Available online on 15.06.2026 at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

Open Access to Pharmaceutical and Medical Research

Open Access

Review Article

Erythromycin-Based Emulgel for Enhanced Anti-Acne Therapy: A Comprehensive Review

Sumedh Prashant Pagare[1], Dr. Ashish Pawar[2], Abdul Kalam[1]

[1]Department of Pharmaceutics, Divine College of Pharmacy, Satana affiliated to Savitribai Phule Pune University, Pune.

[2]Department of Pharmaceutics, MGV College of Pharmacy, Satana affiliated to Savitribai Phule Pune University, Pune.

A B S T R A C T

Acne vulgaris is a chronic inflammatory skin condition affecting about 85 percent of adolescents and a significant percentage of adults across the world, being one of the most common dermatological disorders. Cutibacterium acnes (earlier known as Propionibacterium acnes) causes the disease, due to its ability to colonize the sebaceous follicles and activate innate immunity in the affected area, thus initiating the inflammatory response. Erythromycin, a 14-membered ring macrolide antibiotic, has been successfully used for treatment because of its ability to inhibit bacterial protein synthesis at the level of the 50S ribosome; however, the application of erythromycin in the treatment of acne is largely impeded by several factors, including low aqueous solubility, instability in acid media, increasing drug resistance and poor skin penetrance.

Emulgel, a novel drug delivery system which combines an oil-in-water emulsion with a gel base, is being explored as a possible solution to overcome these challenges. Emulgels are effective in increasing the transdermal penetration of erythromycin due to the synergy between the characteristics of emulsion systems, namely better solubilisation of hydrophobic drugs, and gels, including easy application, sustained drug release, and greasy texture. Additionally, the use of advanced drug delivery vehicles such as solid lipid nanoparticles, niosomes, microemulsions, and polymer nanoparticles optimises drug delivery processes and dosage frequencies.

This review critically evaluates research findings that have been published between the years 2015 and 2026, covering issues such as physicochemical principles underlying erythromycin action within emulgel formulations, formulation design principles, choice of excipients, characterization methods, in vitro and ex vivo permeability studies, clinical performance evaluations, and regulatory considerations. Issues currently challenging this domain include antibiotic stewardship, monitoring of resistance, stability of formulations, and their scalability to larger scales. Future trends that may be encountered include combination therapy, formulation strategies that spare the skin microbiota, and intelligent stimuli-responsive delivery approaches.

Keywords: Erythromycin; Emulgel; Acne Vulgaris; Cutibacterium Acnes; Topical Drug Delivery; Percutaneous Permeation

A R T I C L E I N F O: Received 12 Dec.2025; Review Complete 21 Feb, 2026; Accepted 29 March. 2026; Available online 15 June. 2026

Cite this article as:
Pagare SP, Pawar A, Kalam A, Erythromycin-Based Emulgel for Enhanced Anti-Acne Therapy:A Comprehensive Review, Asian Journal of Pharmaceutical Research and Development. 2026; 14(3) 499-510, DOI: http://dx.doi.org/10.22270/ajprd.v14i3.1830

*Address for Correspondence:
Sumedh Prashant Pagare, Department of Pharmaceutics, Divine College of Pharmacy, Satana affiliated to Savitribai Phule Pune University, Pune.

INTRODUCTION

According to the World Health Organization, acne vulgaris, which is ranked as one of the diseases of significant public health importance, afflicts about 650 million people worldwide and is the eighth most common disease [32]. Acne vulgaris has significant psychosocial consequences such as depression and anxiety apart from its evident effects on physical appearance, which may include comedones, papules, pustules, and nodules and at times even form scarred cysts [33,34]. While generally regarded as a disorder that occurs in adolescents, increasing cases have been recorded among

adults especially women, highlighting the changing nature of its clinical course [35].

Pathogenesis of acne vulgaris is multi-factorial and comprises of four main interconnected pathways, which are (i) overproduction of sebum that is qualitatively different from normal because of the action of androgenic hormones; (ii) alteration in the keratinisation process causing ductal occlusion and formation of micro-comedones; (iii) colonization of the hair follicle-sebaceous gland by cutibacterium acnes (C.acnes); and (iv) an elaborate immune response to the inflammation caused by toll-like receptors and pro-inflammatory cytokines [36,46]. The recent discovery regarding the complexity of the skin microbiota, together with the virulence of particular C. acnes phylotypes, adds to this knowledge base [37,41].

Topical antibacterial treatment, specifically the use of erythromycin, has played an important part in the recommendations regarding the treatment of acne over many years because of its ability to inhibit C. acnes bacteria growth and exhibit its anti-inflammatory effects without being bactericidal while still providing decent tolerance to patients [32,45]. Yet, the efficacy of the traditional formulations of erythromycin topical products (solutions, gels, lotions, and creams) becomes less efficient as a result of increased antibiotic resistance and inability to achieve sufficient skin permeation [38,43].

