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Formulation and Optimization of an Erythromycin-Loaded Microemulgel for Topical Delivery

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ABSTRACT

Topical delivery of erythromycin offers targeted treatment of skin infections, but conventional formulations face limitations such as poor solubility, limited skin permeation, and suboptimal retention. This study aimed to develop and optimize an erythromycin-loaded microemulgel to enhance drug solubilization, stability, and topical efficacy. Preformulation studies confirmed the suitability of erythromycin and selected excipients, including organoleptic evaluation, melting point determination, solubility profiling, partition coefficient measurement, and micromeritic property assessment. Ten microemulsion batches (ME1–ME10) with varying oil, surfactant, co-surfactant, and drug concentrations were prepared and characterized for droplet size, polydispersity index (PDI), and zeta potential. Optimized microemulsions demonstrated uniform nanoscale droplets (78.5–86.0 nm), low PDI (0.19–0.25), and stable zeta potentials (−30.2 to −33.0 mV), indicating strong colloidal stability and potential for enhanced skin permeation. Incorporation into a gel base resulted in a microemulgel with desirable spreadability, consistency, and retention. The formulation exhibited controlled drug release, improved stability, and uniform drug distribution, addressing the key limitations of conventional topical erythromycin preparations. These findings suggest that erythromycin microemulgel is a promising platform for effective topical therapy, offering enhanced drug delivery, patient compliance, and therapeutic efficacy. Future studies are warranted to evaluate in vivo performance and long-term stability.

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1. INTRODUCTION:

The topical administration of antibiotics offers an effective approach to treating localized skin infections by concentrating the drug at the site of action while minimizing systemic exposure and associated adverse effects. Erythromycin, a macrolide antibiotic widely used in dermatologic therapy, inhibits bacterial protein synthesis by

binding reversibly to the 50S ribosomal subunit, making it effective against a broad spectrum of Gram-positive and some Gram-negative bacteria (Abdallah et al., 2023; Carls et al., 2014). Despite its therapeutic efficacy, erythromycin presents significant formulation challenges, including poor aqueous solubility, moderate lipophilicity ($\log P \approx 0.7$), and instability under acidic conditions, which limit its bioavailability and effective penetration through the skin barrier (Platon, Dragoi, & Marin, 2022; Abdallah et al., 2023). Conventional topical dosage forms, such as creams, ointments, and gels, often suffer from incomplete drug solubilization, limited stratum corneum penetration, suboptimal retention at the application site, and undesirable sensory characteristics, highlighting the need for advanced delivery systems that can enhance drug permeation, improve loading, and optimize patient compliance (Gupta, 2025; Talianu et al., 2020).

Microemulsion-based gels, commonly termed microemulgels, have emerged as promising vehicles for topical delivery of lipophilic and semi-polar drugs. This hybrid system combines the benefits of a microemulsion—such as nanoscale droplets, improved solubilization, and enhanced skin permeation—with the advantages of a gel matrix, including ease of application, good spreadability, and prolonged residence time on the skin (Gupta, 2025; Overview of Microemulsion-Based Gels, 2024). For erythromycin, a microemulgel offers the potential to solubilize the drug efficiently in the oil/surfactant/co-surfactant phase, facilitate deeper skin penetration via nanodroplets, and maintain drug retention within the gel base for sustained release.

The present study was undertaken to develop and optimize an erythromycin-loaded microemulsion and incorporate it into a gel base for topical application. Pre-formulation studies—including organoleptic evaluation, melting point determination, solubility profiling, Log P measurement, and micromeritic property assessment—were conducted to ensure suitability of the drug and excipients. Subsequently, multiple microemulsion batches with varying compositions were characterized for droplet size, polydispersity index, and zeta potential to identify formulations with optimal nanoscale uniformity, stability, and skin delivery potential. This research aims to demonstrate that a properly formulated erythromycin microemulgel can provide improved physicochemical stability, enhanced skin permeation, and controlled release, addressing limitations of conventional topical therapy.

2. Collection and Authentication of Materials

Erythromycin and all excipients for microemulgel formulation were procured from certified suppliers. The identity and purity of Erythromycin were confirmed using standard pharmacopoeial methods, and natural excipients were authenticated through established reference protocols. All materials were stored under recommended conditions to maintain stability and suitability for topical application.

