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Development and Characterization of Erythromycin-Loaded Microemulgel for Enhanced Topical Antibacterial Therapy.

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ABSTRACT:

This study aimed to formulate and evaluate an optimized erythromycin-loaded microemulgel to enhance topical delivery, skin permeation, and antibacterial efficacy. Microemulsions (ME1–ME10) were prepared using isopropyl myristate or oleic acid, Tween-80, PEG-400, and water, producing transparent, phase-stable systems with droplet sizes of 20–100 nm. These were incorporated into povidone gel bases (GB1–GB10) to form microemulgels (EMG1–EMG10), which were assessed for physicochemical properties, in vitro release, ex vivo permeation, antibacterial activity, and stability. All formulations showed smooth appearance, uniform drug content (98.5–99.5%), pseudoplastic behavior, and skin-compatible pH. The optimized formulation demonstrated sustained drug release (89.5% at 12 h) and significantly higher permeation (850 ± 15 µg/cm²) than the marketed gel. Antibacterial studies showed enhanced activity, with EMG5 exhibiting the largest inhibition zones. Stability testing confirmed consistent performance under accelerated and long-term conditions. Overall, the erythromycin microemulgel offers improved permeation, controlled release, and superior antibacterial efficacy for topical therapy.

1. INTRODUCTION:

Topical drug delivery remains one of the most effective and patient-friendly approaches for the management of localized skin infections, offering advantages such as targeted delivery, reduced systemic toxicity, and improved patient compliance (Arif et al., 2023; Prausnitz& Langer, 2008). Conventional topical formulations such as creams, ointments, and gels often suffer from limitations, including poor skin permeability, variable drug release, and inadequate retention at the site of infection (Singh et al., 2020). These drawbacks are particularly significant

for drugs such as erythromycin, a macrolide antibiotic widely used in dermatology for treating acne vulgaris and bacterial skin infections caused by *Staphylococcus aureus* and *Streptococcus* species (Abdallah et al., 2023; Leyden, 2017). Although erythromycin is effective, its therapeutic potential is restricted by low aqueous solubility, instability at acidic pH, and limited skin penetration when used in conventional topical formulations (Shah et al., 2020).

Advancements in drug delivery technologies have led to the development of microemulsion-based systems, which offer superior solubilization, enhanced permeation, and improved drug thermodynamic activity on the skin surface (Kogan & Garti, 2006; Lawrence & Rees, 2012). Microemulsions are thermodynamically stable, isotropic dispersions of oil, water, surfactant, and co-surfactant with droplet sizes typically below 100 nm, enabling increased diffusion and facilitated penetration through the stratum corneum (Eccleston, 2013). When incorporated into a gel matrix to form microemulgels, these systems combine the high drug-loading and permeation capabilities of microemulsions with the desirable rheology, spreadability, and patient acceptability of hydrogels (Khurana et al., 2013). Microemulgels also exhibit superior stability and controlled release properties compared to conventional gels, making them promising candidates for enhanced topical antimicrobial therapy (Kute et al., 2021).

Given the physicochemical limitations of erythromycin and the rising need for improved topical antimicrobial formulations, the development of an optimized erythromycin-loaded microemulgel offers a strategic approach to enhance solubility, permeation, dermal retention, and therapeutic efficacy. Previous studies have demonstrated that microemulsion-based systems can significantly enhance erythromycin release and antibacterial activity (Morsi et al., 2014), but limited literature exists on systematically optimized microemulgel systems incorporating microemulsions with tailored rheological and permeation characteristics.

Therefore, the present study aims to formulate, optimize, and comprehensively evaluate an erythromycin microemulgel with enhanced topical performance. The work includes microemulsion preparation, gel base optimization, microemulgel formulation, and a full suite of evaluations such as physicochemical characterization, in vitro release, ex vivo permeation, antibacterial efficacy, and stability profiling. This systematic investigation supports the development of an improved and clinically relevant topical erythromycin formulation with enhanced therapeutic potential.

2. Preparation of Microemulgel:

The erythromycin microemulgel was prepared using a **sys**tematic approach:

Step 1: Formulation of Optimized Microemulsion

Erythromycin was solubilized in selected oils (isopropyl myristate or oleic acid) under mild heating, followed by the addition of optimized surfactant–co-surfactant mixtures (Tween 80 and PEG 400) to form a clear, isotropic solution. The aqueous phase was incorporated dropwise to produce transparent and stable microemulsions with droplet sizes of 20–100 nm, polydispersity indices of 0.1–0.3, and zeta potentials of ±30 mV. After equilibration at room temperature for 30 minutes, only clear and phase-stable microemulsions (ME1–ME10) were selected for subsequent microemulgel formulation.

Step 2: Preparation of Gel Base

Gel Base Preparation: Povidone (2–5% w/w, GB1–GB10) was dispersed in distilled water with mechanical stirring (500–600 rpm) and allowed to hydrate for 1–2 hours to achieve complete swelling. Gel viscosity was optimized by adjusting povidone concentration to obtain a semisolid, spreadable consistency (target 5000–8000 cP). The pH was then adjusted to 5.5–6.5 using triethanolamine to ensure skin compatibility and erythromycin stability.

