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RESEARCH ARTICLE

FORMULATION AND BIOLOGICAL IMPLICATION OF EUCALYPTUS GLOBULUS AND TRACHSPERMUM AMMI ORGANOGEL FOR TOPICAL DELIVERY

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ABSTRACT

Topical delivery is an interesting option because it is convenient and safe. This offers several potential advantages over conventional routes like avoidance of first-pass metabolism, predictable, minimizing undesirable side effects and most importantly, it provides patient compliance as the drug delivery is painless. Eucalyptol is a hydrophobic, anti-inflammatory drug with a shorter biological half-life. In this context, the jellified emulsion was formulated using Na CMC as a polymer, liquid paraffin as oil phase, emulsifying agents like span 80 and tween 80, oleic acid, and clove oil as permeation enhancers. Studies were carried out with the aim to develop Organogel with the different gelling agents for topical application and evaluation of these formulations.

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INTRODUCTION

Topical Drug Delivery System: In Topical Drug Delivery System the medication is distributed throughout the body through the systemic blood circulation. Topical drug administration is anywhere in the body through ophthalmic, rectal, vaginal and dermal as topical routes. Skin is one of the important routes and widely distributed accessible organ on human body for topical administration found to be major route in topical drug delivery system. Skin Route is recognized as an effective means of therapeutic and local dermatological diseases. Topical utilization of medications offers potential points of interest of conveying the medication straightforwardly to the site of activity and representing an amplified timeframe. Topical planning maintains a strategic distance from the GI-irritation, avoid the metabolism of medication. In the form of topical dosage form, endeavors are being made to use sedate bearers that satisfactory restriction or infiltration of the medication inside or through the skin in order to enhance the local and minimize the systemic impact, or to ensure sufficient absorption.

Advantages of Topical Drug Delivery Systems

- Avoid the first pass metabolism.
- Conveniently applicable and easy to use.
- Avoid the dangers and burdens of intravenous treatment and the fluctuated states of assimilation, similar to pH changes, nearness of catalysts, gastric purging time and so on.
- Ability to effectively end the medications, when required.

- Avoids fluctuation in medication levels, between inter and intra-patient varieties.
- A moderately large area of application in correlation with buccal or nasal cavity.
- Capacity to deliver drug more specifically to a particular site.
- Avoidance of gastro-intestinal incompatibility.
- Providing use of medications with short biological half-life, narrow therapeutic window.
- Improve patient compliance.

Principles of Topical Permeation: Before a topically applied drug can act either locally or systemically, it must penetrate the stratum corneum, the skin permeation barrier.Percutaneous absorption involves passive diffusion of substances through the skin. The mechanism of permeation can involve passage through the epidermis itself (trans-epidermal absorption) or diffusion through shunts, particularly those offered by the relatively widely distributed hair follicles and sweat glands (trans-follicular or shunt pathway). In the initial transient diffusion stage, the drug molecules may penetrate the skin along the hair follicles or sweat ducts and then absorbed through follicular epithelium and the sebaceous glands. When steady state has been reached the diffusion through the intact stratum corneum becomes the primary pathway for the topical permeation. The release of a therapeutic agent from a formulation applied to the skin surface and its transport to the systemic circulation is a multistep process.

Types of Organogels

Lecithin Organogels: Lecithin Organogels have emerged as one of the most potential carrier systems. The organogel matrix mainly consists of a surfactant (lecithin) as gelator molecules, a nonpolar organic solvent as external or continuous phase, and a polar agent, usually water. A lecithin organogel is formed. when small amounts of water or other polar substances, such as glycerol, ethylene glycol or formamide, are added to a non-aqueous solution of lecithin. The transfer into jelly-like state has been demonstrated only for non-aqueous solutions of naturally occurring unsaturated lecithin. The latter are mainly separated from soy bean and egg yolk.