Emulgel technology, which was initially developed to be used in delivering non-steroidal anti-inflammatory medications, has received significant attention due to its potential application as a new delivery system for anti-infectives [51,52]. The emulgel is constituted by incorporating an emulsion drug phase in either a hydrophilic or hydrophobic gel framework, thereby offering benefits such as better drug solubilization (especially for drugs belonging to BCS class II, e.g., erythromycin), increased transdermal permeation, controlled drug release, skin moisturization, and better cosmetic performance [56,57]. The latest development in this area involves the incorporation of modern nanoscale carriers in the emulgel system, namely solid lipid nanoparticles (SLN), polymeric nanoparticles, niosomes, and self-nanoemulsifying systems [55,65].

This review summarizes data from peer-reviewed scientific literature between 2015 and 2026, and gives a detailed account of scientific advances related to the erythromycin emulgel formulations in terms of both clinical and translational research. The aim is to assist those who are conducting studies in the area with their ongoing and upcoming work.

Overview of Acne Vulgaris

Epidemiology

Acne vulgaris shows an estimated worldwide prevalence of more than 85% among individuals between 12 to 24 years old, while it is estimated that 15 to 40% may continue suffering from the disease in their adult lives [33,35]. However, its prevalence differs based on ethnicity and location, while Western diet, mental stress, and hormone imbalance have been recently identified as potential risk factors that could be modified [34]. The economic impact is huge, considering that the cost of the condition reaches above 3 billion US dollars each year in the USA alone [32].

Pathogenesis

Pilosebaceous units serve as the primary structural basis for acne formation. Due to androgen stimulation, especially DHT, sebaceous glands grow larger and produce more sebum, which consists of lipids with different proportions of fatty acids, notably lower amounts of linoleic acid. The modified fatty acid profile of sebum leads to damage of the follicular epithelium and excessive keratinocyte proliferation, thus providing conditions suitable for the multiplication of C. acnes. [39,40].

C. acnes synthesises a broad spectrum of virulence factors comprising lipases, proteases, hyaluronidases, and CAMP factors which act to breakdown sebum in the hair follicle and cause injury to the follicular epithelial cells leading to the formation of comedones and releasing inflammatory lipid mediators [41]. Activation of TLR-2 receptors on keratinocytes and monocytes through recognition of cell wall products of C. acnes leads to the synthesis and release of cytokines IL-1β, IL-8, IL-12, and TNF-α setting up an environment conducive to inflammation in acne [46]. Neutrophil influx and the production of ROS through neutrophil myeloperoxidase enzymes also increases tissue injury [36].

Classification and Grading

There are various systems for acne grading that have been scientifically validated, among which include the Global Acne Grading System (GAGS), Leeds Revised Acne Grading System, and Investigator's Global Assessment scale (IGA). In terms of the morphological system, it separates non-inflammatory lesions, such as open and closed comedones, from inflammatory lesions, namely papules, pustules, nodules, and cysts. Treatment is then determined based on the percentage of each lesion type. Treatments may involve topical treatment alone in mild acne, while combined topical treatments and oral antibiotics are recommended for moderate acne.

Therapeutic Role of Erythromycin in Acne Treatment

Pharmacology and Mechanism

Erythromycin was first obtained from Saccharopolyspora erythraea in 1952 and belongs to a group of antibiotics known as 14-membered lactone ring macrolides. From Table 1, the molecular formula for erythromycin is $C_{37}H_{67}NO_{13}$ (molecular weight: 733.93 g/mol) and can be categorized as a BCS Class II drug based on poor solubility (~2 mg