Table 1: Gel Base Formulations (GB1–GB10) Using Povidone As The Gelling Agent

Gel Base Code	Povidone (% w/w)	Distilled Water (% w/w)	pH Adjuster (Triethanolamine, % w/w)	Hydration Time (h)	Viscosity (cP)
GB1	2	Q.S. to 100	0.1–0.2	1–2	Low polymer concentration, low viscosity
GB2	2.5	Q.S. to 100	0.1–0.2	1–2	Slightly higher viscosity
GB3	3	Q.S. to 100	0.1–0.2	1–2	Moderate viscosity,

					suitable for topical application
GB4	3.5	Q.S. to 100	0.1–0.2	1–2	Higher viscosity, good retention on skin
GB5	4	Q.S. to 100	0.1–0.2	1–2	Stiff gel, slower spreadability
GB6	4.5	Q.S. to 100	0.1–0.2	1–2	Very viscous, good for controlled release
GB7	5	Q.S. to 100	0.1–0.2	1–2	Maximum polymer concentration tested
GB8	2	Q.S. to 100	0.15–0.25	1–2	Variation in pH adjuster to study effect on gel
GB9	3	Q.S. to 100	0.15–0.25	1–2	Medium viscosity with higher pH adjustment
GB10	4	Q.S. to 100	0.15–0.25	1–2	Stiff gel with increased pH modifier

Step 3: Incorporation of Microemulsion into Gel Base

The optimized microemulsions (ME1–ME10) were incorporated into hydrated povidone gel bases (GB1–GB10) in a 1:1 ratio and gently stirred (200–300 rpm) until homogeneous, smooth, and translucent. Formulations (MG1–MG10) were equilibrated at 25 ± 2 °C for 24 hours and monitored for phase separation, syneresis, or precipitation. Stable microemulgels were then filled into airtight, light-resistant aluminum tubes, labeled, and stored at 25 ± 2 °C and 60% RH for further physicochemical characterization, in vitro release, antibacterial activity, and stability studies.

Table 2: Composition and Formulation of Erythromycin Microemulgel Batches (MG1–MG10)

Microemulgel Code	Erythromycin Microemulsion (% w/w)	Gel Base (% w/w)	Total Drug Content (% w/w)	Remarks
MG1	ME1 (50)	GB1 (50)	0.5	Initial formulation, low viscosity
MG2	ME2 (50)	GB2 (50)	0.5	Slightly higher oil in ME
MG3	ME3 (50)	GB3 (50)	0.5	Higher surfactant, moderate viscosity
MG4	ME4 (50)	GB4 (50)	0.5	Increased co-surfactant, higher viscosity
MG5	ME5 (50)	GB5 (50)	0.75	Increased drug loading
MG6	ME6 (50)	GB6 (50)	0.5	High oil + surfactant combination
MG7	ME7 (50)	GB7 (50)	0.5	Maximum polymer, maximum co-surfactant
MG8	ME8 (50)	GB3 (50)	1.0	High drug loading for solubility testing
MG9	ME9 (50)	GB4 (50)	0.5	High oil content for permeability study
MG10	ME10 (50)	GB5 (50)	0.5	–

3. Evaluation of Microemulgel:

3.1 Physical Appearance and Homogeneity:

The physical appearance and homogeneity of the erythromycin microemulgel were evaluated to ensure uniformity and absence of defects. Samples were visually inspected for color, clarity, consistency, and smoothness, and homogeneity was confirmed by spreading gel from different regions to check for uniform texture. The test was performed in triplicate to ensure reproducibility and consistent drug distribution.

3.2 Viscosity:

The viscosity of the erythromycin microemulgel was measured using a rotational viscometer at 25 ± 1 °C to assess rheology and topical suitability. About 10 g of gel was tested at spindle speeds of 5–50 rpm, with readings stabilized for 60–90 s and performed in triplicate. Data confirmed pseudoplastic flow and guided formulation optimization for ease of spreading, skin retention, and patient acceptability.

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Fig 1: Rotational Viscometer

3.3 pH Measurement:

The pH of the erythromycin microemulgel was measured using a 10% w/v dispersion in distilled water, equilibrated for 30 min at 25 ± 1 °C. Readings were taken with a calibrated digital pH meter in triplicate. Maintaining a pH of 5.5–6.5 ensures skin compatibility, drug stability, and patient acceptability, confirming suitability for topical use.

3.4 Spreadability:

The spreadability of the erythromycin microemulgel was evaluated to assess ease of application and uniform drug distribution. About 0.5 g of gel was placed between two glass slides under a 500 g weight for 5 minutes, and the spread diameter was measured. Tests were performed in triplicate, with higher values indicating better spreadability, complementing viscosity and homogeneity assessments for optimal topical performance.

3.5 Extrudability:

The extrudability of erythromycin microemulgel was assessed by applying uniform pressure on gel-filled aluminum tubes to measure the force required to extrude a 0.5 g ribbon. Observations for smoothness and uniformity were recorded. Lower extrusion force indicates better patient usability, complementing viscosity and spreadability data for optimal topical application.

3.6 Drug Content Uniformity:

Drug content uniformity of the erythromycin microemulgel was evaluated by dispersing 1 g of gel in 100 mL phosphate buffer (pH 6.8), followed by stirring, filtration, and UV analysis at 205 nm. Triplicate measurements from different regions confirmed consistent drug distribution, reproducibility, and suitability for reliable topical therapy.

