KLE College of Pharmacy

Vidyanagar, Hubli - 580031

(A Constituent unit of KAHER Belagavi,

Deemed-to-be-university) Karnataka.

DISSERTATION PRESENTATION

"FORMULATION AND EVALUATION OF TOPICAL MICROEMULGEL FOR TREATMENT OF MELASMA"

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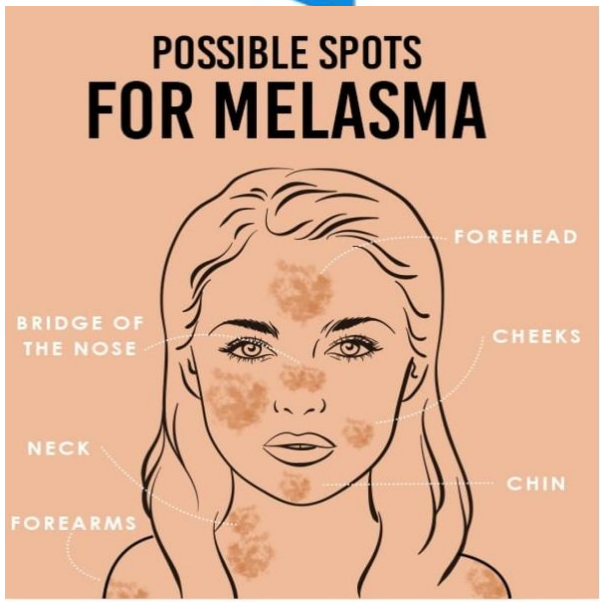
INTRODUCTION

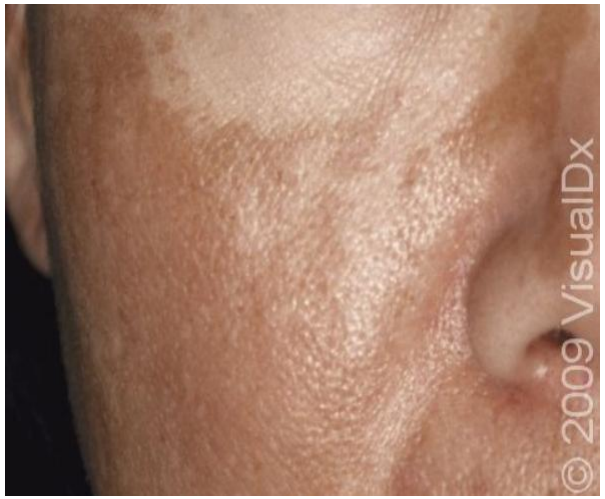
- Melasma , formerely known as choalasma , is a pigamentary disorder that develops over time and most frequently affects the face . Melasma is a common acquired pigmentary disorder that manifestsvas a symmertric hyperpigmented macules and patches on the face, more frequently affecting women of reproductive age.
- The main causees if this condition , which affects more women and those with darker skin tones, include UV exposure and hamonal factors.
- Centrofacial , malar , and mandibular symmetric reticulated hypermelanosis are the three most common facial patterns associated with melasma . it majorily affects mouth , uppper lip , excluding the philtrium , cheeks and chin in the predominant clinical pattern .
- There are certain known triggering variables such as sun exposure , pregnancy , sexual hormones , inflammatory skin conditions , usage of cosmetics , steroids , ovarian tumours . intestinal parasites , hepatopathies hormone replacement therapy and photosensitizing medications.
- 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 deterimental effect on patients quality of life , hurting their psychological and emotional health , which frequently prompts them to look for a dermatologists .

- The quest for an ideal treatment which can achieve efficient depigmentation in melasma without any adverse effects has continued .
- Recently , in vitro studies have shown that topical metformin has melanopenic action , which is due to downregulation of the expression of MITF { Melanocyte inducing transcription factor } which inturn leads to downregulation of transcription of various melanogenic proteins such as tyrosinase , TRP-1 , TRP-2 and protein kinase C-beta .
- The study was undertaken to formulate , optimize and evaluate the safety and efficacy of topical metformin in melasmaicroemulsion based gels .



Microemulgel

- The micron - sized globules of microemulgel have higher penetration , allowing the medicine to reach systemic circulation directly . This improves both the drugs bioavailability and patient compliance .
- 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 improves the skin deposition of API, ultimately increasing its therapeutic activity.



REVIEW OF LITERATURE

SL NO	TITLLE	JOURNAL	RESULTS
1	Melasma Treatment An evidence based review.	American journal of clinical dermatalogy.	Melasma is an chronic condition understanding of melasma through further research will potentially gives us new and improved therapies in future.
2	Melasma an up to date comprehensive review.	American journal of clinical dermatalogy.	Multifactorial etiology of melasma , it is important to have a multimodal therapeutic approach .

