https://doi.org/10.48047/AFJBS.6.12.2024.5074-5091

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

FORMULATION AND EVALUATION OF BENZOYL PEROXIDE ETHOSOMAL EMULGEL FOR THE TREATMENT OF ACNE

GARVITA GOYAL*, Dr. JAI NARAYAN MISHRA, ASHUTOSH KUSHWAHA, PRIYANKA MAURYA

Article History
Volume 6, Issue 12, 2024
Received: June 10, 2024
Accepted: July 5, 2024
doi:
10.48047/AFJBS.6.12.2024.5074-5091

ABSTRACT
This study developed a novel Benzoyl Peroxide ethosomal emulgel formulation to enhance drug delivery to the target site of acne vulgaris. Ethosomes, lipid-based nano-carriers containing phospholipids and ethanol, were integrated into an emulgel matrix to improve BPO's penetration through the stratum corneum, the skin's outermost layer. The ethosome emulgel offers hydration, stability, and optimal drug release characteristics. The formulation was evaluated for various parameters, including particle size, skin permeation studies, drug release profile, and stability assessments. The ethosome emulgel showed a higher percentage of entrapment (97%) of (F3) and an ideal average vesicle size (F3). Future clinical investigations are needed to validate its long-term safety, efficacy in diverse patient populations, and comparative effectiveness against existing treatment modalities.
Key words: Acne, phospholipid, nano-carriers, ethosomal emulgel and benzoyl peroxide

1. INTRODUCTION:

A nano-meter-sized ethosomal emulgel offers benefits in drug formulation, including enhanced bioavailability, targeted delivery, and controlled release. Nanoparticles also protect active ingredients from environmental factors, enhance drug stability, and promote efficient cellular uptake. Ethosomes, advanced lipid carriers, have a unique structure that allows them to penetrate deeper skin layers, enhancing drug absorption and stability.

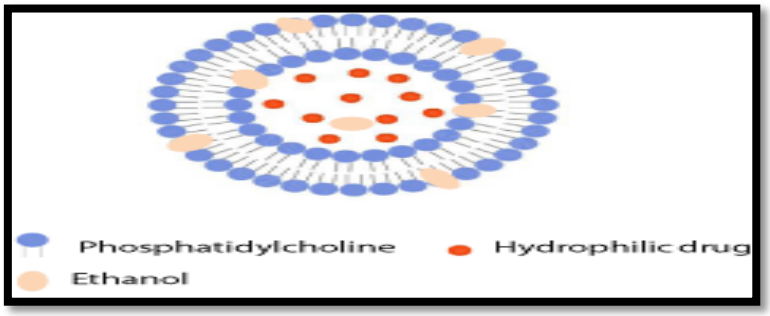

Figure 1: Schematic drawing of Ethosome (Vanic*et al.,* 2015)

Ethosomal formulations consist of varying concentrations of phospholipids, ethanol, and water. High ethanol concentrations improve drug penetration, moderate ethanol balances skin

penetration, high phospholipids create stable vesicles, and low phospholipids may cause leakage. Water content maintains stability. The optimal ethosome formulation requires careful adjustments based on drug and therapeutic target.

Emulgels entered the market as a response to the need for improved topical formulations that could address both cosmetic and therapeutic requirements effectively. Combining the characteristics of emulsions and gels, emulgels offer several advantages over traditional dosage forms. They provide enhanced stability and prolonged drug release, making them adjustable for delivering a broad range of active pharmaceutical ingredients (APIs) with varying solubility. Emulgels also offer superior skin hydration and a non-greasy feel, which improve patient compliance and satisfaction (Stanos, et.al.; 2007).

The development and commercialization of emulgels involved extensive research and formulation optimization to achieve optimal drug delivery profiles and stability. Pharmaceutical and cosmetic industries embraced emulgels due to their versatility in accommodating diverse APIs and their ability to meet stringent regulatory standards. Today, emulgels are widely used in dermatology, pain management, and skincare applications, reflecting their successful integration into modern topical drug delivery systems (Jain *et al*., 2011).

Parts of Emulgel:(Kute, & Saudagar.*et al*.; 2013)

- Emulsion
- Gel

Emulgel Preparation:

Emulgels are a versatile system for delivering active pharmaceutical or cosmetic ingredients. They are created by combining elements of emulsion and gel formulations. The process involves selecting ingredients, preparing the emulsion component, and adding gel-forming chemicals. The emulsion component can be oil-soluble or water-soluble, and high-shear mixing methods are used to ensure uniform droplet size and stability. The gel-forming chemicals are added to the stabilized emulsion, and the emulsion is slowly incorporated into the gel matrix. After preparation, emulgels undergo optimization and characterization to ensure stability, viscosity, and drug release profiles. Emulgels are used in pharmaceuticals and cosmetics due to their enhanced stability, controlled release capabilities, and ability to deliver hydrophilic and lipophilic active ingredients effectively.

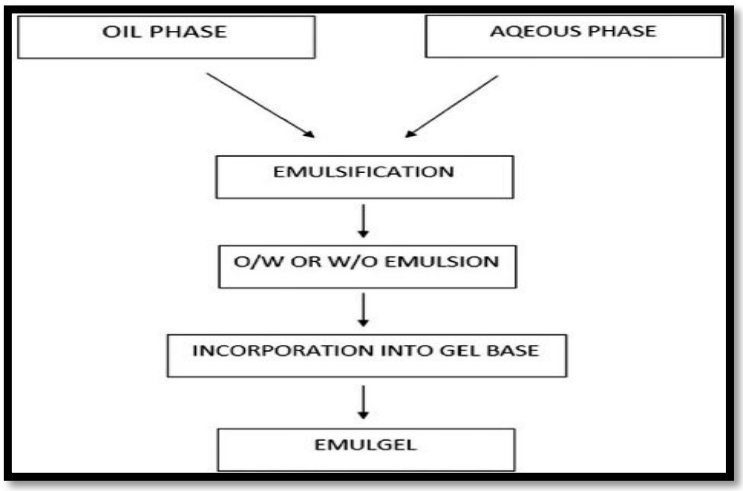

Figure*2*: Basic steps in preparation of emulgel

Evaluation of Emulgel:
Emulgels are characterized and evaluated for stability, efficacy, and suitability for pharmaceutical or cosmetic applications. Key aspects include physical appearance, viscosity, pH measurement, particle size, microscopic analysis, drug content, stability studies, in vitro release studies, and biocompatibility. These tests ensure formulation compatibility with skin and mucous membranes, prevent irritation, sensitization, or adverse reactions.