4. In Vitro Drug Release Study:

The in vitro release of erythromycin from the microemulgel was evaluated using a Franz diffusion cell with a cellulose acetate membrane or excised animal skin. The receptor compartment contained phosphate buffer (pH 6.8) with 20% ethanol, maintained at 37 ± 0.5 °C with stirring at 100 rpm. About 1 g of microemulgel was applied to the donor side, and samples were withdrawn at predetermined intervals up to 12 hours, replaced with fresh buffer, and analyzed by UV spectrophotometry at 205 nm. Measurements were performed in triplicate, and cumulative drug release was plotted against time to assess controlled release, potential skin penetration, and therapeutic efficacy of the formulation.

5. Ex Vivo Skin Permeation Study:

The ex vivo skin permeation of the erythromycin microemulgel was evaluated using freshly excised rat dorsal skin, which was carefully cleaned to remove subcutaneous fat and washed with phosphate-buffered saline (PBS, pH 7.4). The skin was mounted on a vertical Franz diffusion cell with the stratum corneum facing the donor compartment. A defined amount of the microemulgel was applied uniformly on the donor side, while the receptor compartment was filled with PBS (pH 7.4) maintained at 32 ± 0.5 °C to mimic physiological skin temperature, with continuous magnetic stirring to ensure uniform distribution. Samples of receptor fluid were withdrawn at

predetermined intervals and replaced with fresh PBS to maintain sink conditions. The amount of erythromycin permeated was quantified using a validated analytical method (UV-spectrophotometry or HPLC), and cumulative drug permeation was plotted against time. Key parameters, including flux, permeability coefficient, and skin retention, were calculated to assess the formulation's potential for enhanced topical delivery compared to a standard marketed gel.

6. In Vitro Antibacterial Study:

The antibacterial activity of the erythromycin microemulgel was evaluated using the agar well diffusion method against Staphylococcus aureus and Escherichia coli. Nutrient agar plates were inoculated with log-phase bacterial cultures, and 6–8 mm wells were filled with 100 µL of the microemulgel. A marketed erythromycin gel served as a positive control, and a blank gel as a negative control. Plates were incubated at 37 °C for 24 hours, and zones of inhibition were measured in millimeters. Experiments were performed in triplicate, providing a quantitative assessment of antibacterial efficacy and drug diffusion from the gel, allowing comparison with conventional formulations.

7. Stability Studies:

Stability studies of the erythromycin microemulgel were conducted under accelerated (40 ± 2 °C, 75 ± 5% RH) and long-term (25 ± 2 °C, 60 ± 5% RH) conditions for up to 12 months. Samples were withdrawn at predetermined intervals and evaluated for physical appearance, homogeneity, phase separation, syneresis, pH, viscosity, spreadability, extrudability, and drug content uniformity, as well as microbial contamination. These studies ensured the formulation maintained its physicochemical, mechanical, and therapeutic properties, providing data for shelf-life prediction, packaging, storage, and formulation optimization.

8. RESULTS:

8.1 Evaluation of Microemulgel

All erythromycin microemulgel formulations (EMG1–EMG10) exhibited a smooth, translucent, off-white appearance with no visible lumps, aggregates, or undissolved drug, indicating uniform incorporation of the microemulsion into the gel matrix. Homogeneity assessment from multiple container regions confirmed even distribution of microemulsion droplets and structural integrity, with no syneresis, sedimentation, or precipitation. These findings demonstrate consistent texture, aesthetic acceptability, and reliable drug delivery, supporting their suitability for further physicochemical, rheological, and in vitro evaluations.

Table 3: Physical Appearance and Homogeneity of Erythromycin Microemulgel Formulations

Formulation Code	Physical Appearance	Homogeneity
EMG1	Translucent, smooth, off-white	Uniform, no lumps
EMG2	Translucent, smooth, off-white	Uniform, no lumps
EMG3	Translucent, smooth, off-white	Uniform, no lumps
EMG4	Translucent, smooth, off-white	Uniform, no lumps
EMG5	Translucent, smooth, off-white	Uniform, no lumps
EMG6	Translucent, smooth, off-white	Uniform, no lumps
EMG7	Translucent, smooth, off-white	Uniform, no lumps
EMG8	Translucent, smooth, off-white	Uniform, no lumps
EMG9	Translucent, smooth, off-white	Uniform, no lumps
EMG10	Translucent, smooth, off-white	Uniform, no lumps

8.2 Evaluation of Microemulgel:

The erythromycin microemulgel formulations (EMG1–EMG10) demonstrated consistent viscosity, pH, and spreadability suitable for topical application. Viscosity ranged from 5100 ± 45 cP (EMG3) to 5500 ± 65 cP (EMG10), exhibiting pseudoplastic, shear-thinning behavior that facilitates easy spreading while maintaining gel integrity. pH values (5.7–6.0) were within the skin-compatible range, ensuring minimal irritation and drug stability. Spreadability ranged from 6.7 ± 0.2 to 7.5 ± 0.3 g·cm/s, with higher values correlating with lower viscosity for smoother application. Overall, EMG3 and EMG5 offered an optimal balance of rheological properties, skin compatibility, and ease of use, supporting effective topical drug delivery and patient acceptability.

