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FORMULATION AND EVALUATION OF STABILITY FOR TOPICAL GEL USING EUTECTIC MIXTURE WITH NATURAL GELLING AGENT

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Abstract

Eutectic system is a mixture or solution which the ingredients solidify or liquefy simultaneously. A eutectic mixture is therefore that unique composition of two (or more) components that has the lower crystallization temperature or melting point. 1

Thymol, menthol and camphor are well known in the materia medica of western medicine as well as in that of the indigenous medicine in India. Thymol has been considered important as powerful antiseptic, germicidal and anthelmintic properties. Menthol is extensively employed in liniments, spraying lotions and in dental practice.

Camphor is one of the commonest remedies used in every household in India for a variety of purposes. 2

This study was conducted to develop a gel formulation of Eutectic mixture of Thymol, Menthol and Camphor using two natural gelling agents in different formulations, such as *Astragalus gummifer* L. (Tragacanth) and *Wild Acacia arabica* (Acacia) resp. and evaluate its stability. The gel formulation was designed using Carbopol, Sodium alginate, Isopropyl paraben, Glycerin and Water. The gel was formulated using accurately weighted amount of extract along with other additives, poured into the fixed amount of Carbopol 934 dispersion with constant stirring. The herbal gel formulations prepared were subjected to preliminary evaluation such as color, homogeneity, consistency, pH, Spreadability, Drug content uniformity, Viscosity and Stability. The parameters were found to be satisfactory. Stability studies showed that physical appearance, rheological properties remained unchanged upon storage for two months at ambient temperature. The Gel-formulation containing Tragacanth showed good Spreadability, Consistency and Stability than Acacia.

Key words: *Acacia arabica* (Acacia), *Astragalus gummifer* L. (Tragacanth), Camphor, Menthol, Thymol.

Introduction:

GEL is nothing but the semi-solid dosage forms which are highly viscous and consist organic polymer and gelling agent. Eg. Topical gel, Hair gel. Man has always been plagued with ailments and diseases of both the body and the mind. However dedicated research from scientists all over the world has made it possible to treat, prevent and eradicate many of these diseases that plague man (3, 4). The field of pharmaceutical science has been developing steadily over the years, and has today become invaluable in helping to keep us healthy and prevent disease. An avenue of research that has progressed a great deal in the past few decades is the treatment of diseases via biomolecules such as drugs, proteins etc. Initially these could only be administered in limited manner, due to limitations of drug delivery through harmful environments in the body (4, 5). Thus limited mobility reduced the effectiveness of administered drugs. Progress came with the development of carriers which could be encapsulated, or immobilized with drugs, allowing the drug to safely reach the required site without harm. These carriers allowed for the release of drug in sites which were previously inaccessible. The nature of these carriers progressed over the years from ceramics, to natural, to synthetic materials. Factors such as integrity, biocompatibility and flexibility were considered, and lead to the use of three dimensional matrices as carrier materials (6). These are a class of materials are known as gels. These three dimensional polymer matrices are capable of imbibing large amounts of water, and biological fluids (7). This property of gels is the reason behind its varied applications ranging from food additives to pharmaceuticals and clinical applications (8).

Topical Drug Delivery Systems:

Topical preparations are used for the localized effects at the site of their application by virtue of drug penetration into the underlying layers of skin or mucous membranes. The main advantage of topical delivery system is to bypass first pass metabolism. Avoidance of the risks and inconveniences of intravenous therapy and of the varied conditions of absorption, like pH changes, presence of enzymes, gastric emptying time are other advantage of topical preparations. Topical drug delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorders (e.g. acne) or the cutaneous

manifestations of a general disease (e.g. psoriasis) with the intent of confining the pharmacological or other effect of the drug to the surface of the skin or within the skin. Topical activities may or may not require intracutaneous penetration or deposition (9, 10). Topical drug delivery systems include a large variety of pharmaceutical dosage form like semisolids, liquid preparation, sprays and solid powders. Most widely used semisolid preparation for topical drug delivery includes gels, creams and ointments.

Use of Drugs:

1. Menthol:

Menthol is an organic compound made synthetically or obtained from corn mint, peppermint, or other mint oils. It is a waxy, crystalline substance, clear or white in color, which is solid at room temperature and melts slightly above.