Advantages of Emulgel:
Emulgels provide stability, controlled drug release, improved skin penetration, smooth application, patient compliance, efficient delivery of pharmaceutical and cosmetic actives, prolonged therapeutic action, suitable for topical applications like skincare and dermatological treatments, and offer aesthetic benefits like moisturization and anti-aging effects in cosmetic formulations.
Disadvantages of Emulgel:
Formulation processes are complex, requiring precise ingredient selection, with potential instability, skin irritation, sensitization reactions, limited drug loading capacity, higher production costs, compatibility issues with active ingredients, and stringent regulatory requirements adding to development costs and timelines.

Acne:
When oil (sebum) and dead skin cells block hair follicles, acne, a common skin ailment, results. It can appear on the chest, face, shoulders, back, upper arms and neck and usually takes the form of pimples, blackheads, or whiteheads. In certain situations, acne can leave scars and cause emotional anguish, ranging from minor to severe. (Maddiboyina*et al*., 2020, Heath &Usatine 2021).
Benzoyl Peroxide as a Superior Acne Solution
Benzoyl peroxide is a effective acne treatment due to its strong antibacterial properties, particularly against Propioni-bacterium acnes, which reduces inflammation and the likelihood of acne lesions. It also aids in unclogging pores, promoting a clearer complexion, and decreasing inflammation associated with acne lesions.
Benzoyl peroxide works through the generation of free radicals, which play a crucial role in its effectiveness against acne:

1. **Free Radical Generation**: When applied to the skin, benzoyl peroxide decomposes into benzoic acid and oxygen free radicals. The chemical structure of benzoyl peroxide is such that it readily breaks down, releasing these free radicals.
2. **Bacterial Cell Membrane Disruption**: The oxygen free radicals are highly reactive and can disrupt the cell walls of *P. acnes* bacteria. This disruption damages the bacteria, leading to their death. The free radicals oxidize bacterial proteins and lipids, which compromises bacterial integrity and function.
3. **Reduction of Sebum Production**: Although not its primary function, benzoyl peroxide can help reduce the amount of sebum (oil) produced by the skin. This reduction is secondary to its antibacterial effects and the overall improvement in skin health.

2- MATERIALS AND METHODS:

Materials required:

Table 1: Chemicals Used:

S. No	Chemicals	S. No	Chemicals
1	Benzoyl peroxide	7	Ethanol
2	Cholesterol	8	Carbopol 934
3	Methyl Paraben	9	Triethanolamine
4	Methanol	10	Soya lecithin
5	Propylene glycol	11	Span 20
6	Propyl Paraben	12	Tween 20

Pre-formulationstudies:

- **OrganolepticProperties:**By using ocular inspection, the organoleptic qualities of benzoyl peroxide were noted. Studies on benzoyl peroxide's organoleptic properties, such as general appearance (colour, odour, condition, etc.), were carried out.
- **Solubilitystudy:**Solubility study of Benzoyl peroxide was determined qualitatively. This was done by taking 1mg of drug indifferentsolvent of 1 ml. The solubility wasdeterminedaccordingtoUSPNF,2007.
- **pHdetermination:**The pH of Benzoyl peroxide was determined using an electrochemical method and a digital pH meter.
- **MeltingPoint:** The melting point of a sample was determined using Thiele's tube and the open capillary method.
- **Partition coefficient:**The partition coefficient was determined by preparing two immiscible solvents and adding a solute. The solute was agitated and measured in both aqueous and organic layers. The partition coefficient (P) was calculated as the ratio of the solute's concentration in the organic phase to its concentration in the aqueous phase, providing insight into its lipophilicity and potential behavior in biological systems (Zhang. et.al., 2017).

Partition coefficient= (C1/C2)

- **Loss of dryness:** The study assessed moisture content and stability of a medication sample by weighing it, drying it in a hot air oven, cooling it, and reweighing it to determine the loss on drying.
- **Micromeretics study:** This study includes
  - Particle size:
  - DeterminationofLambdamaxand calibrationcurve
  - FouriertransmissionInfra-RedSpectroscopy
  - Powder Property
  - Thin layer chromatography

3. Preparation of Ethosomes:

Lecithin was dissolved in ethanol containing medication, stabilized with cholesterol and propylene glycol, and sealed. Ethosomal colloidal suspensions were prepared by adding distilled water, suspended, and maintained at room temperature for 30 minutes, then stored in the refrigerator.

Table 2: Composition of formulation

Material used	F1	F2	F3	F4	F5
BPO	0.15 gm	0.15 gm	0.15 gm	0.15 gm	0.15 gm
Ethanol (30%)	3ml	3ml	3ml	3ml	3ml
Soyalecithin	0.3 gm	0.4 gm	0.6 gm	0.6 gm	0.6 gm
Cholesterol	0.05 gm	0.05 gm	0.07 gm	0.08 gm	0.1 gm
Propylene glycol	1 ml	1 ml	1 ml	1 ml	1 ml
Water	6ml	6ml	6ml	6ml	6ml

Evaluation parameters of Drug loaded Ethosomes formulation:

Zeta potential:

The zeta potential was measured to determine the velocity of particle movement in an electric field and the charge of the particles. The current study involved diluting the ethosome formulation by a factor of 10 using distilled water, and then analysing it using Zetasizer Malvern tools. Prior to zeta potential measurements, all samples underwent sonication for a duration of 5-10 minutes (Kumar *et al.,* 2018, Penjuri*et al.,* 2016).

Particle size:

The ethosome dimensions were found by means of the Malvern Zeta sizer, an instrument made by Malvern Instruments. Millipore filtered water was used to dilute the dispersions to an appropriate concentration for scattering at 25°C. The resultant sample was subsequently placed in a disposable sized cuvette.The size data is recorded in Table 15 (Sharma and Pathak 2011).