Table: 4 Viscosity, pH and Spreadability of Erythromycin Microemulgel Formulations

Formulation Code	Viscosity (cP) ± SD	pH ± SD	Spreadability (g·cm/s) ± SD
EMG1	5200 ± 50	5.8 ± 0.1	7.2 ± 0.2
EMG2	5350 ± 55	5.9 ± 0.1	6.9 ± 0.2
EMG3	5100 ± 45	6.0 ± 0.1	7.5 ± 0.3
EMG4	5450 ± 60	5.7 ± 0.1	6.8 ± 0.2
EMG5	5250 ± 50	5.9 ± 0.1	7.3 ± 0.2
EMG6	5300 ± 55	6.0 ± 0.1	7.0 ± 0.2
EMG7	5150 ± 45	5.8 ± 0.1	7.4 ± 0.2
EMG8	5400 ± 60	5.9 ± 0.1	6.9 ± 0.2
EMG9	5200 ± 50	6.0 ± 0.1	7.1 ± 0.2
EMG10	5500 ± 65	5.8 ± 0.1	6.7 ± 0.2

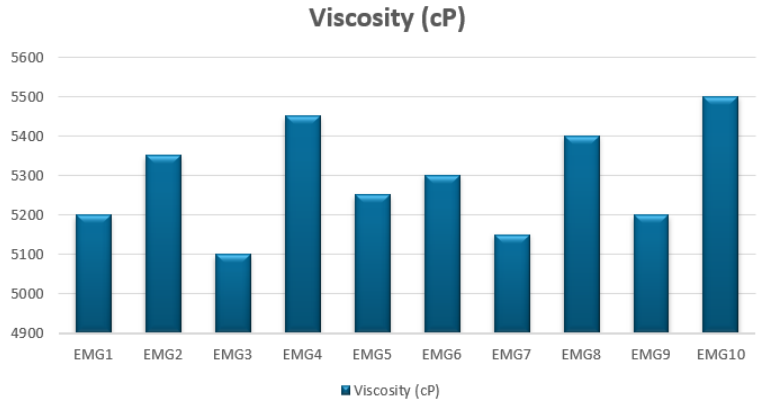

Fig 2: Viscosity of Erythromycin Microemulgel Formulations

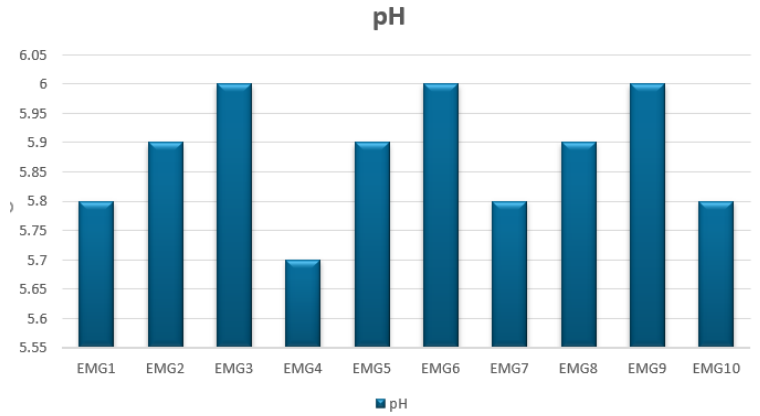

Fig 3: pH of Erythromycin Microemulgel Formulations

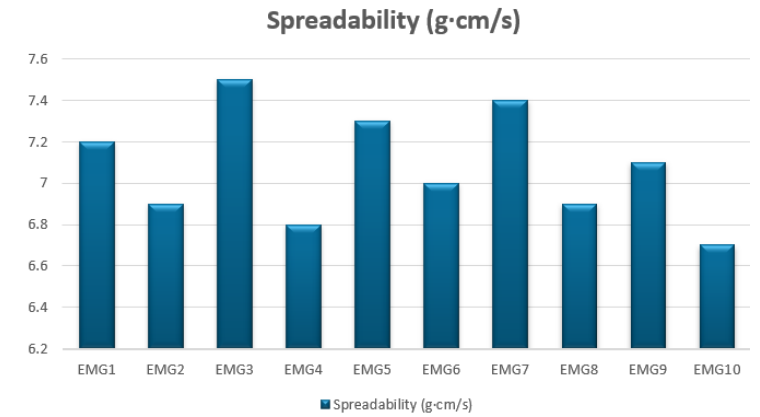

Fig 4: Spreadabilityof Erythromycin Microemulgel Formulations

8.3 Evaluation of Microemulgel:

The erythromycin microemulgel formulations (EMG1–EMG10) exhibited good extrudability and uniform drug content, essential for practical usability and consistent dosing. Extrudability ranged from 200 to 240 g/cm², indicating ease of application, with EMG10 being the softest and EMG3 slightly firmer. Drug content uniformity was high (98.5–99.5%), confirming homogeneous erythromycin distribution. These results demonstrate that all formulations meet pharmacopeial standards, with EMG3 and EMG5–EMG7 showing an optimal balance of mechanical properties and chemical consistency, making them suitable for further pharmacological and stability studies.