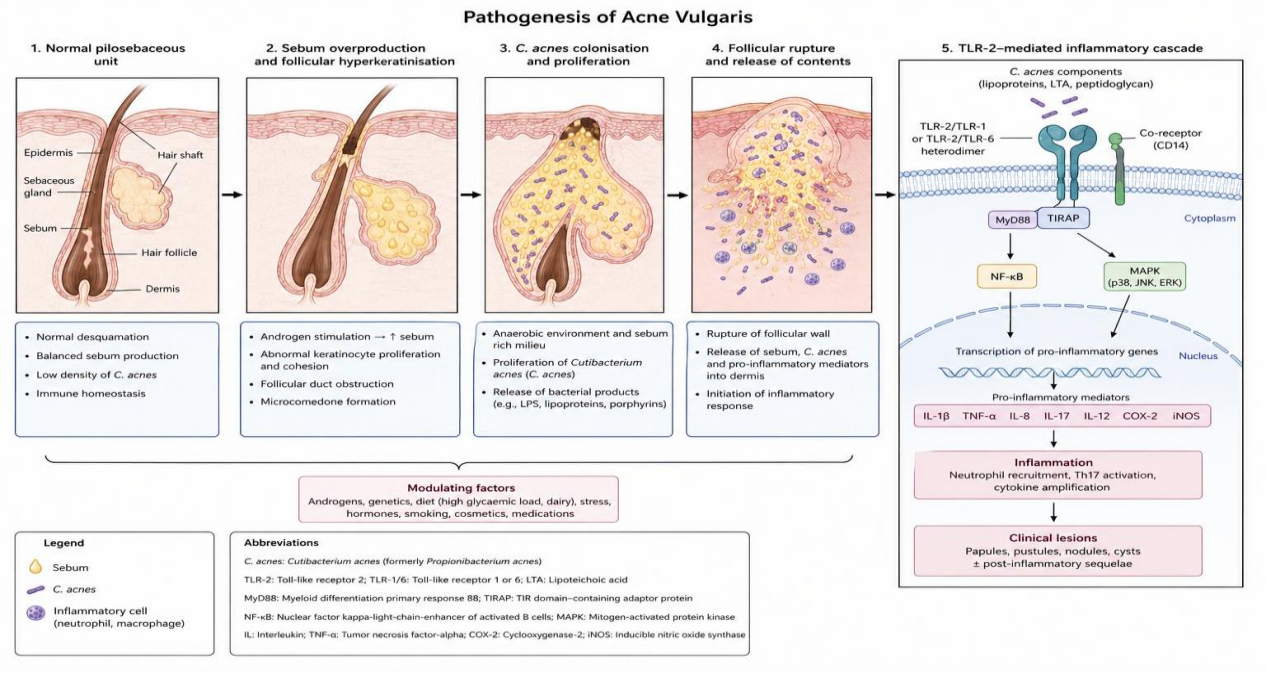

Figure 1 illustrates the interplay among sebum dysregulation, C. acnes colonisation, and the ensuing immune cascade in acne pathogenesis.

Figure 1: Schematic diagram of acne vulgaris pathogenesis — Placeholder for figure showing pilosebaceous unit anatomy, sebum overproduction, C. acnes colonisation, and TLR-2-mediated inflammatory cascade

Table 1: Physicochemical Properties of Erythromycin

Property	Details
IUPAC Name	(2R,3S,4S,5R,6R,8R,10R,11R,12S,13R)-3-[(2R,4R,5S,6S)-4-(dimethylamino)-3-hydroxy-6-methyl-tetrahydropyran-2-yl]oxy-13-ethyl-11-hydroxy-2,4,6,8,10,12-hexamethyl-5-[(3R,4S,6R)-3,4,5-trihydroxy-6-methyltetrahydropyran-2-yl]oxy-1-oxacyclotridecane-1,7,9-trione
Molecular Formula	$C_{37}H_{67}NO_{13}$
Molecular Weight	733.93 g/mol
Appearance	White to off-white crystalline powder
Melting Point	133–138°C
Solubility in Water	Slightly soluble (~2 mg/mL at 25°C)
Log P (Octanol/Water)	3.06
pKa	8.88 (amine group)
Protein Binding	~73–81%
Stability	Acid-labile; stable in alkaline to neutral pH (6.0–8.0)
Mechanism of Action	14-membered macrolide; inhibits bacterial protein synthesis by binding to 23S rRNA of 50S ribosomal subunit
Spectrum	Gram-positive cocci, including Cutibacterium acnes (formerly Propionibacterium acnes)
BCS Classification	Class II (low solubility, high permeability)
Primary References	Awan et al. 2022; Shargel & Yu 2016 [1,2]

The main mechanism of bactericidal activity of erythromycin is based on the reversible binding of erythromycin to 23S ribosomal RNA (rRNA), which is part of the 50S bacterial ribosomal subunit in the peptide exit tunnel, thus hindering the translocation of peptidyl-tRNA and elongation of the new polypeptide chain [38,42]. As a consequence, there is a bacteriostatic effect at low doses and bactericidal effect at high doses in susceptible C. acnes strains. Additionally, erythromycin produces an anti-inflammatory effect, unrelated to its direct bactericidal action, through suppression of neutrophil chemotaxis, reduction of proinflammatory cytokines (IL-1β, TNF-α, IL-8) levels, and inhibition of the activity of metalloproteinases in the follicular matrix, causing comedolysis and post-inflammatory hyperpigmentation [46,60]

Clinical Efficacy Profile

In accordance with the evidence-based medical guideline of the American Academy of Dermatology (AAD) and the European Dermatology Forum (EDF), the use of topical erythromycin (2-4% concentration) is recognized as a proven treatment option for inflammatory acne due to its significant anti-inflammatory activity (with reductions of up to 50-70% in inflammatory lesions when compared to the vehicle) that has been established based on multiple randomized controlled trials [32,45]. The combined use of erythromycin with zinc acetate (commercially available as Zineryt®) or benzoyl peroxide greatly improves the results and decreases resistance development [61].

Limitations of Conventional Topical Formulations

Formulation-Related Barriers

Traditional erythromycin topical formulations (solutions in ethanol (2%–4%), gels, ointments, emulsions in water (simple oil-in-water emulsion), and cellulose gel preparations) possess inherent physicochemical properties that render such preparations inefficient. Erythromycin is a compound sensitive to acidic conditions because of ring opening at a pH lower than 4; therefore, it should be formulated into solutions with pH 6.0-8.0 [1]. Gels are cosmetically appealing but possess weak solubility characteristics for erythromycin; therefore, high levels of solvents (alcohols) are required to attain good drug concentrations [49,56].