Entrapment efficiency:

Weighing and mixing 10 ml of ethosomes with 5 ml of ethanol in a volumetric flask allowed us to accurately calculate the entrapment efficiency. After that, a vortex mixer was used to stir the ingredients for one minute. The capacity was changed to 10 millilitres. After then, the mixture was filtered and then diluted. Spectrophotometry was used at a wavelength of 234.80 nm to measure the amount of benzoyl peroxide (Swetha*et al*., 2011; Solunke*et al*., 2019).

Loading efficiency = Actual drug content in ethosome / Theoretical drug content × 100

Scanning Electron Microscopic (SEM):

Scanning electron microscopy (SEM) was performed by first coating the sample with a thin layer of conductive material, such as gold. The sample was then placed in the SEM chamber, where it was bombarded with a focused beam of electrons. These electrons interacted with the sample's surface, producing various signals that were detected and used to generate a high-resolution image, revealing the sample's surface morphology and composition.

4. FormulationofEmulgel:

- For preparation of oil phase, span 20 and BHT was added in liquid paraffin.
- For preparation of aqueous phase, Tween 20 was dissolved in distilled water.
- Ethosomal vesicles of BPO were separated using centrifuge method.
- Ethosomal vesicles of BPO were then added in propylene glycol with continuous stirring.
- Slowly methyl Paraben, propyl Paraben and disodium EDTA were also added in solution of propylene glycol.
- After continuous stirring for 10 min, the above propylene solution was added into aqueous phase followed by continuous stirring.

- Oil phase solution and aqueous phase solution were heated at 60°C separately for 15 minutes on water-bath.
- Later, oil phase was mixed in aqueous phase slowly with continuous stirring for 15-20 min and were then kept at room temperature

5. Preparation of Ethosomal Emulgel:

After 2 hr in 50 mL of warm water (A), carbopol-934 was homogeneously disseminated at 6000 rpm using a magnetic stirrer. To form stiff gel, carboxymethyl cellulose and methyl paraben were added to 50 ml warm water (B) and mixed continuously. The mixes A and B were continuously stirred. To make gel, tri-ethanol amine (drop-wise) was added to neutralise pH and emulsion was added to the dispersion. Here, propylene glycol was used as a permeation enhancer. Agitating the final dispersion produced a lump-free gel (Abbas*etal*., 2019, Silpa*etal*., 2021)

Table 3: **Composition of Gel formulation**

Quantity (gm)					
Ingredients used	**F1**	**F2**	**F3**	**F4**	**F5**
Carpool 936	1.5	1.5	1.5	1.5	1.5
Benzoyl peroxide Vesicles	0.15	0.15	0.15	0.15	0.15
Liquid paraffin	1ml	2ml	3ml	4ml	5ml
Span 20	1ml	1ml	1ml	1ml	1ml
Tween 20	1ml	1ml	1ml	1ml	1ml
Propylene glycol	5ml	5ml	5ml	5ml	5ml
Methyl Paraben	0.03	0.03	0.03	0.03	0.03
Propyl Paraben	0.01	0.01	0.01	0.01	0.01
Disodium EDTA	0.1	0.1	0.1	0.1	0.1
BHT	0.1	0.1	0.1	0.1	0.1
Tri-ethanolamine	q.s	q.s	q.s	q.s	q.s
Purified water	Upto 50ml	Upto 50ml	Upto 50ml	Upto 50ml	Upto 50ml

CharacterizationofEmulgel:

PhysicalImpression:TheEquippedEmulgelformulationwasevaluatedforOdor, appearance,homogeneity and Color by visualobservation.

pH: Digital pH metre (EI) measured pH of the formulation. If pH deviated slightly, tri-ethanolamine solution was added drop-by-drop to skin pH (McGlynn, W.2003).

Viscosity: The viscosity of the Emulgel formulations was measured at 250C at 100 rpm using a Brookfield viscometer with spindle number 61 (Monica andGautami2014).

Spreadability:The best topical Emulgel needs to have a good spreading coefficient when rubbed or applied to the surface of the skin. To test this, we applied around 1g of the mixture to a glass slide. Over the initial glass slide, another of the same length was placed. The gel was spread out at a particular distance and sandwiched between two glass slides using a 50 mg mass. We timed how long it took for the gel to go that far from its starting point. The subsequent formula was employed to get spreadability:

S=M*L/T

Where,
S-Spreadabilityl, g.cm/s
M- Weight applied to the upper pane
L- glass slide's Length
T- Timefor spreading gelin sec(Sandeep, D. S. 2020).

Skin irritation test: In the patch test for skin irritation, a small amount of the substance was applied to an adhesive patch placed on the skin. It stayed on for a day or two. After removal, the skin is examined for signs of irritation like redness or swelling, helping to evaluate potential skin reactions to the substance, to assess the substance's potential impact on the skin.

In-vitro drug release:

- In vitro drug release test for benzoyl peroxide ethosomal emulgel was performed using an egg cell membrane and a Franz diffusion cell, the procedure involved several steps.
- Initially, a solution containing the benzoyl peroxide gel was placed in the donor compartment of the Franz diffusion cell.
- The drug solution was separated from the receptor compartment by the egg cellophane membrane, with the receptor compartment containing a buffer solution to mimic physiological conditions.
- During the test, benzoyl peroxide diffused through the egg cellophane membrane into the buffer solution.
- Samples were periodically withdrawn from the receptor compartment through inlet and outlet ports.
- These samples were then analyzed using a UV spectrometer to measure absorbance, which correlates with the concentration of benzoyl peroxide released into the buffer solution.
- To calculate the in vitro drug release, the cumulative amount of benzoyl peroxide released over time was determined from the absorbance measurements.

This data was plotted as a cumulative percentage of drug released versus time, providing valuable insights into the release characteristics of the benzoyl peroxide gel formulation.

6. RESULT AND DISCUSSION:

Organolepticproperties:

1. Table 4:OrganolepticpropertiesofBenzoyl peroxide

Drug	Organolepticproperties	Observation
Benzoyl peroxide	Colour	White, granular crystalline solid
	Odor	Odorless
	Physical form	Crystalline in nature
	Appearance	White powder or granules

Organolepticpropertiesofthe Benzoyl peroxide includingappearance,color,odor and Statewere conducted. Benzoyl peroxide was discovered to have a white color, Odorless and has a crystalline powder, according to research conducted on it. Benzoyl peroxide exhibited the same color, state, odorand appearance as the I.P. requirements for these characteristics. Result show in Table7.