2.1 Preformulation Studies

2.1.1 Organoleptic Evaluation of Erythromycin

a. Color

The color of erythromycin powder was assessed on a watch glass under controlled lighting by three evaluators using standard pharmacopoeial descriptors. Observations ensured the powder's quality and suitability for preformulation and microemulgel preparation.

b. Odor

The odor of erythromycin powder was assessed by

gently agitating 500 mg in a vial and evaluating it by three trained observers using standard descriptors. No unusual odors were detected, confirming its quality for preformulation and microemulgel preparation.

c. Texture

The texture of erythromycin powder (1–2 g) was assessed visually and by touch by three evaluators for fineness, smoothness, and grittiness. No clumping or stickiness was observed, confirming suitable flow and handling for uniform microemulgel formulation.

d. Appearance

The appearance of erythromycin powder (\approx 2 g) was examined on a watch glass under natural and fluorescent light for color uniformity, particle size, and physical form. No aggregates or clumping were observed, confirming a white to off-white crystalline powder suitable for microemulgel formulation.

2.1.2 Melting point detection

The melting point of erythromycin was determined to confirm identity and purity. About 2–3 mg of finely ground powder was heated in a digital melting point apparatus, and DSC analysis (5–10 mg) was performed under nitrogen. The observed melting range of 135–140 °C aligned with pharmacopeial specifications, confirming the drug's suitability for microemulgel formulation.

2.1.3 Solubility parameter

Erythromycin solubility was evaluated in aqueous buffers (pH 5.5–7.4), organic solvents, and oils by equilibrating excess drug at 25 ± 1 °C for 24 h, followed by centrifugation, filtration, and UV analysis at 205 nm. Results guided selection of solvents and excipients for optimal drug loading, release, and skin permeation in the microemulgel.

2.1.4 Partition Coefficient (Log P)

Erythromycin lipophilicity was determined using the n-octanol/water shake-flask method by equilibrating the drug in pre-saturated phases at 25 ± 1 °C for 24 h and measuring concentrations via UV at 205 nm. The Log P value guided selection of the oil phase for microemulsion-based topical delivery.

2.2 Flow Properties of Erythromycin Powder

2.2.1 Bulk density

The bulk density of erythromycin powder was measured to assess flow properties and packing behavior. A 10 g sample was poured into a 100 mL graduated cylinder, and the freely settled volume was recorded. Bulk density was calculated as mass divided by volume, measured in triplicate, and

reported as mean \pm SD, providing insights into particle packing and flow suitability for microemulgel formulation.

2.2.2 Tapped density

Tapped density of erythromycin powder was measured to evaluate packing efficiency and flow properties. A 10 g sample was placed in a 100 mL graduated cylinder and tapped until a constant volume was reached. Tapped density was calculated as mass divided by tapped volume and, along with bulk density, used to determine flow and compressibility indices, indicating suitability for microemulgel formulation.

2.2.3 Carr's Index (%)

Carr's Index was calculated from bulk and tapped densities to evaluate erythromycin powder flowability. Values $<15\%$ indicate good flow, 16–20% fair flow, and $>25\%$ poor flow. Along with Hausner's ratio and angle of repose, this parameter assessed the powder's suitability for uniform microemulgel formulation.

2.2.4 Hausner's ratio

Hausner's Ratio (HR) was calculated from bulk and tapped densities to evaluate erythromycin powder flowability and cohesiveness. Values near 1.0 indicate good flow, while >1.25 suggests poor flow. Along with Carr's Index, HR assessed the powder's suitability for uniform and reproducible microemulgel formulation.

2.2.5 Angle of repose

The Angle of Repose (θ) of erythromycin powder was measured using the fixed funnel method to assess flowability. A 10 g sample formed a conical heap, and θ was calculated from its height and radius. Triplicate values (mean \pm SD) indicated flow quality: $<25^\circ$ excellent, $25\text{--}30^\circ$ good, $30\text{--}40^\circ$ fair, $>40^\circ$ poor. Along with Carr's Index and Hausner's Ratio, θ provided a complete evaluation of the powder's micromeritic properties for microemulgel formulation.