Stratum corneum (SC) is a multi-layered lipid membrane comprised of ceramides, free fatty acids, and cholesterol, and is arranged in a "brick and mortar" structure. The SC layer acts as the main hurdle for topically applied drug molecules. A drug molecule needs to pass through 15-20 cell layers, where each layer contains an effective thickness of about 13-15 nm of the lipid bilayer membrane, which requires optimum lipophilicity (log P 1-3), lower molecular weight (less than 500 Da), and hydrogen bond acceptor/donor properties. The molecular weight of erythromycin (733.93 g/mol) surpasses this limit. [50].

Antimicrobial Resistance

Resistance to antibiotics in C. acnes strains is currently an emerging global issue restricting the efficacy of erythromycin therapy on skin disorders. This is because antibiotic resistance is due to acquisition of erm genes such as ermA, ermB, and ermC encoding for methyltransferases that methylate the adenine at position 2058 in the 23S rRNA, thus inhibiting binding of erythromycin [38,44]. Mutation at nucleotides 2058 or 2059 (A2058G, A2059G) on 23S rRNA leads to high-level cross-resistance to macrolides and lincosamides [43]. Several European surveys have recorded higher than 50-60% resistance in a number of countries, with >90% resistance observed in some centres [43]. Walsh et al. estimated the prevalence of 20-60% resistance across global regions after conducting a systematic analysis of literature up to 2016, followed by an upward trend [44]. Clinically, it implies low anti-acne effects from erythromycin treatment, thus warranting formulation modifications.

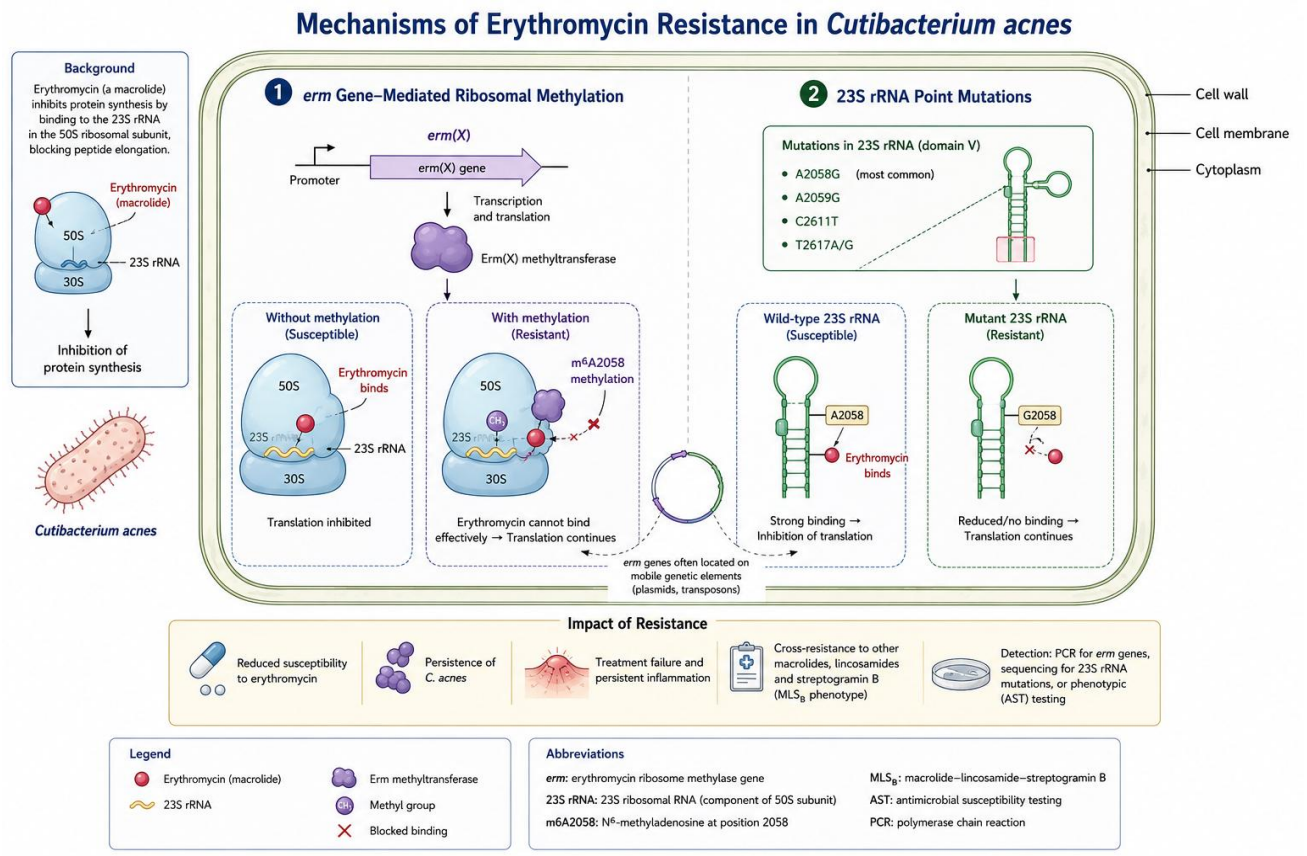

Figure 2 provides a schematic overview of erythromycin resistance mechanisms in C. acnes.