Solubilitystudy:

Table 5: Solubilitystudyof Benzoyl peroxide

S.NO	Solvent	Status
1.	Water	Slightly soluble
2.	Ethanol	Freely Soluble
3.	Methanol	Freely Soluble
4.	DMSO	Freely Soluble
5.	Acetone	Freely Soluble
6.	Acetic Acid	Freely Soluble

pH determination:

Table 6:pHofBenzyl peroxide

S. No	Drugs	Observed	Standard pH value
1.	Benzyl peroxide	3.1	3-4

ThedigitalpHmeterusedto figure outthepHofasubstance.ThepHoftheBenzyl peroxide was found tobe3.1,which falls comfortably within thedrugspecification.

Melting point:

Table 7:Meltingpoint of Benzyl peroxide

Drugs	Observed	Reference
Benzyl peroxide	102°C	104.5°C

The melting point was figured out by using Thiele's tube and the open capillary method. The sample was gently heated using a capillary that was suspended in a thiele's tube; a thermometer was attached for temperature monitoring. We used the temperature that occurred when the sample began to melt as its melting point. The melting pointof the Benzyl peroxide was found to be 102ºC, which falls comfortably within thedrugspecification.

λmax:

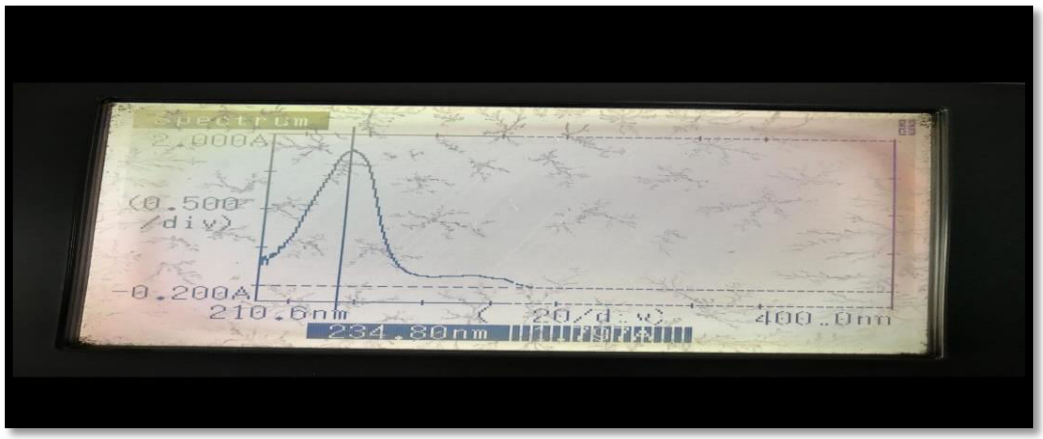

Figure 3: Lambda max

Table 8: Lambda max

S. No	Drug	UV absorption maxima(Lambdamax)
1.	Benzyl peroxide	234.80 nm

UV visible spectrophotometer (Shimadzu- 1700) was employed to figure out thelambda

max (absorption maxima) of the formulation. The absorbance max of the Benzyl peroxide wasfoundtobe234.80 nm. This falls comfortably within thedrugspecification.

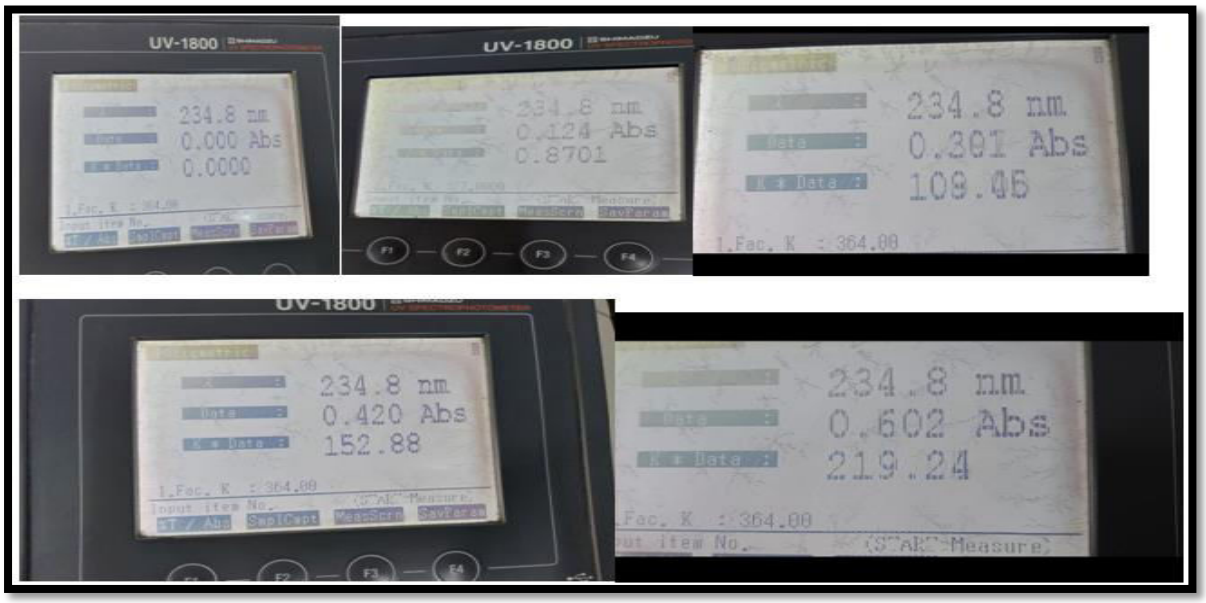

Figure 4: Absorbance at 1ml, 2ml, 3ml and 4ml

Calibration curve of Benzyl peroxide:

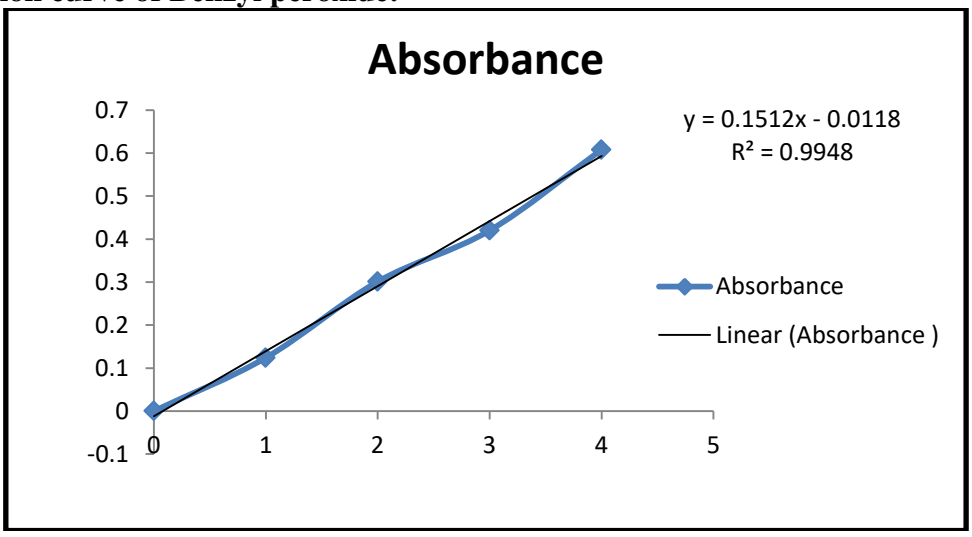

Figure 5: Calibration curve of Benzyl peroxide

Concentration of drug was found to be = 976 ug/ml = 0.9 mg/ml

Partition coefficient:

Table 9: **The partition coefficient of the Benzyl peroxide**

Concentration of drug in solvent	**concentration of drug in organic solvent**
Y=mx+c	Y=mx+c
0.602= 0.15x	0.947= 0.15x
X=4.01	X= 6.31

P.C = concentration of drug in organic solvent /
Concentration of drug in aqueous solvent
= 4.01/ 6.31
= 1.5

Conclusion = partition coefficient came more than 1, hence drug is lipophilic in nature

Table 10: Particle size of Benzyl peroxide

Particle size	264.6 nm

Powder Property:

Flow property of the Benzyl peroxide was performed, and the results are given below.

Table 11: Flow ability properties of Benzyl peroxide

Flow Property	**Benzyl peroxide**
Bulk Density	0.6
Tapped density	0.7
Angle of Repose	22.78
Hausner´s ratio	1.1
Carr's index	14.2

TLC preparation:

$$\mathbf{R_f\ Value} = \frac{\text{Distance traveled by solute}}{\text{Distance traveled by solvent}}$$

$R_f$value = 5.5/6.8 = 0.8

More polar is drug, it would have slow or low movement. More **R_f**value, least polar is drug. Hence proved, Benzyl peroxide our API, is non-polar in nature.

Functional group identification by FTIR:

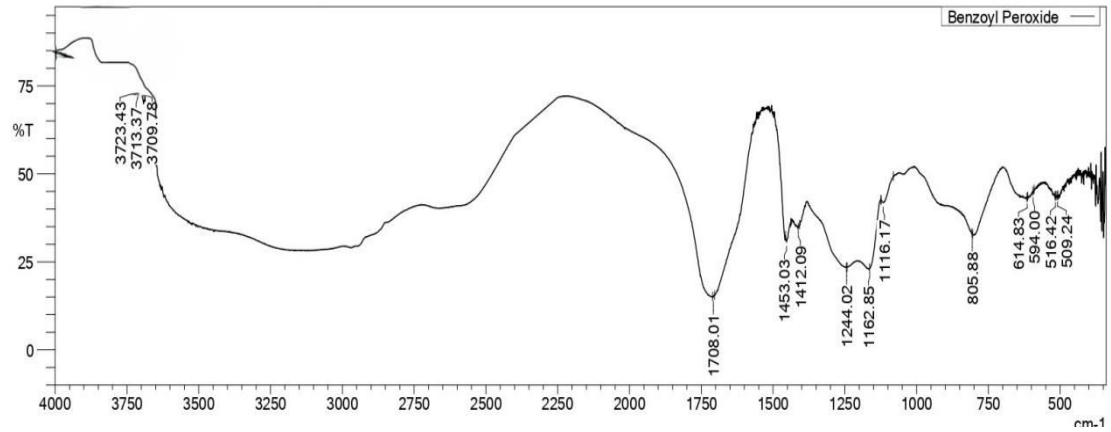

Figure 6: FTIR of Benzyl peroxide

7. Evaluation parameter of Benzyl peroxide loaded ethosomes formulation:

Particle size determination:

DISCUSSION

One of the most vital variables for characterising ethosomes is the particle size. The drug-loaded ethosomes formulation was tested using a Malvern zeta sizer to determine the average particle sizes. Ethosomes had an average particle size ranging from 186.25 to 451.52 nm, according to the particle size study. The particle size data in table 15 demonstrate that all of the ethosomes that were formulated fall within the range of less than 1000 nm, with the lowest particle size being F3.

			Size (d.n...	% Number:	St Dev (d.n...
Z-Average (d.nm):	186.25	Peak 1:	200.0	100.0	186.9
PdI:	0.321	Peak 2:	0.000	0.0	0.000
Intercept:	0.877	Peak 3:	0.000	0.0	0.000
Result quality	Good				

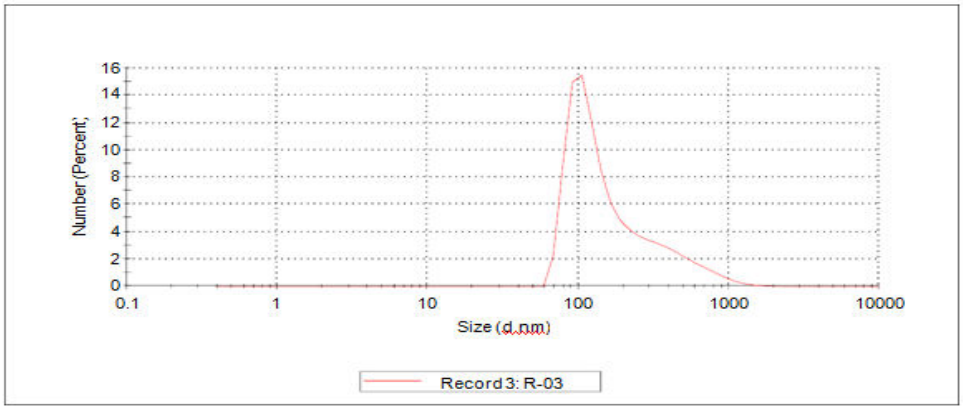

Figure 7: Particle size (F3)