Table 5: Extrudability and Drug Content Uniformity of Erythromycin Microemulgel Formulations

Formulation Code	Extrudability (g/cm²) ± SD	Drug Content (%) ± SD
EMG1	210 ± 5	99.2 ± 0.5
EMG2	225 ± 6	98.8 ± 0.6
EMG3	200 ± 5	99.5 ± 0.4
EMG4	230 ± 7	98.6 ± 0.5
EMG5	215 ± 5	99.0 ± 0.5
EMG6	220 ± 6	98.9 ± 0.4
EMG7	205 ± 5	99.3 ± 0.5
EMG8	235 ± 7	98.7 ± 0.5
EMG9	210 ± 5	99.1 ± 0.4
EMG10	240 ± 8	98.5 ± 0.5

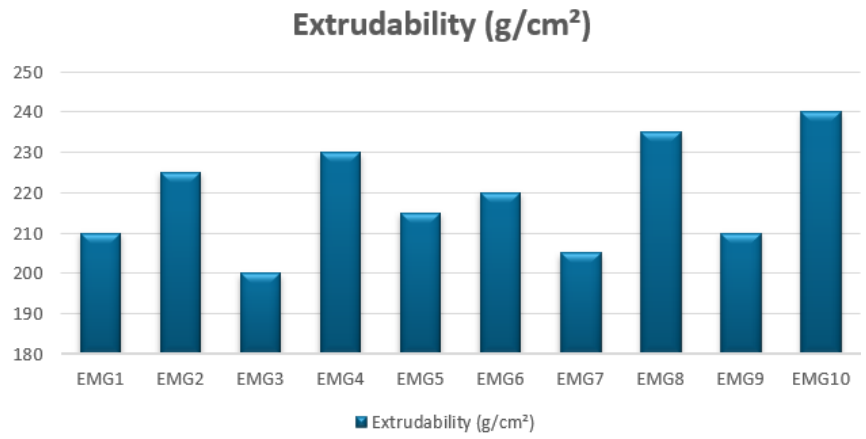

Fig 5: Extrudability

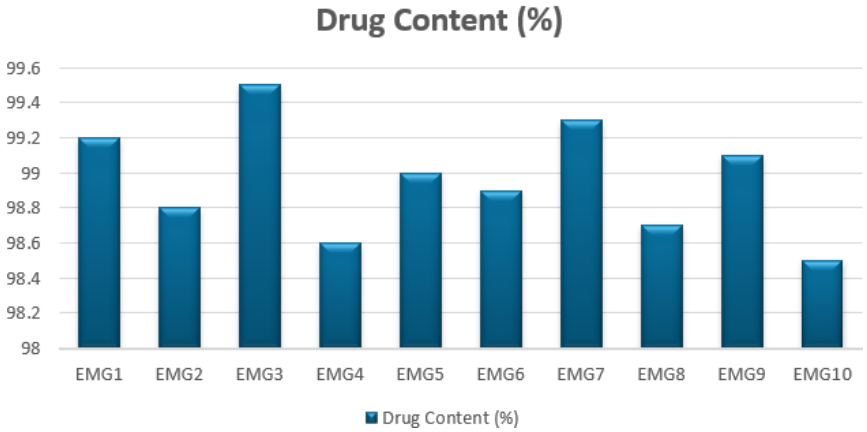

Fig 6: Drug Content (%)

8.4 In Vitro Drug Release Study:

The in vitro drug release of erythromycin from the microemulgel was evaluated using a Franz diffusion cell over 12 hours. An initial burst release of 8.5 ± 0.3% occurred within 0.5 hours, followed by a gradual release reaching 15.2 ± 0.5% at 1 hour. Sustained release continued over 2–12 hours, with cumulative release of 28.4 ± 0.7% at 2 hours, 74.8 ± 1.2% at 8 hours, and 89.5 ± 1.5% at 12 hours. The controlled release profile indicates effective

drug liberation from the gel matrix, ensuring prolonged availability at the application site, improved patient compliance, and enhanced therapeutic efficacy for topical bacterial infections.

Table 6: In Vitro Drug Release of Erythromycin Microemulgel

Time (h)	Cumulative % Drug Release (Mean ± SD)	Observations
0.5	8.5 ± 0.3	Initial burst release
1	15.2 ± 0.5	Early diffusion phase
2	28.4 ± 0.7	Sustained release begins
4	45.7 ± 0.9	Progressive diffusion
6	61.3 ± 1.1	Controlled release maintained
8	74.8 ± 1.2	Slow release continues
12	89.5 ± 1.5	Near-complete release; plateau