Figure 2: Schematic illustration of erythromycin resistance mechanisms in Cutibacterium acnes — Placeholder for figure depicting erm gene-mediated ribosomal methylation and 23S rRNA point mutations

Concept of Emulgel Drug Delivery

Definition and Rationale

An emulgel can be described as a two-phase drug delivery vehicle where an emulsion, O/W or W/O, forms part of a gel structure formed by either hydrophilic or hydrophobic polymer systems [51,57]. In essence, the name emulgel represents both properties of the gel as well as those of the emulsion. The reason for choosing to develop an emulgel in treating acne is the synergistic benefits that both the emulsion and the gel provide when considered separately [52,56].

The benefits of emulsions include increased ability to solubilise lipophilic medications (like erythromycin), easy mixing with oils known for their follicular penetration capability (isopropyl myristate, oleic acid) and surfactants, which cause temporary disruption of stratum corneum lipid organization, thus improving cutaneous absorption [13,55]. Gels offer improved rheology with thixotropy for optimal application to the skin, control over drug delivery via the 3D network of polymers, hygroscopic properties aiding water retention by the skin damaged by acne, and no greasy feel typical of ointments and creams. [16,56].

The emulgel that forms as a result of the above process is therefore a combination of the solubility properties of an emulsion and the patient-friendly characteristics of a gel, which makes it suitable for the formulation of poorly water-soluble anti-acne compounds like erythromycin. The O/W type of emulgels is more common in the dermatology field due to their ability to be spread and washed off without causing occlusion, just like today's cosmetics. [64].

Advantages Over Conventional Vehicles

Some of the significant advantages offered by emulgels compared to traditional topical formulations are: higher drug solubilization and drug loading; better skin penetration via both hydrophilic and lipophilic routes; prolonged drug release leading to less frequent doses; better skin hydration and bioadhesion; reduced skin irritation due to organic co-solvents; thermodynamic stability if properly prepared; simple manufacturing and scaling up; and high patient acceptability due to elegance of appearance and non-greasy nature. [51,56,57].

Components of Emulgel Formulation

Physicochemical performance and therapeutic effectiveness of erythromycin emulgels are highly dependent on the choice and optimization of individual components. Table 2 presents some of the most common excipients for erythromycin emulgels along with their concentrations and functions.

Table 2: Excipients Used in Erythromycin Emulgel Formulation

Excipient Category	Example(s)	Concentration (%)	Role in Formulation
Gelling Agent	Carbopol 934/940	0.5–2.0	Provides gel matrix; controls viscosity and consistency
Gelling Agent	HPMC K4M / K15M	1.0–4.0	Film-forming; moisture retention; sustained release
Gelling Agent	Sodium CMC	1.0–3.0	Thickening; emulsion stabilization
Emulsifying Agent	Tween 80 (Polysorbate 80)	1.0–5.0	O/W emulsification; solubilization of lipophilic drug
Emulsifying Agent	Span 60 / Span 80	0.5–2.0	Co-emulsifier; HLB balancing
Oil Phase	Liquid paraffin	5.0–20.0	Emollient; drug vehicle; occlusive moisturizer
Oil Phase	Isopropyl myristate	2.0–10.0	Penetration enhancer; reduces skin irritation
Oil Phase	Castor oil / Olive oil	5.0–15.0	Natural emollient; anti-inflammatory adjuvant
Penetration Enhancer	Propylene glycol	5.0–15.0	Humectant; enhances drug permeation
Penetration Enhancer	Dimethyl sulfoxide (DMSO)	1.0–5.0	Potent penetration enhancer; use limited by irritation
Penetration Enhancer	Oleic acid	0.5–5.0	Disrupts stratum corneum lipid bilayer
Humectant	Glycerin	2.0–10.0	Moisture retention; skin softening
Preservative	Methylparaben / Propylparaben	0.1–0.3	Antimicrobial preservation; stability
pH Modifier	Triethanolamine (TEA)	q.s. to pH 6–7	Neutralizes Carbopol; forms stable gel network
Antioxidant	BHT / BHA	0.01–0.1	Prevents oxidative degradation of oil phase
Solvent/Co-solvent	Ethanol / Isopropanol	5.0–20.0	Drug solubilization; antiseptic adjuvant
References			Al-Suwayeh et al. 2015; Shukr & Mahmoud 2013 [3,4]

Gelling Agents

The Carbopol (polyacrylic acid) family of polymers – more specifically carbopol grades 934, 940, and 934P – are the most commonly used gelling agents for the study of erythromycin emulgels, at levels between 0.5% and 2.0% w/w [9, 51]. Carbopol gel is formed when it undergoes cross-linking to form a three-dimensional network when neutralized with triethanolamine (TEA) or sodium hydroxide, thus forming a highly viscous material with pseudoplastic rheology, and exhibiting bioadhesion. Other cellulosic polymers such as hydroxypropyl methyl cellulose (HPMC) and sodium carboxymethyl cellulose (CMC) can also be considered as potential alternatives due to their enhanced pH range and lesser irritancy [57]. Natural polymer-based

systems consisting of xanthan gum, sodium alginate, and chitosan are also promising owing to their biocompatible