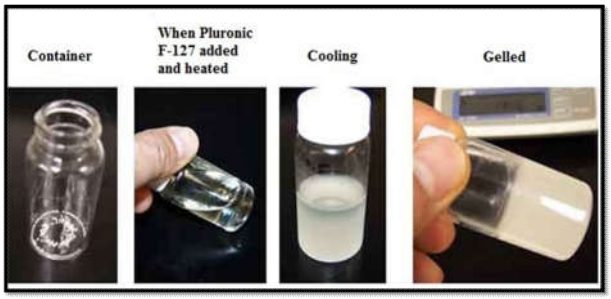

Fig. 1. Preperation and formulation of various types of Organogel

Sorbitanmono stearate Organogels: Made up of combination of Sorbitanmono stearate (Span 60) and sorbitanmono palmitate (Span40) have been found to gel a number of organic solvents at low concentrations.

Nano-emulsion based Organogels: Microemulsions are defined as thermodynamically stable transparent, single optically isotropic liquid system of water, oil and surfactants frequently in combination with suitable co-surfactants. Microemulsions are known to enhance the bioavailability of drugs via topical and systemic routes.

Poly (ethylene) Organogels: Very few polymeric organogels have been geared towards pharmaceutical applications. The only two such systems have been widely tested for drug delivery applications are poly (ethylene) organogels. PO patches were shown to be non-irritating and have low sensitizing properties.

Supramolecular Organogels: Although a low molecular mass gelator was discovered in the early nineteenth century, the supramolecular nature of these materials was poorly understood and they were largely neglected until the late 20th century. The diversity of gel structural architectures has allowed them to be utilized as templates to prepare novel inorganic superstructures for possible applications in catalysis and separation.

Eudragit Organogels: Eudragitorgano gels are really mixtures of Eudragit (L or S) and polyhydric alcohols, such as glycerol, propylene glycol and liquid polyethylene glycol containing high concentrations (30 or 40% w/w) of Eudragit. Gel consistency and spreading is described using a penetrometer. Gel viscosities were found to increase with increasing concentrations of Eudragit and to decrease with increasing drug content.

METHODOLOGY

Materials, Chemicals and Reagents: The following materials used in the study are Pharma grade or the best possible Laboratory Reagent (LR) supplied by the manufacturer.

Table 1. List of chemicals and reagents

Sl. No.	Materials	Source
1	Eucalyptol	Yarrow chemicals, Mumbai
2	Thymol	Yarrow chemicals, Mumbai
3	Sodium Alginate	Otto chemical reagents
4	Guar gum	Yarrow chemicals, Mumbai
5	Xanthan gum	Merck ltd
6	Methyl paraben	Nice Chemicals Pvt. Ltd., Kerala
7	Pluronic F127	Yarrow chemicals, Mumbai
8	Methanol	Karnataka fine chem., Bangalore

Preparation of Eucalyptol and Thymol Organogels:

Method of Preparation of Organogel: Organo gelators precipitates out as fibers which undergo, physical interactions amongst each other thereby forming, a 3-dimentional networked structure, which immobilizes the polar solvent.

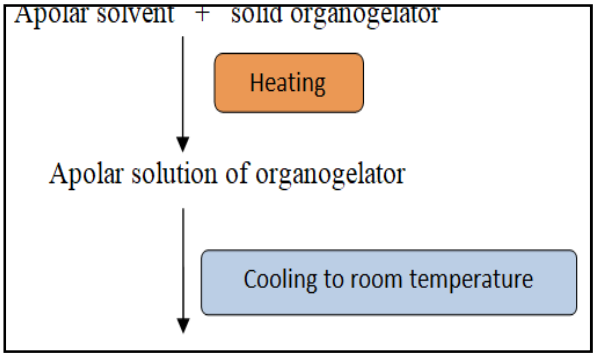

Fig 2. Method of Formation of Organogel by Solid Fiber Mechanism

Table 2. Organogel composition of different formulations of Eucalyptol and Thymol organogel F1-F6

Ingredients(mg)	F1	F2	F3	F4	F5	F6
Eucalyptol(ml)	12	12	12	12	12	12
Thymol	40	60	80	40	60	80
Sodium Alginate	20	40	60	-	-	-
Guar Gum	-	-	-	20	40	60
Xanthan Gum	-	-	-	-	-	-
Pluronic F-127	40	40	40	40	40	40
Methyl Paraben	30	30	30	30	30	30
Methanol(ml)	10	10	10	10	10	10
Water	QS	QS	QS	QS	QS	QS