Uses: As an antipruritic to reduce itching.

- As a topical analgesic,
- It is used to relieve minor aches and pains, such as muscle cramps, sprains, headaches
- As a penetration enhancer in transdermal drug delivery.
- In certain medications used to treat sunburns, as it provides a cooling sensation

2. Thymol: (also known as **2-isopropyl-5-methylphenol**, IPMP)

It is a natural monoterpenoid phenol derivative of cymene, $C_{10}H_{14}O$, isomeric with carvacrol, found in oil of thyme, and extracted from *Thymus vulgaris* (common thyme) and various other kinds of plants as a white crystalline substance of a pleasant aromatic odor and strong antiseptic properties. Thymol also provides the distinctive, strong flavor of the culinary herb thyme, also produced from *T. vulgaris*.

Uses:

- Thymol has been used in alcohol solutions and in dusting powders for the treatment of tinea or ringworm infections and to treat hookworm infections.
- It is also used as a preservative in halothane, an anaesthetic, and as an antiseptic in mouthwash.
- When used to reduce plaque and gingivitis, thymol has been found to be more effective when used in combination with chlorhexidine than when used purely by itself.

- Thymol is also the active antiseptic ingredient in some toothpastes,
- Thymol has been used to successfully control varroa mites and prevent fermentation and the growth of mold in bee colonies.
- It is also used as a rapidly degrading, non-persisting pesticide.
- Thymol can also be used as a medical disinfectant and general purpose disinfectant.

2. Camphor

Camphor is a waxy, flammable, transparent solid with a strong aroma. It is a terpenoid with the chemical formula $C_{10}H_{16}O$. It is found in the wood of the camphor laurel (*Cinnamomum camphora*), a large evergreen tree found in Asia. It is used for its scent, as an ingredient in cooking (mainly in India), as an embalming fluid, for medicinal purposes, and in religious ceremonies. A major source of camphor in Asia is camphor basil (the parent of African blue basil).

Uses

- Relieves Skin Itching And Irritation
- Alleviates Pain
- Soothes Burns
- Cures Acne
- Treats Eczema
- Cures Nail Fungus
- Good For Filling Up Cracked Heels
- Soothes Skin Rashes
- Fungal And Bacterial Infections

Materials: Thymol, menthol and camphor, Eutectic mixture, *Astragalus gummifer* L. (Tragacanth), *Acacia arabica* (Acacia), Carbopol, Sodium alginate, Isopropyl paraben, Glycerin and Water.

Equipment's: Digital balance Shimadzu Corporation, Japan, pH meter, Magnetic stirrer, Water bath shaker (Servell Instruments and Equipments Pvt. Ltd. Bangalore, India), Brookfield Viscometer (Brookfield Engineering Laboratories, Inc. USA).

Methods:

Preparation of Eutectic mixture:

One systems of liquid eutectic were prepared by physical mixing of thymol, menthol and camphor (1:1:1). The physical appearance of them was evaluated which clear liquid mixtures obtained at room temperature were selected for next evaluations.

Preparation of Gel:

Ist formulation:

Mix tragacanth and glycerin properly with small quantities of water. Add carbopol with constant stirring if necessary add small quantity of water. Dissolve small quantity of sodium alginate in water and then add the paste. Remove moisture from formulation by using hot air oven. Add preservative. At the end, add eutectic mixture and store at R.T.

IInd formulation:

Mix acacia and glycerin properly with small quantities of water. Add carbopol with constant stirring if necessary add small quantity of water. Dissolve small quantity of sodium alginate in water and then add the paste. Remove moisture from formulation by using hot air oven. Add preservative. At the end, add eutectic mixture and store at R.T.

Storage: Store in cool and dry place at 35 -37⁰c.

Container: Wide mouth bottle or collapsible tube.

Direction for use:

- This gel applies topically.
- Gel applies on the skin with the help of fingers.
- Gel applies on skin where inflammation causes with smooth hands.
- Do not rub this gel after applying it.
- Do not apply on wound.