Emulsifying Agents and Oil Phase

The effectiveness of emulsification, droplet size, and stability will depend on the HLB balance of the surfactant system and compatibility with the oil component. In general, non-ionic surfactants (mainly Tween 80 (HLB = 15.0) and Span 60 (HLB = 4.7), mixed in appropriate concentrations) are selected due to their biocompatibility and low irritancy [3, 55]. The choice of oil phase affects the drug distribution and enhancing permeation: IPM has been extensively used for its skin penetration enhancing activity and capacity to dissolve erythromycin [3], while liquid paraffin contributes to occlusive lubrication of the skin surface. Moreover, natural oils can be considered for their anti-inflammatory properties and emollients suitable for acne-prone skin [22].

Penetration Enhancers

Because erythromycin has a high molecular weight, enhancing penetration becomes essential. Chemical enhancers like propylene glycol, oleic acid, and pyrrolidones enhance SC permeation by different means: propylene glycol functions as a moisturizer and co-solvent that enhances the thermodynamic activity and solubility of drugs in the SC; oleic acid modifies the crystalline structure of lipids in the SC to make fluid lipid zones for drug transfer; and laurocapram (Azone) embeds itself in the lipid bilayer of the SC, widening lamellar spaces [13,16,50]. Ethanol, which acts as a co-solvent, dissolves erythromycin while extracting SC lipids, temporarily improving permeability. The optimal concentration of penetration enhancers needs consideration because higher concentrations can cause skin irritation [55].

Preparation Methods

Conventional Emulgel Preparation

The common protocol for the two-phase preparation of erythromycin emulgel includes the following steps: (i) preparation of aqueous phase – hydration of gelling agent like Carbopol 934 in purified water (12-18 hours) and then neutralization of the gel mass with TEA to bring its pH to 6.0-7.0; (ii) preparation of oil phase – dissolving erythromycin along with other lipophilic components like emulsifier, oil, penetration enhancer with warming (50-60°C) in presence of nitrogen atmosphere; (iii) emulsification process – pouring the oil phase into the aqueous phase and mixing continuously (2000-10,000 rpm; ultra-turrax or silverson mixer) or ultrasonic probe method; (iv) homogenization of the prepared mass until a homogeneous mass is formed; and (v) quality control – pH, viscosity, appearance, drug content determination [51,57,58].

Nanoparticle-Incorporated Emulgel

Erythromycin emulgels with advanced formulation involve the incorporation of pre-formed nanocarriers into the gel system. SLNs can be produced via either the melt-emulsification method or the hot high-pressure homogenization method: erythromycin is dissolved in the melted lipid (glyceryl monostearate, tripalmitin) matrix, which is then dispersed in an aqueous surfactant solution, homogenized at 500–1500 bar, and rapidly cooled to produce SLN particles of sizes ranging from 100–400 nm [24,65]. PLGA nanosphere formulations using erythromycin as the active drug ingredient have been reported using the nanoprecipitation or double emulsion methods, achieving an entrapment efficiency of 60-85%, which is then further incorporated into Carbopol gel formulations [28,53]. Niosomal emulgels consist of niosomes prepared via thin film hydration of Span 60, cholesterol, and erythromycin, and are sonicated after hydration [26]. SNEDDS undergo spontaneous nanoemulsification to generate droplets less than 50 nm in size, [31].

Characterization Parameters

The properties, safety, and efficacy of emulgels of erythromycin are evaluated using a series of physicochemical, microbial, and biological tests as described in Table 3 below. Figure 3 illustrates the complete procedure that should be undertaken for the evaluation of emulgels.

Table 3: Characterization Parameters and Evaluation Methods for Erythromycin Emulgels

Parameter	Method / Instrument	Acceptance Criterion	References
Physical Appearance	Visual inspection; tactile assessment	Uniform, homogeneous, translucent/opaque gel without phase separation or lumps	USP <1151> [5]
pH	Digital pH meter (calibrated); 1% w/v dispersion	6.0–7.4 (skin-compatible)	Saeedi et al. 2019 [6]
Viscosity	Brookfield viscometer (RVT); cone-plate rheometer	2000–50,000 mPa·s (formulation-dependent)	Radulescu et al. 2016 [7]
Spreadability	Parallel-plate method (weight-loaded for 5 min)	>8 cm (good spreadability)	Hussain et al. 2020 [8]
Extrudability	Crimped tube; force to extrude 0.5 g	>90% extrusion efficiency	Khullar et al. 2012 [9]
Drug Content / Assay	HPLC; UV-Vis spectrophotometry (262 nm)	95–105% of label claim	IP/BP/USP [10]
In Vitro Drug Release	Franz diffusion cell; dialysis membrane; synthetic membrane	Follows Higuchi / zero-order / Korsmeyer-Peppas kinetics	Franz 1975; Costa & Lobo 2001 [11,12]
Ex Vivo Skin Permeation	Excised human/rat/porcine skin; Franz cell; HPLC quantification	Flux, Kp, diffusion coefficient determined	Prausnitz & Langer 2008 [13]
Globule / Droplet Size	Dynamic light scattering (DLS); laser diffraction (Malvern	<1 µm (o/w emulgel); PDI	Calixto et al. 2015 [14]