REVIEW OF LITERATURE

SL NO	TITTLE	JOURNAL	RESULTS
3	Microemulgel an overwhelming approach to improve therapeutic action of drug moiety.	Saudi pharmaceutical journal	Selection of oil, emulsifiers and co-emulsifiers for penetration through the skin depends upon skin.
4	Topical metformin in the treatment of melasma : A preliminary clinical trial.	Journal of cosmetic dermatalogy	In vitro study has shown that metformin , the most commonly used oral hypoglycemic drug , has melanopenic actionwhen applied topically.
5	Topical metformin : A promising alternative .	Journal of cosmetic dermatalogy	A higher drug bioavailability may be achieved.

NEED FOR THE STUDY

- Microemulsions have a broad spectrum of applications in drug targetting and controlled drug release. They have unique distinguishing features like enhanced bioavailability , due to their ability to solubilize lipophillic drugs.
- Microemulsions demonstrate greater longevity as compared to other biphasic dosage forms .Microemulsions are designed keeping in mind the utilization of their unique properties like toxic side effects and reduction in the volume of carrying vehicle .
- Focusing on the treatment of melasma numerous things like sun exposure heridity and female sex harmones can cause it. Despite the fact that melanocytes alone were once believed to be the main factor , the pathophysiology of melasma is complex .
- Melasma significantly affects the one's appearance , brings on psycho social and emotional anguish and lowers one's quality of life . Patients frequently describe having low self esteem , anhedonia , a sense of unhappiness and lack of motivation to leave the house .
- The precise causes of melasma are unknown .
- Therefore , considering the depigmenting potential of metformin on melasma need to be formulated , evaluated in the form of topical microemulgel.

OBJECTIVES

- **AIM OF THE STUDY**
- Formulation and evaluation of topical microemulgel by using metformin for treatment of melasma.

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

MATERIALS

MATERIALS USED

- API : Metformin HCL
- OIL : Linseed oil , lemon oil .
- SURFACTANT : Tween 80 , span 20 , span 80 .
- CO SURFACTANT : Polyethylene glycol , propylene glycol .
- GELLING AGENT : HPMC
- HUMECTANT : Glycerine
- VEHICLES : Distilled water.
- OTHER PRESERVATIVES : Preservatives and fragnance.

METHODOLOGY

- ✓ Identification of API
- ✓ Scanning and Caliberation curve of API in solvent and in phosphate buffer at specific pH .
- ✓ Identification of excipients .
- ✓ Short listing oils that have no interference of absorbance of API . [Generally between 200 to 400 nm]
- ✓ Screening of oil among the shortlisted oils , emulsifier , and co-emulsifier on the basis of solubility study.
- ✓ Selection of emulsifier , co-emulsifier , its ratio and oil .
- ✓ API - Excipients compatibility study .

- ➢ Formulation of microemulsion : By phase titration method for preparation of Pseudo ternary diagram .
- ➢ Formulation of gel base for microemulsion.
- ➢ Preparation of API loaded micro - emulsion.
- ➢ Incorporation of prepared microemulsion in to gel with continous stirring to form microemulsion based gel.
- ➢ Optimization of microemulsion .
- ➢ Formulation and development of API loaded microemulgel using suitable design of expereinments.
- ➢ EVALUATION PARAMETERS.

DEVELOPMENT OF PSEUDO TERNARY DIAGRAM BY USING PHASE TITRATION METHOD

Linseed oil , lemon oil and olive oil was selected as oil phase from solubilities studies .Tween 80 and polyethylene glycol was selected as surfactant and co-surfacrtant respectively. Tween 80 was selected also on the basis of HLB value which is 15 and suitable for o/w formulation.

Surfactant and Co-surfactant were mixed [Smix] in 1:2,2:1,3:1 and 4:1 ratios. For each phase diagram , oil and Smix at specific ratio were mixed thoroughly in vortex mixer to give oil : Smix at different ratio from 9:1 to 1:9 ratio.

Each mixture was titrated with water and visual observation was made transparent o/w microemulsion.

End point for the titration was turbid appearance of mixture.

From findings of water titration method pseudoternary phase diagram was constructed with one axis representing aqueous phase, oil and surfactant and co-surfactant.

