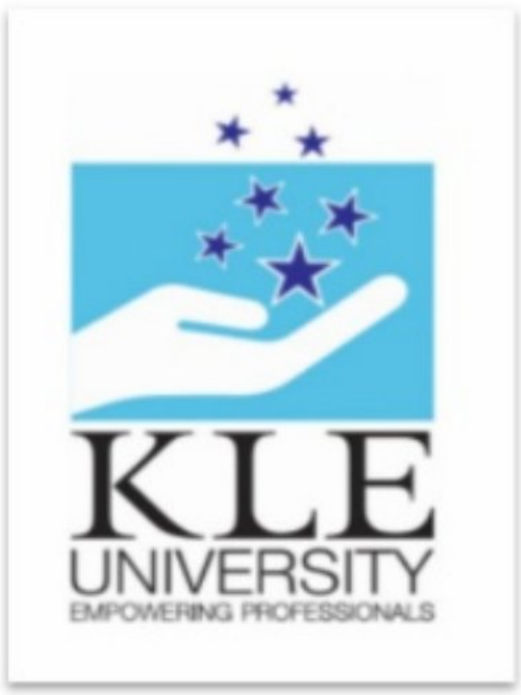
FORMULATION AND EVALUATION OF TOPICAL MICROEMULGEL FOR TREATMENT OF MELASMA

SUBMITTED TO

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH, BELAGAVI,

KARNATAKA



BY

MAHIMA. A. MUDHOLE

M PHARM- II

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UNDER THE GUIDANCE

Mr. HARISH K H

Assistant Professor

Department of Pharmaceutics

KLE COLLEGE OF PHARMACY

HUBBALLI

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KLE COLLEGE OF HIGHER EDUCATION AND RESEARCH BELAGAVI ,

KARNATAKA

PROFORMA FOR REGISTRATION OF SUBJECTS FOR

DISSERTATION

1.	NAME OF THE CANDIDATE AND ADDRESS	MAHIMA . A. MUDHOLE DEPT OF PHARMACEUTICS, KLE COLLEGE OF PHARMACY, VIDYANAGAR, HUBBALLI-580031.
2.	NAME OF THE INSTITUTION	KLE COLLEGE OF PHARMACY, VIDYANAGAR HUBBALLI-580031.
3.	COURSE STUDY AND SUBJECT	MASTER OF PHARMACY IN PHARMACEUTICS.
4.	DATE OF ADMISSION TO COURSE	SEPTEMBER 2022
5.	TITLE OF THE TOPIC: FORMULATION AND EVALUATION OF TOPICAL MICROEMULGEL FOR TREATMENT OF MELASMA	

6.	BRIEF RESUME OF THE INTENDED WORK

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6.1 - NEED FOR THE STUDY:

Topical drug delivery is a viable method for delivering a medication that has less side effects. There are numerous standard dosage forms for topical applications, such as ointment, cream and gel, however they all exhibit variations in the bioavailability of the pharmaceuticals and have additional restrictions, such as gel's limited capacity to deliver hydrophilic medications. To deliver the hydrophilic medication known as microemulgel, which can enjoy the gelling property and whose rate can be controlled, a new method in the field of topical drug delivery is introduced. It is essentially the process where a drug's microemulsion is made utilising oils, surfactants and co-surfactants, then mixed with gelling agents to create microemulgel.(1)

The micron-sized globules of microemulgel have higher penetration, allowing the medicine to reach systemic circulation directly. This improves both the drug's bioavailability and patient compliance.(1)

The Microemulgel for dermatological and cosmetic use has a variety of desirable qualities, including good consistency, being thixotropic, easily spreadable, non-staining, emollient, biofriendly, clear, transparent and elegant appearance. Additionally, these Microemulgel-based formulations improve the skin deposition of API, ultimately increasing its therapeutic activity.(2)

The dosage form is referred to as "microemulgel" when gel and microemulsion are combined. Microemulgel has significant advantages over both novel and conventional vesicular systems in a number of ways, including being thixotropic, greaseless, easily spreadable, quickly removed, emollient, nonstaining, water-soluble, longer shelf life, biocompatible, transparent and pleasing to the eye.(2)

Topical medications like ointment, cream and lotion have numerous drawbacks. They are uncomfortable for the patients since they are sticky, have a low spreading coefficient, and may require rubbing while applying. They demonstrate the stability issue as well. The usage of translucent gel has increased in both cosmetics and medicinal preparations as a result of all these factors within the main group of semisolid preparations. However, although having many advantages, gels as a colloid system have significant drawbacks, such as the inability to transport hydrophobic medicines. An technique based on microemulsions is being employed to solve this issue, allowing even hydrophobic medicinal moiety to be successfully integrated and administered through gel mixes.(1)

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Advantages of microemulsions over other dosage forms

• Microemulsions have a broad spectrum of applications in drug targeting and controlled drug release.