Zeta potential:

DISCUSSION

Zeta potential testing determines particle surface charge and colloidal stability. According to these numbers, all of the ethosomes that have been created are firm. Best was our (F3) formulation having zeta potential **-11.7 mV.**

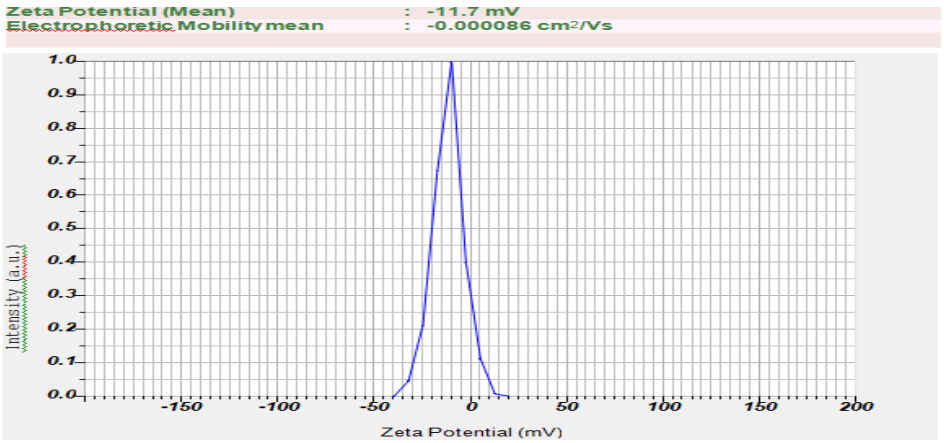

Figure**8**: Zeta potential (F3)

SEM of F3 formulation:

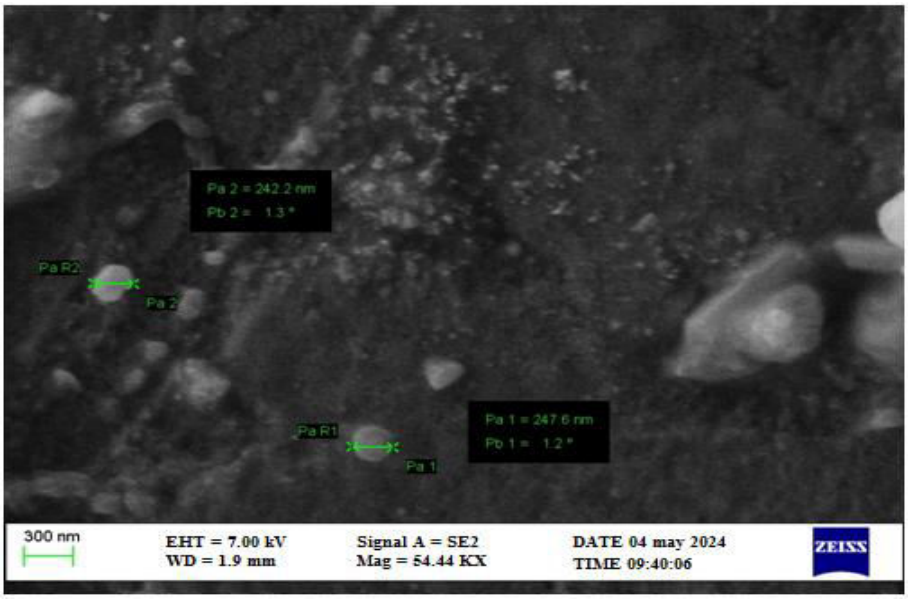

Figure9: SEM (F3)

Discussion

The generated drug-loaded ethosomes were characterised by their shape and morphology using SEM analysis. Scanning electron microscopy was used to capture images of ethosomes that had been produced using benzoyl peroxide and thoroughly dried to remove any moisture content. At 54.44 kx magnification, a scanning electron micrograph revealed that the produced ethosomes had a spherical form and a smooth surface morphology. Using scanning electron microscopy, we were able to make out the ethosomes' smooth surface morphology and round form.

Entrapment efficiency:

Table 12: **Entrapment efficacy**

F1	**F2**	**F3**	**F4**	**F5**
0.240	0.110	0.025	0.190	0.180
0.320	0.121	0.027	0.230	0.200
0.410	0.130	0.108	0.310	0.290
0.510	0.141	0.110	0.408	0.340
Average				
0.37	0.12	0.07	0.28	0.25
Y=mx+c	Y=mx+c	Y=mx+c	Y=mx+c	Y=mx+c
Y=mx	Y=mx	Y=mx	Y=mx	Y=mx
X= 0.37/0.15	X= 0.12/0.15	X= 0.07/0.15	X= 0.28/0.15	X= 0.25/0.15
X1= 2.4 ug	X2= 0.8 ug	X3= 0.4 ug	X4= 1.8 ug	X5= 1.6 ug
D1= 15 ug drug On-double dilution	D1= 15 ug drug On-double dilution	D1= 15 ug drug On-double dilution	D1= 15 ug drug On-double dilution	D1= 15 ug drug On-double dilution
EE%= D1-X1/D1*100	EE%= D1-X2/D1*100	EE%= D1-X3/D1*100	EE%= D1-X4/D1*100	EE%= D1-X5/D1*100
EE%= 15-2.4/15 *100	EE%= 15-0.8/15 *100	EE%= 15-0.4/15 *100	EE%= 15-1.8/15 *100	EE%= 15-1.6/15 *100
EE%= 84%	EE%= 94%	EE%= 97%	EE%= 87%	EE%= 89%

Discussion

This could be because the shifts in polymer concentration caused the entrapment efficiency to vary.The prepared drug entrapped ethosomes possess drug entrapment range (84 to 97). Ethosomes loaded with F3 Benzyl peroxide have a drug entrapment effectiveness in the 97% range, which is very high.

Characterization of Ethosomes loaded Emulgel:

Physical Impression:

Table 13: Physical Impression

S. No	Impression	Result
1.	Homogeneity	Homogeneous
2.	Odour	Odour-less
3.	Colour	White
4.	Appearance	Transparent

Discussion

The gel was examined for its homogeneity, colour, smell, and overall appearance. Upon testing, it was found that Emulgel had a white hue. Previous studies on gel have shown that it is odourless and appears translucent. Gel looked, smelled, and met all of the colour and appearance standards set by the I.P.