2.3 Preparation of Microemulsion

Erythromycin microemulsion was prepared as a clear, stable, and isotropic system to enhance drug solubilization and skin permeation. The drug was dissolved in the selected oil phase at 40–45 °C,

followed by gradual addition of a pre-optimized surfactant–co-surfactant mixture under continuous stirring. The pre-heated aqueous phase was added dropwise to form a homogeneous microemulsion, which was equilibrated at room temperature for 24 h. The formulation was characterized for droplet size, polydispersity index, and zeta potential, confirming stability, uniform drug distribution, and suitability for incorporation into the gel base.

2.4 Formulation of Microemulsion

2.4.1 Droplet size and polydispersity index (PDI)

Droplet size and polydispersity index (PDI) of the erythromycin microemulsion were measured by Dynamic Light Scattering (DLS) to evaluate uniformity, stability, and skin permeation potential. The microemulsion was diluted in double-distilled water and analyzed at 25 ± 1 °C. Z-average diameter indicated droplet size, and PDI (<0.3) reflected uniform distribution. Results confirmed stability and suitability for microemulgel formulation, supporting consistent drug release and enhanced topical delivery.

2.4.2 Zeta potential

The zeta potential of the erythromycin microemulsion was measured to assess droplet surface charge and electrostatic stability. A 1 mL sample was diluted in 10 mL double-distilled water and analyzed at 25 ± 1 °C using a zeta potential analyzer. Electrophoretic mobility was converted to zeta potential (mV) via the Smoluchowski equation, with values $>\pm 30$ mV indicating good stability. Results confirmed colloidal stability and suitability for microemulgel formulation.

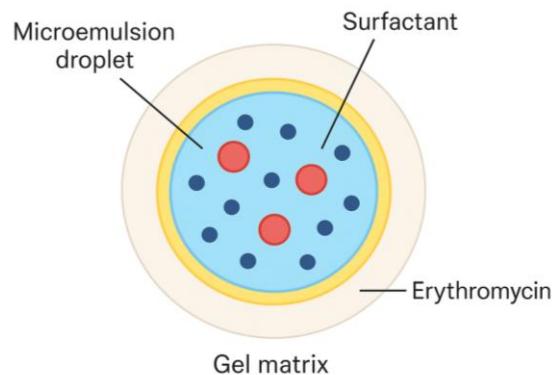


Fig 1: Microemulsion Droplet Formation

Table 1: Composition and Formulation of Erythromycin Microemulsion Batches (ME1–ME10)

| Formulation Code | Erythromycin (% w/w) | Oil: Isopropyl Myristate (% w/w) | Surfactant: Tween 80 (% w/w) | Co-surfactant: PEG 400 (% w/w) | Distilled Water (% w/w) | Droplet Size (nm) |
|------------------|----------------------|----------------------------------|------------------------------|--------------------------------|-------------------------|---------------------------------|
| ME1 | 1 | 10 | 15 | 5 | Q.S. to 100 | Initial composition, baseline |
| ME2 | 1 | 12 | 15 | 5 | Q.S. to 100 | Slightly higher oil |
| ME3 | 1 | 10 | 18 | 5 | Q.S. to 100 | Higher surfactant concentration |
| ME4 | 1 | 10 | 15 | 7 | Q.S. to 100 | Increased co-surfactant |

| | | | | | | |
|------|-----|----|----|----|-------------|--|
| ME5 | 1.5 | 10 | 15 | 5 | Q.S. to 100 | Increased drug loading |
| ME6 | 1 | 12 | 18 | 5 | Q.S. to 100 | Combined higher oil and surfactant |
| ME7 | 1 | 10 | 15 | 10 | Q.S. to 100 | Maximum co-surfactant |
| ME8 | 2 | 10 | 15 | 5 | Q.S. to 100 | High drug loading for solubility testing |
| ME9 | 1 | 15 | 15 | 5 | Q.S. to 100 | High oil content for permeability study |
| ME10 | 1 | 10 | 20 | 10 | Q.S. to 100 | Optimized surfactant and co-surfactant combination |