• They have unique distinguishing features like enhanced bioavailability, due to their ability to solubilize lipophilic drugs.

• Microemulsions can carry water-soluble drugs into aqueous phase, and hence demonstrate the ability to carry both lipophilic as well as hydrophilic drugs.

• Microemulsions have a wide range of applicability, as they can be delivered by all major routes of drug delivery.

• Microemulsions demonstrate greater longevity as compared to other biphasic dosage forms.

• Microemulsions are designed keeping in mind the utilization of their unique properties like minimum toxic side effects and reduction in the volume of carrying vehicle.

• Ease of application makes them far better dosage forms than others

• They provide protection from hydrolysis and oxidation.

• They facilitate increased patient compliance .(3)

Melasma, formerly known as chloasma, is a pigmentary disorder that develops over time and most frequently affects the face. The main causes of this condition, which affects more women and those with darker skin tones, include UV exposure and hormonal factors. Centrofacial, malar,and mandibular symmetric reticulated hypermelanosis are the three most common facial patterns associated with melasma. The centrofacial pattern, which affects the forehead, nose and mouth, upper lip, excluding the philtrium, cheeks and chin is the predominant clinical pattern in 50–80% of patients.(4)

Numerous things, including as sun exposure, heredity and female sex hormones, can cause it. Despite the fact that melanocytes alone were once believed to be the main factor, the pathophysiology of melasma is complex.(5)

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The condition affects patients' quality of life since it frequently affects the face. Although there are certain known triggering variables such sun exposure, pregnancy, sexual hormones, inflammatory skin conditions, usage of cosmetics, steroids and photosensitizing medications, its pathogeny is not yet fully understood. Additionally, there is a definite genetic susceptibility since over 40% of patients reported having relatives who had the illness. The writers of this publication go through the key clinical and epidemiological facets of melasma.(5)

Melasma significantly affects one's appearance, brings on psychosocial and emotional anguish and lowers one's quality of life. Additionally, there are large costs associated with medical operations and treatments, even though the outcomes are not always what people hope for.

Melasma causes patients distress since it mostly affects the face, is readily visible, and is always present in daily life. In this situation, it has a detrimental effect on patients' quality of life, hurting their psychological and emotional health, which frequently prompts them to look for a dermatologist.

Patients frequently describe having low self-esteem, anhedonia, a sense of unhappiness and a lack of motivation to leave the house. There have also been reports of suicidal thoughts in the literature.(6)

The precise causes of melasma are unknown, but some triggering factors have been identified, including sunlight exposure, pregnancy, the use of oral contraceptives and other steroid medications, consumption of specific foods, ovarian tumours, intestinal parasites, hepatopathies hormone replacement therapy. The use of cosmetics and photosensitizing medications, procedures and inflammatory skin processes and stressful events. This shows that melasma development is influenced by a variety of factors and depends on the interaction of hormonal and environmental impacts with genetic susceptibility.(6)

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6.2-REVIEW OF LITERATURE

1} **Ashara K.C et al.,[2014]** had reviewed on microemulgel an overwhelming approach to improve therapeutic action of drug moiety- Microemulgel was created by screening oils, emulsifiers and co-emulsifiers based on the solubility of an API compared to gel and other topical formulations. Due to the high solubility of an API and the potential pharmacological properties of oil, the therapeutic effects of an API may be aided. The presence of the oil component causes more API to penetrate the skin . Oil Micelle Size was less than 500 nm, providing more surface area for API absorption in the skin, resulting in more penetration and greater effectiveness than macro-emulsion.(2)