OIL : Smix	Smix %	Water [Solvent]
0.1 + 1	0.5 + 0.5	1.4
0.2 + 0.99	0.66 + 0.33	2.1
0.3 + 1	0.75 + 0.25	2.5
0.4 + 1	0.8 + 0.2	2.7
0.5 + 0.99	0.83 + 0.16	3.4
0.6 + 0.99	0.85 + 0.14	4.0
0.7 + 0.99	0.87 + 0.12	5.0
0.8 + 0.99	0.88 + 0.11	5.3
0.9 + 1	0.9 + 0.1	5.7

FORMULATION OF MICROEMULSION BASED GEL

EMULSION
Linseed oil + tween 80 + span 20 + water [3:2:1ratio]

HPMC + Water [soaked overnight]
GEL BASE

Mixed in 1:1 ratio
Glycerine , sodium benzoate and
water is added to above mixture

Mixture is mixed evenly
by using ultra stirrer

FORMULATION TABLE OF PLACEBO

SL NO	INGREDIENTS	QUANTITY	FUNCTIONS
1	HPMC	0.75 g	Gelling agent
2	LINSEED OIL	10 ml	Oil
3	TWEEN 80	1.7 ml	Emulsifier
4	SPAN 20	1.7 ml	Emulsifier
5	GLYCERINE	5 ml	Humectant
6	SODIUM BENZOATE	0.6 g	Preservative
7	WATER	qs	Vehicle

FORMULATION FOR METFORMIN MICROEMULGEL

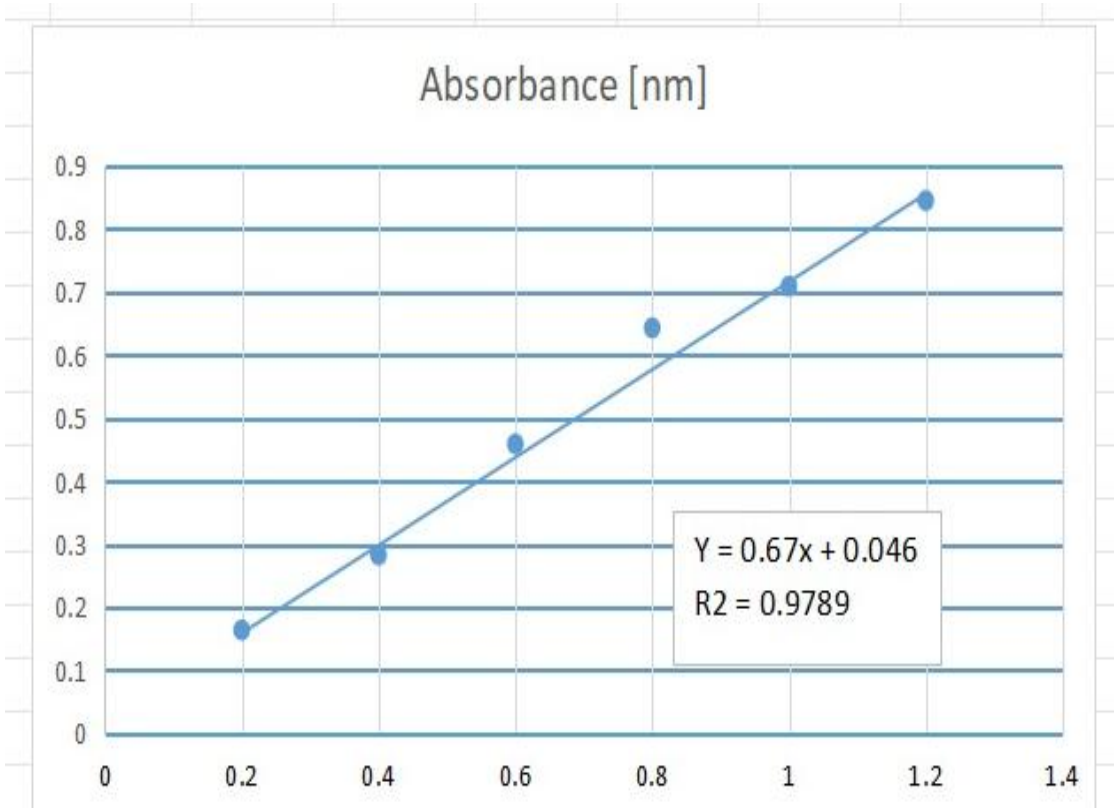
INGREDIENTS	F1	F2	F3	F4	F5
Metformin	1g	1g	1g	1g	1g
HPMC	2%	4%	6%	2%	4%
Linseed oil	5	5	5	5	5
Tween 80	0.25	0.25	0.25	0.4	0.4
Span 20	1	1	1	0.85	0.85
Distilled water	qs	qs	qs	qs	qs