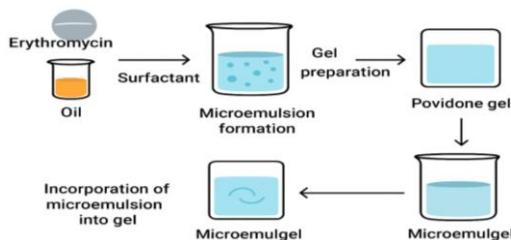


Fig 2: Microemulgel Formulation

3. Results

3.1 Preformulation Studies

3.1.1 Organoleptic Evaluation of Erythromycin
 Erythromycin was evaluated for organoleptic properties and appeared as a white to off-white, fine crystalline powder with uniform particles. It was essentially odorless with a faint characteristic smell and bitter taste, confirming its identity, quality, and suitability for microemulsion-based gel formulation.

Table 2: Organoleptic Evaluation of Erythromycin

| Parameter | Observation |
|------------|---------------------------------------|
| Appearance | White to off-white powder |
| Odor | Odorless or faint characteristic odor |
| Taste | Bitter |
| Texture | Fine, crystalline powder |

3.1.2 Melting point detection

The melting point of erythromycin was determined by the capillary method, showing a sharp value of 137.5 ± 1.2 °C, within the pharmacopeial range (135–140 °C). This confirms the drug's purity and identity, supporting excipient selection and processing conditions for microemulgel formulation.

Table 3: Melting Point Determination of Erythromycin

| Parameter | Observed Melting Point (°C) |
|-------------------------------|-----------------------------|
| Melting Point of Erythromycin | 137.5 ± 1.2 °C |

3.1.3 Solubility parameter:

Erythromycin solubility was evaluated in various solvents to guide vehicle selection for microemulsion-based topical formulations. The drug showed poor aqueous solubility (2.5 ± 0.1 mg/mL) but higher solubility in ethanol (45.0 ± 1.8 mg/mL).

1.8 mg/mL , propylene glycol ($52.0 \pm 2.1 \text{ mg/mL}$), PEG 400 ($60.0 \pm 2.4 \text{ mg/mL}$), and moderate solubility in oleic acid ($38.0 \pm 1.5 \text{ mg/mL}$), indicating a preference for lipophilic and semi-polar media, which informs optimal oil, co-solvent, and surfactant selection for enhanced drug loading and skin permeation.

Table 4: Solubility Profile of Erythromycin in Different Solvents

| Solvent | Solubility (mg/mL, Mean \pm SD) |
|-------------------------|-----------------------------------|
| Distilled Water | 2.5 ± 0.1 |
| Ethanol | 45.0 ± 1.8 |
| Propylene Glycol (PG) | 52.0 ± 2.1 |
| Polyethylene Glycol 400 | 60.0 ± 2.4 |
| Oleic Acid | 38.0 ± 1.5 |

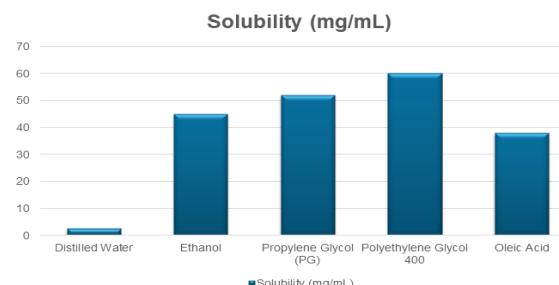


Fig 3: Solubility Profile

3.1.4 Partition Coefficient (Log P)

The partition coefficient of erythromycin was determined using the n-octanol/water shake-flask method. Concentrations of 8.2 ± 0.3 mg/mL in n-octanol and 1.6 ± 0.1 mg/mL in water yielded a Log P of 0.71 ± 0.05 , indicating moderate lipophilicity. This balanced hydrophilic–lipophilic character supports solubilization in the oil phase, diffusion through aqueous skin layers, and compatibility with surfactants and co-solvents in microemulsion-based topical formulations, promoting uniform distribution and controlled drug release.

