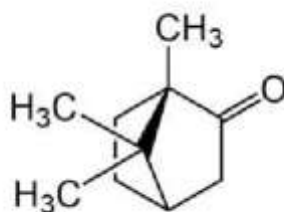
INGREDIENT PROFILE**1. CAMPHOR**

Generic Name: - camphor

Chemical IUPAC Name: - 1,7,7-Trimethylbicyclo[2.2.1]heptan-2-one

**➤ PHYSICAL PROPERTIES**

Structure Formula



Molecular Formula: - C₁₀H₁₆O

Molecular Weight: - 152.237 g.mol⁻¹

State: - Translucent crystals

Color: - White,

Melting Point: - 175-177 C

Uses: - This can help open up nasal passages and provide relief from congestion Camphor may have decongestive properties and decreases inflammation in the lungs and throat.

2. MENTHOL

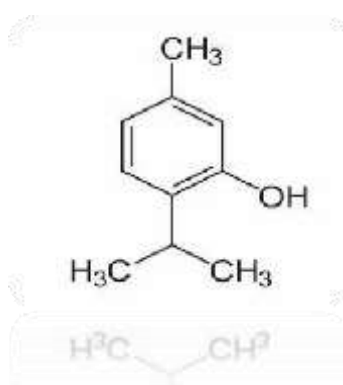
Generic Name: - Menthol

IUPAC Name: - 5-Methyl-2-(propan-2-yl)phenol



➤ PHYSICAL PROPERTIES

Structure Formula



Molecular Formula:- C₁₀H₁₄O

Molecular Weight:- 150.221 g.mol⁻¹

State: - Colorless crystalline solid

Color: - White,

Melting Point:- 49-51 C

Uses: - Menthol crystals for inhalation can provide immediate relief from mcongestion and discomfort associated with respiratory issues such ascolds, allergies, and sinusitis.

3. EUCALYPTUS

Generic Name:- Eucalyptus globulus

IUPAC Name:- 1,3,3-Trimethyl-2-oxabicyclo[2.2.2]octane



➤ PHYSICAL PROPERTIES



Structure Formula

$C_{10}H_{18}O$

Molecular formula: - 154.249g/cm

Molecular weight:- liquid

State: - 15.4°C

Melting Point: - 176–177 °C (349–351 °F; 449–450 K)

Boiling point: - Eucalyptus ointments are also used on the nose and chest to relieve congestion. Eucalyptus oil helps loosen phlegm, so many

Uses: - people breathe in eucalyptus steam to help treat bronchitis, coughs, and the flu.

PROFILE OF AN 'IDEAL' DRUG CANDIDATE FOR NASAL DELIVERY

An ideal nasal drug candidate should possess the following attributes:

- Appropriate aqueous solubility to provide the desired dose in a 25-150 ml volume of formulation administration per nostril.
- Appropriate nasal absorption properties.
- No nasal irritation from the drug.
- A suitable clinical rationale for nasal dosage forms, e.g. rapid onset of action.
- Low dose. Generally, below 25 mg per dose.
- No toxic nasal metabolites.
- No offensive odors/aroma associated with the drug.
- Suitable stability characteristics

MATERIAL AND METHOD

Oily formulation containing Camphor, Menthol and Eucalyptus in 1:1:1 W/W ratio.

MATERIAL

Drug and Chemical

1. Camphor is to use in lab solution
2. Crystal Menthol is purchase by market in chemical shop.
3. Eucalyptus is purchase by market in chemical shop.

INSTRUMENT

1. Electric weight balance
2. Digital PH meter

Formulation of Herbal Nasal Roll – On

INGREDIENTS	QUANTITY REQUIRED
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CAMPBOR	5 gm
MENTHOL	5 gm
EUCALYPUTS	5 ml

METHOD

- Clean to all glass ware property wash and dry it.
- Frist for Camphor (Kapoer) in weight to 3.3 gm in butter paper after add in porcelain dish.
- To add in equal amount of crystal Menthol and mixing in glass rod.

- After add in equal amount Eucalyptus in mixing in room temperature.
- That is mixer in camphor is dissolute in room temperature.
- To all ingredient is equal amount in 1:1:1 w/w ratio.
- To mixer solid is soluble in all an ingredient.
- After fill in roll-on bottle and check to properly roll-on worked.

EVALUTION AND PARAMETER

1. Preformulation studies of MIG

Preformulation studies were performed on the MIG, which include extraction, purification and physiochemical characterization of the mixer in oil.

2. Organoleptic Evaluation

The herbal roll-on was evaluated for its organoleptic properties such as colour , odor , and texture.

- Homogeneity:** Homogeneity can be tested by visual appearance and by touch.
- After Feel:** Emolliency, slipperiness and residue left after roll-on application is observed.
- Removal:** Roll-on is applied on the skin and removed by washing with tap water.
- Irritancy test:** Roll-on is applied on the skin and checked for redness, edema, inflammation, and irritation.
- pH Evaluation:** The pH of the 1% roll-on solution was measured using a digital pH meter.

EXPERIMENTAL WORK





PREFORMULATUION STUDIES OF NASAL ROLL-ON☐ **SOLUBILITY**

The solubility of pure drug in solvent was carried out and found to be soluble in acetone, and ethanol, insoluble in water.

☐ **MELTING POINT**

Melting point of Nasal roll-on was found to be 108 C from this we concluded that the drug sample is pure.

☐ **FLAME PROJECTION**

The aerosol product is sprayed to an open flame for about extension in after flow rate is proper not worked in after irritation in the skin part in other flow rate increase.

☐ **LEAKAGE TEST**

To fill in solution in 10 ml a roll-on bottle in the room temperature to 24 hours and after check in quantity.

No leakage in bottle to the mixer

☐ **ROLL-ON QUALITY TEST**

The roll-on is best to apply in nasal close cloth in apply and not irritation in the skin part.

To amount of drug is properly size to reduced.

PHYSIOCHEMICAL PROPERTIES OF NASAL ROLL ON

PARAMETER	RESULT
SOLUBILITY	Soluble in acetone, and ethanol, insoluble in water.
MELTING POINT	108° C
STATE	Liquid
COLOUR	Pale yellow

RESULT

After formulating the herbal roll-on, evaluation tests were done and compared with the marketed preparation (amrutanjan roll-on). Based on the results of evaluation studies, the herbal roll-on shows similar reports as per marketed preparation. This invention relates to an improved herbal-based decongestant nasal roll-on which includes known constituents in specific ratios. They work to very quickly open up nasal passages by constricting blood vessels in the lining of the nose. The camphor, menthol, Eucalyptus oil are used in this formulation.

CONCLUSION

Nasal drug delivery is a novel platform and it is a promising alternative to injectable route of administration. There is possibility in the near future that more drugs will come in the market in the form of nasal formulation intended for systemic treatment. Development of a drug with a drug delivery system is influenced by several factors. For the treatment of long illnesses such as diabetic, osteoporosis, fertility treatment novel nasal products are also expected to be marketed. Bioavailability of nasal drug products is one of the major challenges in the nasal product development. In contrast, a huge amount of money is investigated by pharmaceutical companies in the development of nasal products, because of growing demand of nasal drug products in global pharmaceutical market. So, for the avoidance of side effect and improve effectiveness of nasal products we should pay attention to basic research in nasal drug delivery.

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