Table 3. Organogel composition of different formulations of Eucalyptol and Thymol tablets F7-F12

Ingredients(mg)	F7	F8	F9	F10	F11	F12
Eucalyptol(ml)	12	12	12	12	12	12
Thymol	40	60	80	40	60	80
Sodium Alginate	-	-	-	25	40	55
Guar Gum	-	-	-	30	45	60
Xanthan Gum	20	40	60	35	50	70
Pluronic F127	40	40	40	40	40	40
Methyl Paraben	30	30	30	30	30	30
Methanol	10	10	10	10	10	10
Water	QS	QS	QS	QS	QS	QS

Biological properties

Insecticidal: Plant secondary metabolites play an important role in the plant-insect interactions. Some compounds extracted from plants have insecticidal activity. Essential oil extracted from the seeds of ajwain exhibited insecticidal activity against Callosobruchus chinensis in the ovi-position step as well as egg hatching and developmental inhibitory activities.

Antibacterial: Ethanol and acetone extract of ajwain seeds possessed an antibacterial activity against two Gram negative food spoilage bacteria Pseudomonas aeruginosa and Escherichia coli. The in vitro antibacterial activity was performed by disc diffusion method. Ethanol extract of ajwain seeds possessed highest activity against P. aeruginosa whereas acetone extract exhibited highest activity against E. coli. Antibacterial effect of ajwain was studied by applying cream containing 5% essential oil of ajwain for healing wound in rabbits and compared its effect with iodine solution. Wound contraction on the 15th day in ajwain group was 99.68%, compared with the healing effect of iodine solution group and non-treatment group which was found to be 100 and 96.57%, respectively which indicated a wound healing effect of ajwain.

Antifungal: Ethanol extract of ajwain seeds showed antifungal activity against selected fungi (Aspergillus flavus, A. ochraceus, A. niger, A. orzyae, Fusarium moniliforme, Penicillium sp.) using agar well diffusion assay (Odhav et al. 2002). Ajwain seed essential oil also exhibited a broad spectrum of fungitoxic behavior against A. niger, A. flavus, A. oryzae, A. ochraceus, F. monoliforme, F. graminearum, P. citrium, P. viridicatum, P. madriti and Cheilomenes lunata and absolute mycelial zone inhibition was obtained at a 6 µl dose of the oil.

Anthelmintic: Anthelmintic activity in ajwain was exerted by interference with the energy metabolism of parasites through potentiation of ATPase activity and thus loss of energy occured. Anthelmintic activity of ajwain, showed its effect against specific helminths, e.g. Ascaris lumbricoides in humans and Haemonchus contortus in sheep.

The plant was also reported to possess cholinergic activity with peristaltic movements of the gut, thus helped in expulsion of intestinal parasites which might also be a contributory factor to its anthelmintic activity.

CONCLUSION

Eucalyptol and Thymol are volatile oil is a hydrophobic in nature, anti-inflammatory agent with shorter biological half-life. It has GIT, renal and hepatic disorder if taken orally. Hence, to overcome the above drawback it is required to administer the drug topically. The Pre-formulation studies involving solubility and melting point of the drug were found to be comparable with the standard. The drug Eucalyptol and Thymol was checked for compatibility with selected polymers by FTIR and found to be compatible. Formulation of Organogel was carried out using Sodium Alginate, Guar Gum and Xanthan gum as gelling agent. The prepared topical Organogel of Eucalyptol and thymol were formulated and subjected to physicochemical studies i.e. viscosity, Spreadability studies and in vitro release studies. Drug content of all the formulations were found to be in the range of 86-103 % and pH was found to be between 6-7 for all the formulations. All the formulations showed good Spreadability. The stability study as per ICH guidelines was performed for the optimized formulation. F6 formulation at Accelerated testing of 40°C ± 2°C/70 ± 5% RH. No major change in appearance, pH and drug content was seen. Finally, it could be concluded that the prepared Organogel formulation was found to be an effective vehicle for the delivery of the drug and showing the biological properties i.e. Insecticidal, Antifungal, Antibacterial and Anthelmintic. Further studies should be carried out to prove the clinical effectiveness of the formulation.

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