2} **Kumar . S . G.N et al.,[2016]** has reviewed on Microemulgel as a topical drug delivery system - The Microemulgel for dermatological and cosmetic use has a variety of desirable qualities, including good consistency, being thixotropic, easily spreadable, non-staining, emollient, biofriendly, clear, transparent and elegant appearance. Additionally, these Microemulgel-based formulations improve the skin deposition of API, ultimately increasing its therapeutic activity. As a results in direct entry of biomoleucules in to a systemic circulation thereby avoiding first pass metobolism, efflux transporters as well as metabolizing enzymes.(3)

3} **Sharma . K. A et al.,[2016]** has studied on Role of microemulsions in advanced drug delivery system - Microemulsions have drawn a lot of interest from formulation scientists due to their remarkable stability, solubility, simplicity and formulation-related characteristics. Microemulsions can also be used in cosmetics, immunology, sensor technology, coating, textiles, analytical chemistry and spermicide in addition to medication administration via oral, topical or ocular routes. The final goal of this review is to briefly go over how microemulsions are used in enhanced medication delivery.(3)

4} **Jadhav . A . et al.,[2018]** reviewed on microemulsion a novel approach for drug delivery system - The word "microemulsion" refers to an interfacial coating of surfactant molecule that stabilises a thermodynamically stable isotropically transparent dispersion of two immiscible liquids, such as oil and water. A growing industry of global significance in numerous technical applications is microemulsion. Among these uses are increased oil recovery, combustion, enzymatic catalysis, organic and bio-organic processes, the chemical synthesis of nanoparticles, cosmetics, medicines, agriculture, metal cutting, lubrication, food and others. The purpose of this review article is to discuss the use of microemulsions. An overview of the microemulsion's structure, type, features of formation, stability, phase behaviour and the impact of additives,

pressure and temperature on that behaviour is provided.(7)

5} **Oluwatobi A. Ogbechieb-Godec Nada Elbuluk et al.,[2017]** had reviewed on melasma up to date comprehensive review- Melasma is a normal acquired disorder of symmetric hyperpigmentation that usually affects the face. It is more common in women and people with darker skin types. The pathophysiology of this condition has been linked to a number of aetiologies, including familial history, hormonal influences and exposure to light. Increased epidermal and/or dermal pigmentation, expanded melanocytes, increased melanosomes, solar elastosis, dermal blood vessels and perivascular lymphohistiocytic infiltrates are all possible symptoms of melasma. Notably, combination therapies within or across treatment modalities generally results in better efficacies than monotherapies.(4)

6} **M D Vashi . N A[2019]** Melasma pathognesis: pathological findings and investigational therapies - The majority of women with darker skin types are more frequently affected by the acquired hyperpigmentation illness known as melasma. Numerous things, like as sun exposure, genetic predispositions and female sex hormones cause it. Recent studies suggest that interactions between keratinocytes and mast cells, anomalies in gene regulation, neovascularization and disruption of the basement membrane are part of the pathophysiology of melasma, which goes beyond melanocytes. Aims to provide summary of the more novel pathological findings.(5)

7} **Handel carolina . A et al.,[2014]** Melasma : a clinical and epidemiological review - Most often affecting women (particularly after the menopause) and more pigmented phenotypes (Fitzpatrick skin types III–V), it is a common reason for the need for dermatological care. The condition affects patients' quality of life since it frequently affects the face. Although there are certain known triggering variables such sun exposure, pregnancy, sexual hormones, inflammatory skin conditions, usage of cosmetics, steroids and photosensitizing medications, its pathogeny is not yet fully understood. Additionally, there is a definite genetic susceptibility since over 40% of patients reported having relatives who had the illness. The writers of this publication go through the key clinical and epidemiological facets of melasma.(6)

8} **M C Kesey . J et al.,[2019]** Melasma Treatment ; An evidence based review - The most effective treatment for melasma continues to be the triple combination cream (hydroquinone, tretinoin and corticosteroid), as well as hydroquinone by itself. The effectiveness of chemical peels, laser and light-based devices varies. A promising new therapy for moderate to severe recurrent melasma is oral tranexamic acid. The most common side effects from all treatments

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include moderate skin irritation, dryness, burning, erythema and post-infammatory hyperpigmentation. As a results, triple combination cream [hydroquinone, treteroin and corticosteroids] remains the most effective treatment for melasma. (8)