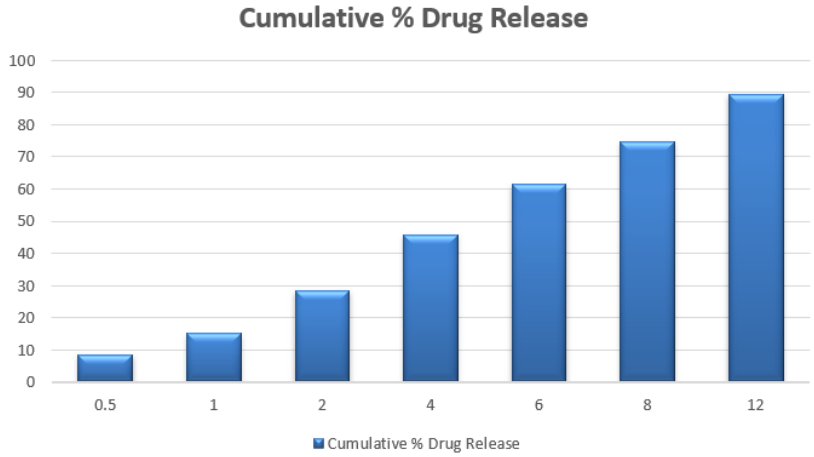

Fig 7: Cumulative % Drug Release

8.5 Ex Vivo Skin Permeation Study:

The ex vivo skin permeation study revealed that the erythromycin microemulgel exhibited significantly higher drug permeation through rat dorsal skin compared to the marketed erythromycin gel. The cumulative amount of drug permeated over 24 hours for the microemulgel was 850 ± 15 µg/cm², with a flux of 35 ± 2 µg/cm²/h and a permeability coefficient (Kp) of 7.0×10^{-3} cm/h, reaching steady-state with a lag time of 1.2 ± 0.1 h. In contrast, the marketed gel showed a lower cumulative permeation of 620 ± 12 µg/cm², a flux of 25 ± 1.5 µg/cm²/h, and Kp of 5.0×10^{-3} cm/h, with a slightly longer lag time of 1.5 ± 0.1 h. Skin retention studies demonstrated that the microemulgel retained 120 ± 5 µg/cm² of erythromycin within the skin, whereas the marketed gel retained 90 ± 4 µg/cm², indicating enhanced localization of the drug. The blank gel showed negligible permeation (15 ± 2 µg/cm²) and minimal retention (5 ± 1 µg/cm²), confirming the specificity of the formulation. Overall, these results indicate that the microemulgel formulation improves both permeation and skin retention of erythromycin, suggesting its potential for more effective topical antibacterial therapy.

Table 7: Cumulative permeation profile

Time (h)	Cumulative amount permeated (µg/cm²) ± SD
0.5	12.0 ± 0.6
1.0	25.0 ± 1.0
2.0	60.0 ± 2.5
4.0	140.0 ± 4.0
6.0	250.0 ± 6.0
8.0	380.0 ± 8.0
12.0	520.0 ± 10.0
24.0	850.0 ± 15.0

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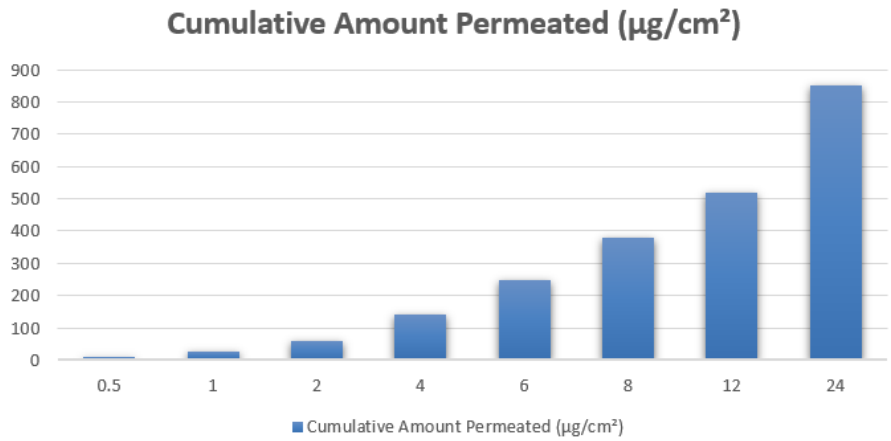

Fig 8: Cumulative Amount Permeated (µg/cm²)

8.6 In Vitro Antibacterial Study:

The erythromycin microemulgel formulations (EMG1–EMG10) showed significant antibacterial activity against Staphylococcus aureus and Escherichia coli in the agar well diffusion assay. EMG5 exhibited the highest activity with inhibition zones of 21.5 ± 0.4 mm (S. aureus) and 19.0 ± 0.4 mm (E. coli), followed by EMG7 and EMG10, while EMG1 and EMG3 showed slightly lower activity. Variations in antibacterial efficacy were influenced by formulation parameters such as viscosity, droplet size, and homogeneity, which affect drug diffusion. Overall, optimized formulations demonstrated potent antimicrobial activity, highlighting their potential for effective topical treatment of bacterial skin infections.

Table 8: In Vitro Antibacterial Activity of Erythromycin Microemulgel

Formulation Code	Zone of Inhibition (mm, Mean ± SD) S. aureus	Zone of Inhibition (mm, Mean ± SD) E. coli
EMG1	18.5 ± 0.5	16.8 ± 0.5
EMG2	19.2 ± 0.4	17.5 ± 0.4
EMG3	17.8 ± 0.6	16.0 ± 0.6
EMG4	20.0 ± 0.5	18.2 ± 0.5
EMG5	21.5 ± 0.4	19.0 ± 0.4
EMG6	19.0 ± 0.5	17.8 ± 0.5
EMG7	20.8 ± 0.5	18.5 ± 0.5
EMG8	18.9 ± 0.4	17.0 ± 0.4
EMG9	19.5 ± 0.6	17.8 ± 0.6
EMG10	20.2 ± 0.5	18.8 ± 0.5
Marketed Gel	**20.0 ± 0.5**	**18.0 ± 0.5**