Viscosity of Emulgel:

Table 14: Viscosity

S. No	Formulation	Viscosity (cps)
1.	Gel	6891±0.29

Discussion

At 100 revolutions per minute, using spindle no. 61 and the most known Brookfield viscometer, the viscosity was measured. Table 19 displayed the outcome. According to the results, the viscosity of emulgel is 6891 centipoise.

pH determination:

Table 15: pH

S.No.	Formulation	pH
1.	Emulgel	6.6

Discussion

With a pH of6.6, the emulgel formulation is safe for use on the skin since it is within the normal pH range. The relationship between time and pH values was not significantly altered. There was excellent concordance between the developed emulgel formulation's physicochemical characteristics.

Spreadability:

Table 16: Spreadability

S.No	Formulation	Spreadability (g.cm/s)
1.	Emulgel	13.15

Discussion

The ability to be easily spread is a must-have quality for every emulgel. How well a formulation spreads is influenced by its viscosity and the physical properties of the polymers utilised. The spreadability of a thicker formulation would be lower. When applied to the skin, the word "spreadability" indicates the area across which the gel spreads easily. A formulation's spreading value is another factor that determines its medicinal efficacy. We measured a spreadability of 13.15 g cm/s for the emulgel formulation.

Report on skin irritation study:

Table 17 : skin irritation study

S. No	Formulation	Results
1.	Emulgel	Non-irritantion observed

The produced gels did not cause any cutaneous reactions, redness, or irritation when applied, according to the results of a skin irritation test.

Figure 10: Emulgel

In-vitro drug release:

A Franz diffusion cell was employed to obtain the in vitro drug release. The absorbance was next measured using UV-spectroscopy at predetermined intervals.

Table 18: Time interval of Drug release

Time (min)	F1	F2	F3	F4	F5
15	10.5	14.6	15.1	13.5	14.1
30	18.7	28.2	30.2	22.4	25.4
45	26.89	43.8	45.1	33.5	43.5
60	34.62	58.9	65.4	45.6	55.8
120	47.73	70.4	80.3	60.4	67.4
180	50.83	70.6	86.5	60.7	70.5
240	50.78	71.2	87.8	61.5	70.9
300	55.23	71.6	88.5	61.4	71.4
360	55.47	71.9	88.7	61.7	71.4
420	55.69	71.9	88.5	61.9	71.4

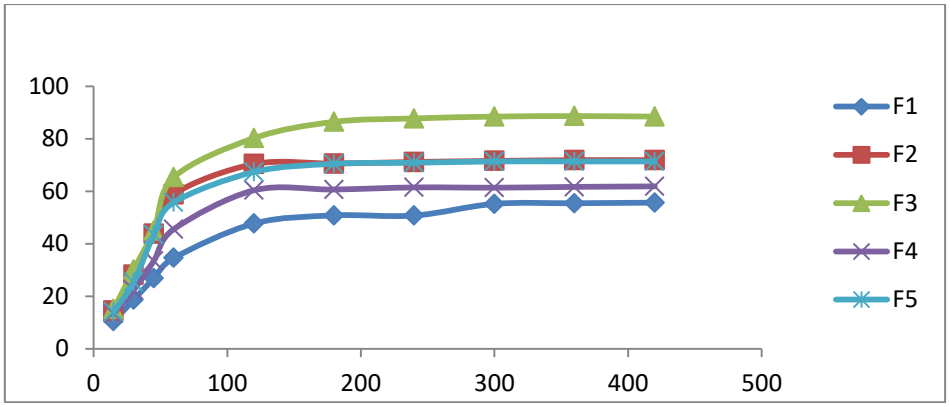

Figure11: Graph of Drug release F1-F5

Release kinetics study of optimized formulation

Figure displayed the statistics for the % medication release formulation. Plots of cumulative percentage of drug release vs time were created for the kinetic investigation in accordance with zero order kinetic models. A zero-order kinetic model explains how a drug delivery system maintains a constant release of the drug at any concentration.

Stability studies

Table 19: Stability Study of F3 formulation (Emulgel)

S. No	Time (Days)	25^0C±2 ^{0}C and 60 ± 5% RH	
		Viscosity	pH
1.	0	6891	6.6
2.	30	6893	6.8
3.	45	6895	7.0
3.	60	6897	7.3
4.	90	6901	7.6

After three months of accelerated stability at 25^0C±2 ^{0}C temperature and 60 ± 5% RH, the formulation was determined to be physically and chemically stable. There was no discernible change in the evaluation metrics, such as the pH studies or viscosity. At various intervals throughout stability investigations, the results of the assay and other evaluation criteria are summarised in Table

Table 20: Stability Study of F3 formulation (Emulgel)

S. No	Time (Days)	40^0C±2 ^{0}C and 70 ±5% RH	
		Viscosity	pH
1.	0	6891	6.6
2.	30	6895	6.7
3.	45	6899	6.9
3.	60	6905	7.5
4.	90	6908	7.8

Simultaneously, accelerated stability at400C±2 ^{0}C temperature and 70 ±5% RH, the formulation was determined to be physically and chemically stable. There was no discernible change in the evaluation metrics, such as the pH studies or viscosity. At various intervals throughout stability investigations, the results of the assay and other evaluation criteria are summarised in Table.

CONCLUSION

The Benzoyl Peroxide ethosomes emulgel is a significant advancement in topical dermatological treatments, particularly in acne management. The emulgel formulation incorporates lipid-based nanocarriers, enhancing drug permeation and enhancing the bioavailability and therapeutic efficacy of Benzoyl Peroxide. The emulgel matrix provides a stable and aesthetically acceptable dosage form, ensuring prolonged contact with the skin. Evaluation studies have shown promising results in drug release profile, skin permeation, stability, and therapeutic efficacy. Further clinical studies are needed to establish its safety profile and effectiveness against existing treatments. The ethosome emulgel is well encapsulated within ethosomes and maintains its pH and physical stability over three months.