9} **Soon-Hyo Kwon et al.,[2016]** Melasma : Updates and Perspectives - Melasma management is extremely difficult due to uneven treatment outcomes and frequent relapses. Recent research, however, suggests that melasma may possibly be a skin ailment caused by photoaging rather than just a melanocyte disease. Here, they describe the histopathologic signs of melasma, including solar elastosis, altered basement membrane, enhanced vascularization and increased mast cell count, in an effort to confirm that the condition is, in fact, a photoaging disorder. We also explore some therapeutic implications based on these discoveries, as well as the most recent developments and viewpoints on treatment.(9)

10} **Sardana . K . et al .,[2015]** Rational of using hypopigmenting drugs and their clinical applications in melasma : - Melasma is the prototypical pigmentary condition that is characterised by hyperpigmentation. Although triple combination creams are typically utilised, there is a need for hydroquinone replacements due to the drug's limitations on general use. Understanding the processes involved in melanogenesis and the medications that block the essential processes is necessary for this. Before a rationally formulated fixed pharmacological product that inhibits the key steps in the pigmentation pathway is marketed, the data on in-vitro inhibition must be converted into clinical in-vivo results. Additionally, it is necessary to hunt for medications that are more effective than hydroquinone since only then will they have real-world clinical value.(10)

6.3 - OBJECTIVES OF THE STUDY

- **The main objective of the present research work is to ,**
- To formulate and optimize the microemulsion based gels for topical application .
- To evaluate the microemulsion based gels.

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7.	**MATERIALS AND METHOD** **A] METHOD** OIL : Oleic acid , clove oil, propylene glycol monolaurate, isopropyl myristate,borage oil or any other suitable oil. SURFACTANT : Tween 80, Tween 20 , lecithin , transcutol, or any other suitable surfactants. CO-SURFACTANTS : Propylene glycol , polyethylene glycol , iso-propyl alcohol, ethanol or any other suitable co-surfactants. **B] METHOD** ✓ Formulation of microemulsion : Phase titration method or any other suitable method. ✓ Formulation of gel base for microemulsion. ✓ Incorporation of prepared microemulsion in to gel with continuous stirring to form microemulsion based gel. **7.1 - SOURCES OF DATA** Data is collected from A. Books such as IP,BP and USP. B. International and Indian journals. C. Textbooks and reference books. D. Websites. **7.2 - METHOD OF COLLECTION OF DATA** 1. Compatability studies between drug and excipients. ■ Fourier Transform Infra Red spectroscopy { FTIR } ■ Differential scanning calorimetry { DSC } 2. Preparation of standard caliberation curve.

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3. Experimental design and optimization.

4. Characterisation of the prepared microemulsion gel includes the

Determination of :

- ✧ Physical Appearance
- ✧ pH
- ✧ Viscosity
- ✧ Percentage of drug content.
- ✧ In - vitro permeation study.
- ✧ Stability study as per ICH guidelines.

7.3 - DOES THE STUDY REQUIRES ANY INVESTIGATIONOR INTERVENTION TO BE CONDUCTED ON PATIENTS OR OTHER HUMAN OR HUMANS OR ANIMALS ? IF SO , PLEASE DESCRIBE BRIEFLY.

NO

7.4 - HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3 ?

NO

LIST OF REFERENCES

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Signature of the candidate	
Remarks of the guide	The work which is assigned to **Ms. MAHIMA A MUDHOLE** is under my guidance
11.1 Name and designation of the guide	**Mr HARISH K H** **Assistant Professor** KLE COLLEGE OF PHARMACY HUBBALLI-580031
11.2 Signature	
11.3 Name and Designation of the co- guide	
11.4 Signature	
11.5 Head of the Department	**Dr. S.P HIREMATH** **PROFESSOR AND HEAD OF DEPARTMENT** KLE College of Pharmacy, Vidyanagar Hubballi- 580031.
11.6 Signature	
12.1 Remarks of the principal	The above-mentioned information is correct, and I recommend the same for approval.
12.2 Signature	**Dr A.H.M VISHWANATHA SWAMY** **PRINCIPAL, HEAD** KLE College of Pharmacy Vidyanagar, Hubballi - 580031.

KLE'S COLLEGE OF PHARMACY HUBBALLI 580 031