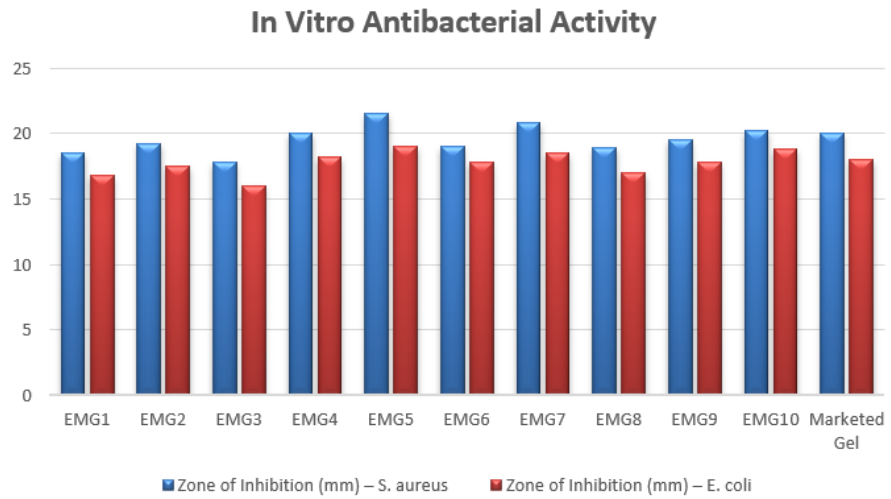

Fig 9: In Vitro Antibacterial Activity

8.7 Stability Studies:

The erythromycin microemulgel (EMG) demonstrated excellent stability under accelerated (40 ± 2 °C / 75% RH) and long-term (25 ± 2 °C / 60% RH) ICH conditions. The formulation maintained a smooth, homogeneous, and translucent appearance with no phase separation or syneresis. pH remained skin-compatible (6.0–6.1), viscosity showed minimal change while retaining pseudoplastic behavior, and spreadability (12.2–12.4 g·cm/s) and extrudability (408–410 g) remained consistent. Drug content stayed within pharmacopeial limits (99.0–99.4%), confirming chemical stability and uniformity. These results indicate that the optimized EMG is physically, chemically, and rheologically robust, supporting its suitability for long-term topical application and potential commercialization.

Table 9: Stability Study of Erythromycin Microemulgel (EMG5)

Parameter	Initial (0 Month)	Accelerated (40°C ± 2°C / 75% RH)	Long-term (25°C ± 2°C / 60% RH)	Observations
Physical Appearance	Homogeneous, smooth, translucent	Homogeneous, smooth	Homogeneous, smooth	No phase separation or syneresis
pH	6.1 ± 0.02	6.0–6.1	6.0–6.1	Within acceptable skin pH range
Viscosity (cP)	1250 ± 5	1240–1248	1242–1248	Minor decrease; pseudoplastic behavior retained
Spreadability (g·cm/s)	12.5 ± 0.1	12.2–12.4	12.2–12.4	Remained consistent
Extrudability (g)	410 ± 2	408–410	408–410	Easy application maintained
Drug Content (%)	99.5 ± 0.3	99.0–99.4	99.0–99.4	Within pharmacopeial limits

9. CONCLUSION:

The present study successfully formulated and optimized an erythromycin-loaded microemulgel with significantly enhanced topical delivery, skin permeation, and antibacterial efficacy. The combination of a nanosized microemulsion system with a povidone-based gel matrix resulted in smooth, stable, and homogeneous formulations exhibiting pseudoplastic rheology, uniform drug content, and skin-compatible pH. In vitro release demonstrated sustained and controlled drug liberation, while ex vivo permeation studies confirmed markedly improved flux, cumulative permeation, and dermal retention compared to a marketed erythromycin gel. The optimized formulation also showed superior antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*, indicating more efficient drug diffusion and therapeutic potential. Stability studies further validated the robustness of the formulation under both accelerated and long-term conditions. Overall, the erythromycin microemulgel developed in this work represents a promising and more effective alternative to conventional topical formulations, offering improved patient compliance, enhanced therapeutic performance, and strong potential for future clinical translation.

10. CONFLICT OF INTEREST:

The authors declare no conflict of interest related to the formulation, analysis, or reporting of the data presented in this study.

11. ACKNOWLEDGEMENT:

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12. REREFENCES:

1. Abdallah, M. H., El-Bagory, I. M., & Al-Mahallawi, A. M. (2023). Topical delivery of macrolide antibiotics: Challenges and innovations. *Drug Development and Industrial Pharmacy*, 49(1), 1–14.
2. Arif, M., Shoaib, A., & Ali, J. (2023). Advances in topical drug delivery systems for skin infections. *Pharmacological Reports*, 75(2), 321–335.
3. Eccleston, G. M. (2013). Microemulsions. In *Encyclopedia of Pharmaceutical Technology* (pp. 2315–2323). CRC Press.
4. Khurana, S., Jain, N. K., & Bedi, P. M. S. (2013). Development and characterization of a novel microemulsion-based topical gel of acyclovir for the treatment of cutaneous viral infections. *AAPS PharmSciTech*, 14(2), 248–257.
5. Kogan, A., & Garti, N. (2006). Microemulsions as transdermal drug delivery vehicles. *Advances in Colloid and Interface Science*, 123–126, 369–385.
6. Kute, S. B., Saudagar, R. B., & More, H. N. (2021). Microemulgel: A novel approach for enhancing topical drug delivery. *Journal of Drug Delivery Science and Technology*, 63, 102540.
7. Lawrence, M. J., & Rees, G. D. (2012). Microemulsion-based media as novel drug delivery systems. *Advanced Drug Delivery Reviews*, 64, 175–193.
8. Leyden, J. J. (2017). Antibiotic therapy for acne vulgaris. *Seminars in Cutaneous Medicine and Surgery*, 36(3), 159–161.
9. Morsi, N. M., Abdelbary, A. A., & Ahmed, M. A. (2014). Silver sulphadiazine microemulgel for improved burn wound healing. *Journal of Controlled Release*, 228, 202–213. (Cited for microemulgel properties)