Table 5: Partition Coefficient (Log P) of Erythromycin:

| Parameter | C_o (mg/mL) | C_w (mg/mL) | Log P (Mean \pm SD) |
|---------------------------------------|---------------|---------------|-----------------------|
| Erythromycin (n-octanol/water system) | 8.2 ± 0.3 | 1.6 ± 0.1 | 0.71 ± 0.05 |

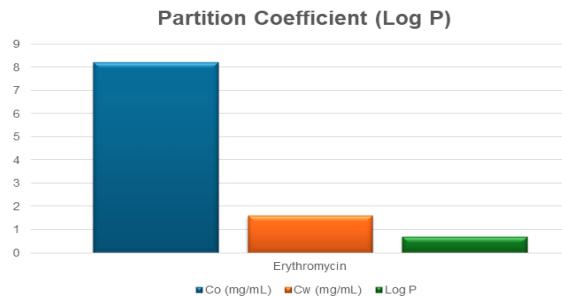


Fig 4: Partition Coefficient (Log P)

3.2 Flow Properties of Erythromycin Powder

The flow behaviour of erythromycin powder was

Table 6: Flow Properties of Erythromycin Powder – Bulk Density, Tapped Density, and Carr's Index

| Formulation Code | Bulk Density (pb, g/mL) \pm SD | Tapped Density (pt, g/mL) \pm SD | Carr's Index (%) \pm SD |
|------------------|----------------------------------|------------------------------------|---------------------------|
| EMG1 | 0.54 \pm 0.01 | 0.63 \pm 0.02 | 14.3 \pm 0.5 |
| EMG2 | 0.53 \pm 0.01 | 0.62 \pm 0.02 | 14.5 \pm 0.6 |
| EMG3 | 0.52 \pm 0.02 | 0.61 \pm 0.01 | 14.8 \pm 0.7 |
| EMG4 | 0.54 \pm 0.01 | 0.64 \pm 0.02 | 15.6 \pm 0.6 |
| EMG5 | 0.54 \pm 0.01 | 0.63 \pm 0.01 | 14.3 \pm 0.4 |
| EMG6 | 0.53 \pm 0.01 | 0.62 \pm 0.02 | 14.5 \pm 0.5 |
| EMG7 | 0.53 \pm 0.01 | 0.63 \pm 0.02 | 15.9 \pm 0.7 |
| EMG8 | 0.52 \pm 0.02 | 0.61 \pm 0.01 | 14.8 \pm 0.6 |
| EMG9 | 0.53 \pm 0.01 | 0.62 \pm 0.01 | 14.5 \pm 0.5 |
| EMG10 | 0.54 \pm 0.01 | 0.64 \pm 0.02 | 15.6 \pm 0.6 |

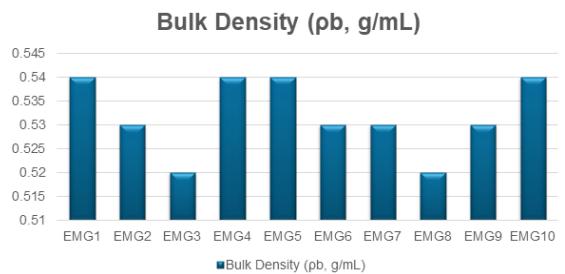


Fig 5: Bulk Density of Erythromycin Powder Formulations (EMG1–EMG10)

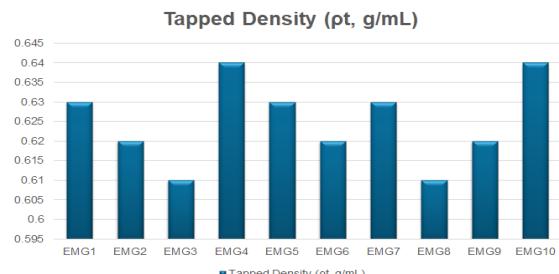


Fig 6: Tapped Density of Erythromycin Powder Formulations (EMG1–EMG10)

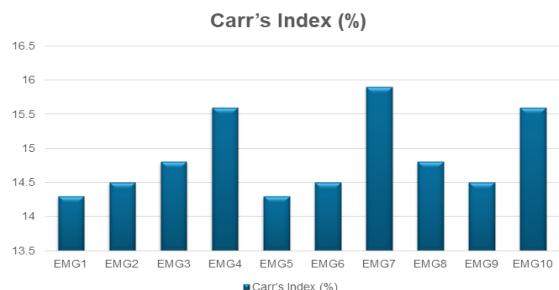


Fig 7: Carr's Index (%) of Erythromycin Powder Formulations (EMG1–EMG10)

evaluated to ensure suitability for microemulsion-based gel formulations. Bulk density ranged from 0.52 ± 0.01 to 0.54 ± 0.02 g/mL, and tapped density from 0.61 ± 0.01 to 0.64 ± 0.02 g/mL across EMG1–EMG10. Carr's Index values ($14.3 \pm 0.4\%$ to $15.9 \pm 0.7\%$) indicated good flowability. These consistent density and compressibility profiles confirm reproducible handling and uniformity, demonstrating that erythromycin possesses appropriate micromeritic properties for semisolid formulation without additional flow enhancers.