	Mastersizer)	<0.3	
Zeta Potential	Electrophoretic light scattering (Zetasizer)	±20 to ±40 mV (good stability)	Müller et al. 2011 [15]
Rheological Behavior	Oscillatory / rotational rheometry; thixotropy test	Pseudoplastic (shear-thinning); thixotropic recovery >90%	Barry 2001 [16]
Skin Irritation	HET-CAM; patch test; Draize rabbit test	No erythema/edema (primary irritation index <0.5)	OECD TG 404 [17]
Antimicrobial Activity	Agar well diffusion; MIC/MBC determination vs C. acnes	Zone of inhibition comparable to or greater than reference standard	EUCAST 2023 [18]
Stability Studies	ICH Q1A(R2); 25°C/60% RH (LTZ); 40°C/75% RH (AZ)	No significant change in appearance, pH, viscosity, drug content over 6 months	ICH Q1A(R2) 2003 [19]
Occlusion Factor	TEWL measurement; gravimetric method	Higher occlusion = enhanced hydration; OF > 0.4 preferred	Loden 2003 [20]

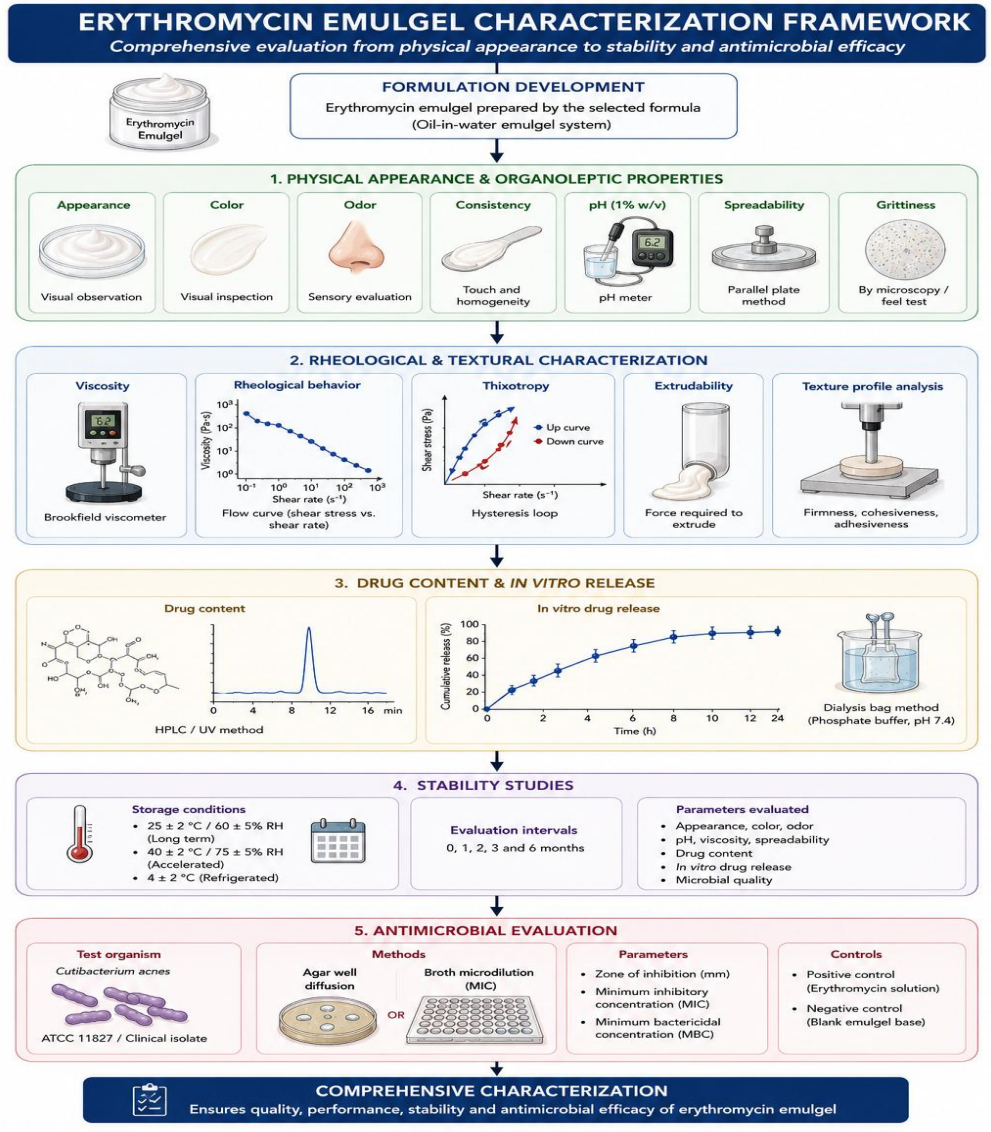

Figure 3: Flowchart of erythromycin emulgel characterization framework — Placeholder for figure depicting the complete characterization workflow from physical appearance through stability and antimicrobial evaluation