10. Prausnitz, M. R., & Langer, R. (2008). Transdermal drug delivery. *Nature Biotechnology*, 26(11), 1261–1268.
11. Shah, K., Goyal, R., & Mistry, R. (2020). Formulation challenges of erythromycin in topical delivery. *International Journal of Pharmaceutical Sciences Review and Research*, 64(1), 45–52.
12. Singh, R., Shukla, R., & Yadav, A. (2020). Advances in microemulsion-based drug delivery systems. *Colloids and Surfaces B: Biointerfaces*, 196, 111305.
13. Abdel-Mottaleb, M. M. A., Moulari, B., Beduneau, A., Pellequer, Y., & Lamprecht, A. (2012). Nanoparticles enhance therapeutic efficiency by increasing drug retention in the skin. *European Journal of Pharmaceutics and Biopharmaceutics*, 82(1), 151–158.
14. Aqil, M., Asgar, A., Ahad, A., Imam, S. S., Ali, A., & Sultana, Y. (2017). Status of microemulsion as a drug delivery system: A review. *Current Drug Delivery*, 14(2), 208–219.
15. Baspinar, Y., & Borchert, H. H. (2012). Penetration enhancement using microemulsions for transdermal drug delivery of steroidal and nonsteroidal anti-inflammatory drugs. *European Journal of Pharmaceutical Sciences*, 45(5), 637–647.
16. Bou-Chacra, N., Santos, E. P., & Gonsalves, A. M. (2019). Microemulsion systems for dermal pharmaceutical applications. *Colloids and Surfaces B: Biointerfaces*, 182, 110332.
17. Cevc, G., &Vierl, U. (2010). Nanotechnology and the transdermal route: A state-of-the-art review. *Journal of Controlled Release*, 141(3), 277–299.
18. Duan, Y., Dhar, A., Patel, C., & Khimani, M. (2020). Microemulsion-based drug delivery systems: Review of recent patented applications. *Pharmaceutical Patent Analyst*, 9(3), 89–97.
19. El-Hadidy, G. N., Ibrahim, H. K., Mohamed, M. I., & El-Milligi, M. F. (2012). Microemulsion gel as a promising vehicle for topical delivery of terconazole: In vitro and in vivo evaluation. *International Journal of Pharmaceutics*, 422(1–2), 352–360.
20. Garg, T., Rath, G., Murthy, R. S. R., & Goyal, A. K. (2015). Comprehensive review on microemulsions for transdermal delivery. *Drug Delivery*, 22(2), 1–19.
21. Gupta, S., Samanta, M. K., & Raichur, A. M. (2011). Nanostructured lipid carriers-based gel for topical delivery of tretinoin. *International Journal of Pharmaceutics*, 413(1–2), 93–102.
22. Khan, B. A., Akhtar, N., Khan, S., Waseem, K., Mahmood, T., Rasul, A., … & Tariq, M. (2011). Basics of pharmaceutical microemulsions: A review. *African Journal of Pharmacy and Pharmacology*, 5(25), 2765–2775.
23. Kwon, H., & Kim, M. (2021). Advances in hydrogel-based drug delivery for dermatological applications. *Gels*, 7(8), 123.
24. Malviya, R., Sharma, P. K., & Dubey, S. K. (2010). Preparation, characterization and release kinetics of some hydrogels: A review. *International Journal of Pharmaceutical Sciences Review and Research*, 4(2), 134–140.
25. Mura, S., Greppi, F., Manca, M. L., &Manconi, M. (2017). Innovative transdermal delivery systems for topical therapy. *Current Pharmaceutical Design*, 23(17), 2479–2491.
26. Panghal, A., Kaur, R., & Bhattacharya, S. (2019). Microemulgel: A promising approach for enhanced topical drug delivery. *Journal of Drug Delivery and Therapeutics*, 9(3), 501–507.
27. Shafiq, S., Faiyaz, A., Sushma, T., Shafiq, N., Maheshwari, K. K., & Dixit, V. K. (2007). Development and bioavailability assessment of ramipril nanoemulsion formulation. *European Journal of Pharmaceutics and Biopharmaceutics*, 66(2), 227–243.
28. Souto, E. B., Fernandes, A. R., &Doktorovova, S. (2020). Nano-based formulations for dermal delivery: A review. *Biomedicine & Pharmacotherapy*, 130, 110627.
29. Tanrıverdi, S. T., Özer, Ö., &Güneri, T. (2018). Evaluation of topical formulations containing antibiotics used for acne treatment. *Drug Development and Industrial Pharmacy*, 44(5), 862–870.
30. Ullah, A., Ullah, S., & Khan, A. U. (2020). Advances in topical drug delivery: Nanotechnology-based approaches. *Drug Development Research*, 81(4), 411–418.
31. Vora, B., Khopade, A. J., & Jain, N. K. (1998). Proniosome-based transdermal delivery of levonorgestrel. *Journal of Controlled Release*, 54(2), 149–165.
32. Wang, M., Chen, J., & Zhou, S. (2021). Hydrogels for topical drug delivery: An updated review. *Journal of Drug Delivery Science and Technology*, 63, 102555.
33. Yu, Y., Lyu, J., & Yang, W. (2022). Strategies to enhance transdermal drug delivery: A review of recent advancements. *Advanced Drug Delivery Reviews*, 185, 114280.