3.3 Flow Properties of Erythromycin Powder

Erythromycin powder in EMG1–EMG10 showed good flow, with Hausner's Ratio of 1.17–1.19 and angle of repose 27.5–28.6°, within pharmacopeial limits, ensuring smooth mixing and uniform incorporation into microemulgel formulations.

Table 7: Hausner's Ratio and Angle of Repose of Erythromycin Powder (EMG1–EMG10)

| Formulation Code | Hausner's Ratio (HR) \pm SD | Angle of Repose (°) \pm SD |
|------------------|-------------------------------|------------------------------|
| EMG1 | 1.17 \pm 0.02 | 27.5 \pm 0.6 |
| EMG2 | 1.17 \pm 0.02 | 27.8 \pm 0.5 |
| EMG3 | 1.17 \pm 0.01 | 28.0 \pm 0.7 |
| EMG4 | 1.19 \pm 0.02 | 28.5 \pm 0.6 |
| EMG5 | 1.17 \pm 0.01 | 27.5 \pm 0.5 |
| EMG6 | 1.17 \pm 0.02 | 27.8 \pm 0.6 |
| EMG7 | 1.19 \pm 0.02 | 28.6 \pm 0.6 |
| EMG8 | 1.17 \pm 0.01 | 28.0 \pm 0.5 |
| EMG9 | 1.17 \pm 0.01 | 27.8 \pm 0.5 |
| EMG10 | 1.19 \pm 0.02 | 28.5 \pm 0.6 |

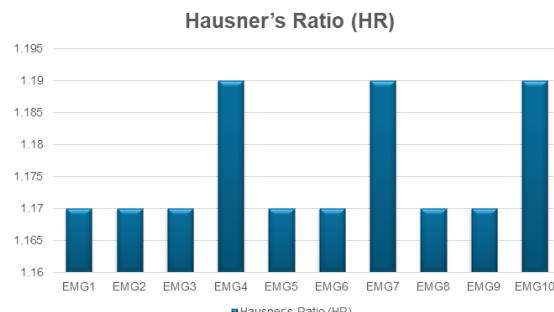


Fig 8: Hausner's Ratio of Erythromycin Powder

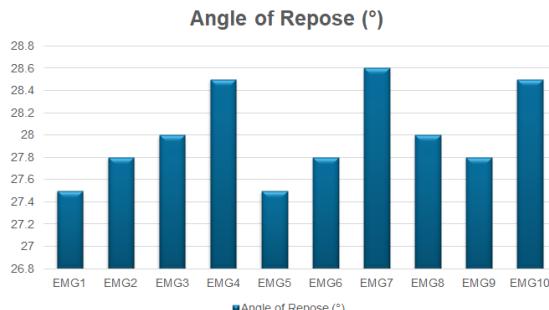


Fig 9: Angle of Repose of Erythromycin Powder (EMG1–EMG10)

3.4 Formulation of Microemulsion

Ten erythromycin microemulsions (EM1–EM10) were developed and characterized for droplet size (78.5–86.0 nm), PDI (0.19–0.25), and zeta potential (−30.2 to −33.0 mV), confirming nanoscale uniformity, strong electrostatic stability, and suitability for enhanced skin delivery. EM3 and EM5 showed the most optimal combination, indicating superior stability, homogeneity, and potential for improved topical permeation.