REFERENCE

- Roe, D., Karandikar, B., Bonn-Savage, N., Gibbins, B. and Roullet, J. B. (2008). Antimicrobial surface functionalization of plastic catheters by silver nanoparticles. Journal of Antimicrobial Chemotherapy. 61, 869–76
- Hahens WI., Oomen AG., deJong WH., Cassee FR. What do we (need to) know about the kinetic properties of nanoparticles in the body? Regulatory Toxicology and Pharmacology. 2007.
- Couvreur P., Dubernet C., Puisieux F. Controlled drug delivery with Nano particles:current possibilities and future trends. Eur J Pharm Biopharm. 1995.
- ŽeljkaVanic, Phospholipid Vesicles for Enhanced Drug Delivery in Dermatology, J Drug Discov Develop and Deliv. 2014
- SP Vyas, RK Khar. Controlled drug delivery – Concepts and advances VallabhPrakashan New Delhi, FirstEdition. 2002, 173-243.
- Sune B, Folke E, Liisa T.K, Maria R; "Selective enzymatic reactions using microemulsion-based gels." Colloidal and Surfaces B: Biointerfaces. 1995, 4, 121-127.
- Joshi B et al; "Emulgel: A Comprehensive Review on the Recent Advances in Topical Drug Delivery." International Research Journal of Pharmacy. 2011, 2(11), 66-70.
- Gangwar S., Singh S., Garg G., Ethosomes: A Novel toolfor Drug Delivery through the Skin, Journal of PharmacyResearch 2010; 3(4):688-691.
- Stanos, S. P. (2007). Topical agents for the management of musculoskeletal pain. *Journal of pain and symptom management*, *33*(3), 342-355.
- Jain, A., Deveda, P., Vyas, N., Chauhan, J., Khambete, H., & Jain, S. (2011). Development of antifungal emulsion based gel for topical fungal infection (s). *IJPRD*, *2*(12), 18-22.
- Kute, S., &Saudagar, R. (2013). Emulsified gel A Novel approach for delivery of hydrophobic drugs: An overview. *Journal of Advanced Pharmacy Education & Research Oct-Dec*, *3*(4).
- Shivappa, N., Arjun, M., Rohini, B., & Ganesh, N. (2018). Design, development and evaluation of microemulgel containing econazole nitrate. *Int J Curr Res*, *10*(8), 72727-33.

- Sharma, V., Nayak, S. K., Paul, S. R., Choudhary, B., Ray, S. S., & Pal, K. (2018). Emulgels. In *Polymeric Gels* (pp. 251-264). Woodhead Publishing.
- Javed, N., SN, H. S., Saeed, J., Nisar, M., Javed, H., Riaz, R., &Karim, K. (2022). Formulation development and evaluation of transdermal emulgel using Aloevera extract and natural penetration enhancers. *Pakistan Journal of Pharmaceutical Sciences*, *35*(3 (Special)), 953-964.
- Surekha, M., Khan, P. M., Reddy, G. G., Tabassum, S. A., Wilson, K. V., &Siddiqua, S. A. (2019). Emulgel-An Overview. *World Journal of Pharmaceutical Research*, *8*(4), 394-406.
- Maddiboyina, B., Jhawat, V., Ramesh, K., Nakkala, R. K., &Jakka, A. L. (2020). A Review on Nanoparticle Based Herbal Remedies for the Management of Alopecia.
- Heath, C. R., &Usatine, R. P. (2021).Acne vulgaris. Cutis, 108(3).
- Tan, A. U., Schlosser, B. J., &Paller, A. S. (2018).A review of diagnosis and treatment of acne in adult female patients. International journal of women's dermatology, 4(2), 56-71.
- Conforti, C., Giuffrida, R., Fadda, S., Fai, A., Romita, P., Zalaudek, I., &Dianzani, C. (2021).Topical dermocosmetics and acne vulgaris. Dermatologic therapy, 34(1), e14436.
- Fallah, H., &Rademaker, M. (2021).Isotretinoin in the management of acne vulgaris: practical prescribing. International journal of dermatology, 60(4), 451-460.
- Tobiasz, A., Nowicka, D., &Szepietowski, J. C. (2022). Acne vulgaris—Novel treatment options and factors affecting therapy adherence: A narrative review. Journal of Clinical Medicine, 11(24), 7535.
- Makrantonaki, E., Ganceviciene, R., &Zouboulis, C. C. (2011).An update on the role of the sebaceous gland in the pathogenesis of acne. Dermato-endocrinology, 3(1), 41-49.
- Feneran, A. N., Kaufman, W. S., Dabade, T. S., & Feldman, S. R. (2011).Retinoid plus antimicrobial combination treatments for acne. Clinical, Cosmetic and Investigational Dermatology, 79-92.
- Toyoda, M., &Morohashi, M. (2001).Pathogenesis of acne. Medical Electron Microscopy, 34, 29-40.
- Davis, E. C., &Callender, V. D. (2010). A review of acne in ethnic skin: pathogenesis, clinical manifestations, and management strategies. The Journal of clinical and aesthetic dermatology, 3(4), 24.
- Kurokawa, I., Danby, F. W., Ju, Q., Wang, X., Xiang, L. F., Xia, L., ...&Zouboulis, C. C. (2009). New developments in our understanding of acne pathogenesis and treatment. Experimental dermatology, 18(10), 821-832.
- Sari, P. K., Zulkarnain, A. K., &Lukitaningsih, E. (2023). Evaluation of the Physical Properties and Anti-aging Microemulgel Sunscreen Nyamplung Oil (*Calophylluminophyllum L.). Tropical Journal of Natural Product Research*, *7*(2).
- Giri, Y., Habibullah, S., Dixit, P. K., Mahalik, G., Mohanty, B., &Behera, A. (2024). Development of microemulgel formulations with varied permeation enhancers for transungual delivery of luliconazole in onychomycosis management. *Colloids and Surfaces B: Biointerfaces*, *234*, 113718.
- Manure Hirakant, S., &NagobaShivappa, N. Design, Development And Evaluation Of Novel Nanoemulgel For Topical Drug Delivery System.
- Tasneem, R., Khan, H. M. S., Rasool, F., Khan, K. U. R., Umair, M., Esatbeyoglu, T., & Korma, S. A. (2022). Development of Phytocosmeceuticalmicroemulgel containing

flaxseed extract and it's *in vitro* and *in vivo* characterization. *Pharmaceutics*, *14*(8), 1656.