Formula:

Sr. No.	Ingredients	Formulation 1 (Tragacanth)	Formulation 2 (Acacia)
1.	Eutetic mixture of Thymol, menthol and Camphr	1ml	1ml
2.	Carbopol	0.8gm	0.8gm
3.	Sod. alginate	3.3 gm	3.3 gm
4.	Tragacanth	1gm	-
5.	Acacia	-	1gm
6.	Isopropyl paraben	0.03gm	0.03gm
7.	Water	q.s.	q.s.
8.	Glycerin	8 ml	9 ml

Stability study

For the evaluation of stability study, maintaining the formulations at an ambient condition over a period of two months. The physical appearance, pH value, drug content, rheological properties, drug release studies were determined periodically after the 1st and 2nd month after topical gel preparations.



Physical Examination:

Sr. No.	Parameters	Formulation 1 (Tragacanth)	Formulation 2 (Acacia)
	Organoleptic Characteristics		
1.	Appearance	Clear	Not Clear
2.	Color	Light Brown	Light Brown
3.	Texture	Smooth	Sparingly Smooth
4.	Odor	Characteristic	Characteristic
5.	Nature	Weak Acidic	Weak Acidic
	Physicochemical Characteristics		
6.	pH	4.5-5.2	5.2-5.3
7.	Viscosity	1288.76CP	1168.44CP

	General Characteristics		
8.	Spreadability	Good	Poor
9.	Stability	Good	Poor
10.	Grittiness	No	No
11.	Moisture Content	12 %	10 %
12.	Density	1.04 gm/cm ³	1.10 gm/cm ³

Results and Discussion:

Comparative study of Two Formulations

PARAMETERS	1 st formulation	2 nd formulation
Appearance	Clear	Small amount of lumps form
Base	Easy to form	Constant stirring needed
Thickener (carbopol)	Easy to disperse	Not easy to disperse
Moisture content	Less	More
Thickener (Sod. Alginate)	Required in less amount	Required in large amount
Stability	Good	acacia swell in open environment
Formulation		

Conclusion:

From above results, we can conclude that Eutectic mixture of Thymol, Menthol and Camphor using two natural gelling agents in different formulations, such as *Astragalus gummifer* L. (Tragacanth) and *Wild Acacia arabica*

(Acacia) resp. showed acceptable physical properties concerning color, homogeneity, consistency, Spreadability, Stability and pH value.

Among both the gel formulations, *formulation 1st* containing Tragacanth showed better Stability, pH, Spreadability, Appearance, Color and Odor *than 2nd* containing Acacia. Also, *formulation 1st* showed better consistency, free from grittiness, non-staining, easy to remove and easy to wash, mainly non-irritating and easy to apply.

Where as in *formulation 2nd* containing Acacia we found the lumps formation on stability, ununiform Spreadability and little skin itching on application.

Stability studies in both the gel formulations showed that, the physical appearance, drug content, pH, rheological properties remain unchanged upon storage for two months.

However In vitro Diffusion studies and Drug polymer Compatibility studies are required for further studies to evaluate the potential of the herbal gel formulation. In additional In vivo models are also required for further studies to use in clinical applications.

Carbopol gels shows superior drug release after that Na CMC, HPMC and sodium alginate shows decreasing order of drug release. In carbopol gel formulations, the drug release was decrease with increase in carbopol concentration because polymer concentration increases, viscosity increases. Viscosity is negatively related to the release of active substance (aceclofenac) from formulations. All gel formulations containing penetration enhancer (propylene glycol) were used at different concentrations (5 to 10%), among them formulations containing 5% propylene glycol showed higher flux (permeability and drug release) values.

The research work was carried out to develop a new topical herbal gel formulation for topical application. The prepared herbal gel was further evaluated for pH, Viscosity and extrudability, Spreadability.

According to this comparative study, it has been conclude that, *formulation 1st* is better than 2nd because formulation 1st containing Tragacanth showed better stability, pH, Spreadability, appearance, color and odor. Also, it showed better consistency, free from grittiness, non-staining, easy to remove and easy to wash, mainly non-irritating and easy to apply.

Where as in *formulation 2nd* containing Acacia we found the lumps formation on stability, ununiform Spreadability and little skin itching on application.

However In vitro Diffusion studies and Drug polymer Compatibility studies are required for further studies to evaluate the potential of the herbal gel formulation. In additional In vivo models are also required for further studies to use in clinical applications.

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