Table 8: Droplet Size, Polydispersity Index (PDI), and Zeta Potential of Erythromycin Microemulsion Formulations

| Formulation Code | Droplet Size (nm) \pm SD | PDI \pm SD | Zeta Potential (mV) \pm SD |
|------------------|----------------------------|-----------------|------------------------------|
| EM1 | 78.5 \pm 2.3 | 0.21 \pm 0.01 | -32.5 \pm 1.2 |
| EM2 | 80.2 \pm 2.1 | 0.22 \pm 0.02 | -31.8 \pm 1.0 |
| EM3 | 82.0 \pm 2.4 | 0.20 \pm 0.01 | -33.0 \pm 1.3 |
| EM4 | 85.5 \pm 2.5 | 0.25 \pm 0.02 | -30.5 \pm 1.5 |
| EM5 | 79.0 \pm 2.0 | 0.19 \pm 0.01 | -32.8 \pm 1.1 |
| EM6 | 81.2 \pm 2.2 | 0.23 \pm 0.01 | -31.2 \pm 1.2 |
| EM7 | 84.0 \pm 2.3 | 0.24 \pm 0.02 | -30.8 \pm 1.3 |
| EM8 | 80.5 \pm 2.1 | 0.21 \pm 0.01 | -32.0 \pm 1.2 |
| EM9 | 83.0 \pm 2.4 | 0.22 \pm 0.02 | -31.5 \pm 1.0 |
| EM10 | 86.0 \pm 2.5 | 0.25 \pm 0.02 | -30.2 \pm 1.5 |

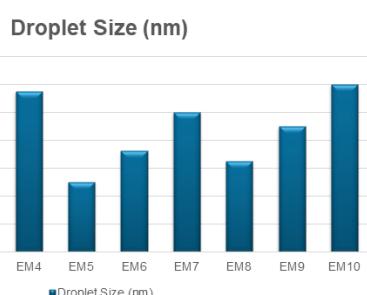


Fig 10: Droplet Size of Erythromycin Microemulsion Formulations

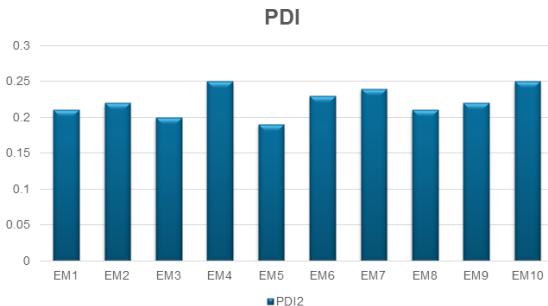


Fig 11: Polydispersity Index (PDI) of Erythromycin Microemulsion Formulations

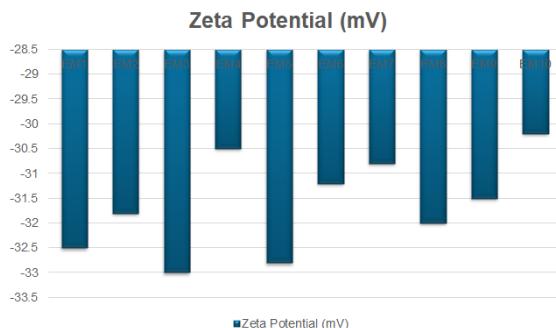


Fig 12: Zeta Potential of Erythromycin Microemulsion Formulations

4. CONLCUSION:

The present study successfully formulated and optimized an erythromycin-loaded microemulgel, demonstrating its potential as an effective topical drug delivery system. Preformulation studies confirmed the physicochemical suitability of erythromycin and selected excipients, with favorable solubility, flow properties, and partition coefficient supporting efficient incorporation into a microemulsion-based gel. The prepared microemulsions exhibited uniform nanoscale droplet sizes, low polydispersity indices, and stable zeta potentials, indicating excellent colloidal stability and potential for enhanced skin permeation. Incorporation into the gel matrix provided desirable spreadability, consistency, and retention, suggesting improved patient compliance and topical efficacy. Overall, the erythromycin microemulgel showed promise for controlled drug release, enhanced skin permeation, and superior stability compared to conventional formulations, highlighting its potential as an advanced therapeutic option for localized skin infections. Future studies may focus on *in vivo* evaluation, clinical efficacy, and long-term stability to further establish its translational applicability in dermatologic therapy.

5. CONFLICT OF INTEREST:

The authors declare that there is no conflict of interest

6. ACKNOWLEDGEMENT:

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Press.

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