PHYSICAL EVALUATION

- Colour - white
- Odour - Pleasant
- Texture - smooth
- State - Semi solid

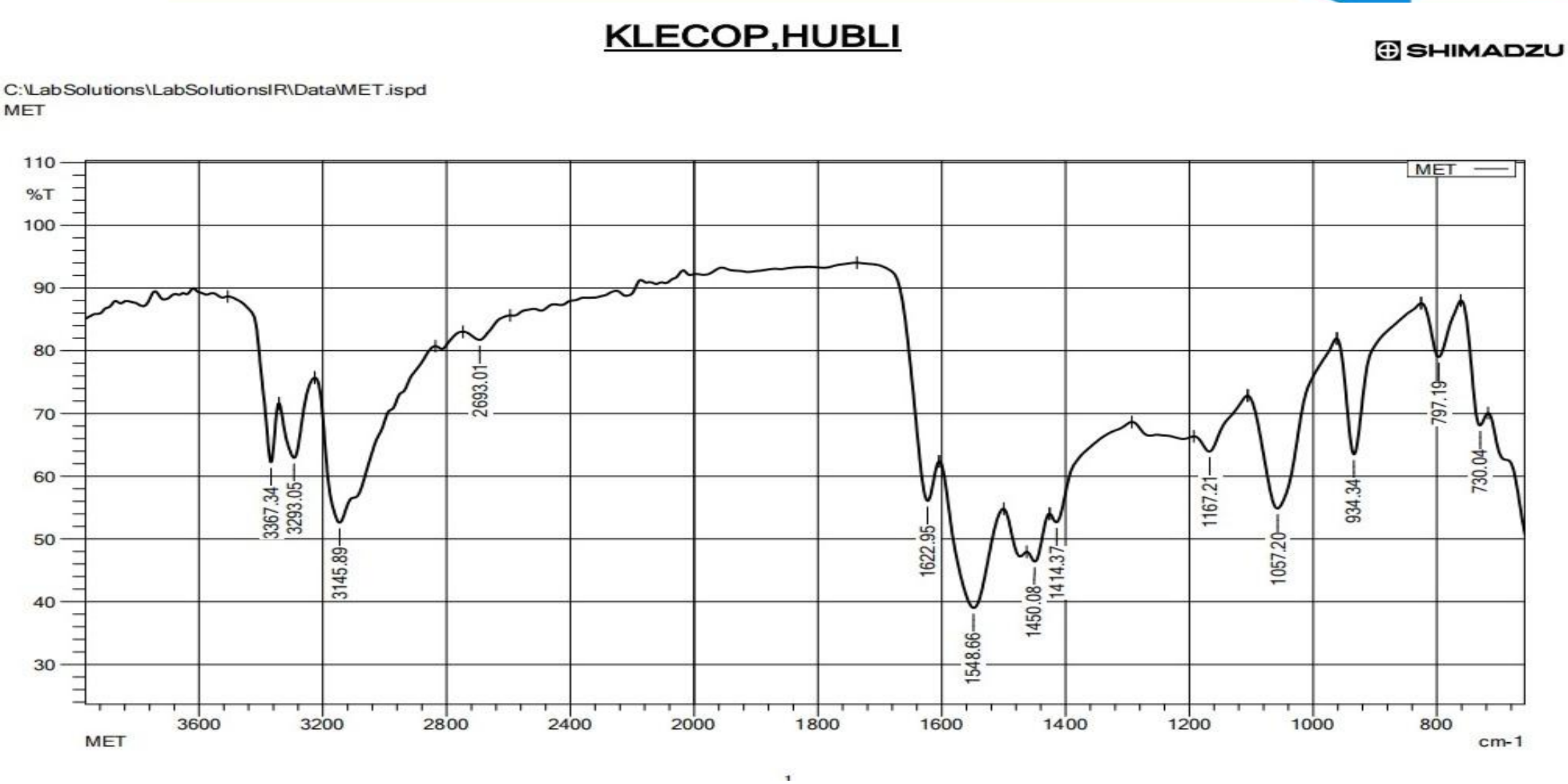
UV Estimation of metformin

SL NO	Concentration	Absorbance [nm]
1	0.2	0.164
2	0.4	0.283
3	0.6	0.459
4	0.8	0.643
5	1	0.709
6	1.2	0.845



Calibration curve of metformin at 234nm

FTIR OF METFORMIN



FUTURE WORK PLANS

- Evaluation of Placebo
- Compactibility studies between drug and excipients
  Differential scanning calorimetry [DSC]
- Preparation and evaluation of more formulation
- Experimental design and optimization
- Charaterisation 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

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DURATION / ACTIVITY	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APRIL
SEMESTER 3										
Literature search										
Protocol submission										
Drug and excipients procurement										
Extraction and analytical techniques										
Placebo and Pre-formulation studies										
Journal club 1st presentation & Biostatistics 1st internal										
Microbial studies										
1st dissertation protocol presentation										
Trial batch formulation and optimization										
Journal club 2nd presentation										
Biostatistics 2nd sessional										
Characterization studies										
2nd dissertation protocol presentation										
Biostatistics theory examination										
Journal club 3rd presentation										
Final dissertation protocol presentation										
SEMESTER 4										
Journal club presentation 1st,2nd & 3rd										
Stability test										
Thesis writing										
Publication										

THANK YOU