Physical and Rheological Characterization

Rheological analysis assumes a specific significance when developing emulgels for topical applications. In an ideal case, emulgels exhibit shear-thinning rheological behavior – high rest viscosity for providing good adhesion on the skin and low viscosity under the influence of shear force for easy

spreadability – described using the power law equation and Herschel-Bulkley equation [16]. The thixotropic effect (>80% recovery within 60 seconds after cessation of shearing) helps ensure rapid restoration of the structure after the application and avoid dripping/migration from the applied area [7]. Rheological oscillation analysis gives viscoelastic parameters of gel strength and stability (G' and G"), important for the shelf life properties of the product [16].

Drug Release and Permeation Studies

Erythromycin emulgels' in vitro release kinetics are usually tested using Franz diffusion cells that have synthetic cellulose acetate or nitrocellulose membranes (12,000–14,000 Da MWCO) and phosphate buffered saline (PBS, pH 5.5 or 7.4) as receptor solution at 32±0.5°C temperature, mimicking the temperature of the skin surface [11]. In vitro release kinetic data is analyzed with different mathematical models such as zero order, first order, Higuchi, and Korsmeyer-Peppas to understand the nature of the release mechanism. The value of diffusion exponent n in Korsmeyer-Peppas model determines if the transport type is Fickian ($n \leq 0.5$) or non-Fickian [12]. Ex vivo skin permeation testing on full thickness human or porcine ear skin (abdominoplasty) gives more accurate results related to in vivo skin permeation, allowing determination of parameters such as flux (Jss, µg/cm²/h), permeability coefficient (Kp), and lag time values [3,13]. CLSM was used in ex vivo studies to examine follicular or transdermal delivery in emulgels [14].

Mechanism of Enhanced Anti-Acne Action

The enhanced effectiveness of erythromycin emulgels over other drug delivery systems for the treatment of acne can be attributed to the following factors at the level of physicochemistry, pharmacokinetics, and pharmacodynamics [55,56]:

The first one concerns the fact that emulsion technology helps enhance the thermodynamic activity of erythromycin in the drug delivery system by making the process of solubilization more efficient and creating a greater concentration gradient through passive diffusion across the SC. Oil droplets help partition the lipophilic drug directly into the SC lipids, avoiding the slow process of diffusion through the aqueous medium found in hydrophilic gels. [13,56].

Second, chemical permeation enhancers contained in the oil layer (oleic acid, propylene glycol, IPM) synergize to interfere with the structure of the SC lipid bilayer (intercellular pathway) as well as improve the solubility of drugs in skin lipids. Surfactants (Tween 80) temporarily interfere with the structure of SC lipid bilayer, and also allow drugs to penetrate via the follicular transfollicular pathway — an important point to be considered in the case of acne, which involves pilosebaceous follicles as the major pathological site of interest [50,55].

Thirdly, inclusion of nanocarriers (SLN, niosomes, PLGA nanoparticles) achieves extended delivery of drugs into the skin layer that maintains drug levels above the MBC level of C. acnes while minimizing systemic absorption and the formation of resistant organisms due to sub-therapeutic drug concentrations [24,28,65]. The minute size (100–400 nm) of these nanocarriers increases the tendency of their deposition within the follicular infundibulum, which is the main location of C. acnes [55].

Together, the overall effect is a marked improvement in skin deposition and follicular delivery of erythromycin, leading to higher local concentrations of the drug within the area of C. acnes infection, increased bactericidal activity (even in cases of minor resistance), and lower systemic levels — thereby providing the physiological rationale for the therapeutic superiority of erythromycin emulgels compared to traditional formulations. [21,26,28].

Recent Research on Erythromycin Emulgel

There has been a considerable advancement in research relating to the use of emulgel formulation containing erythromycin due to advancements made simultaneously in the fields of nanotechnology, polymer chemistry, and computational formulae optimisation during the past decade. This is elaborated in Table 4 below.

Table 4: Recent Studies on Erythromycin Emulgel for Acne Therapy (2015–2025)

Year	Formulation System	Key Excipients / Technology	Key Findings	Reference
2015	Erythromycin nanoemulsion-based gel	Carbopol 940, Tween 80, isopropyl myristate, oleic acid	8.5-fold increase in cumulative drug permeation vs conventional gel; improved bactericidal action against C. acnes ATCC 11827	Al-Suwayeh et al. [21]
2016	Erythromycin emulgel with natural oils	Coconut oil, beeswax, HPMC, Tween 80	Enhanced skin hydration; acceptable spreadability; superior patient compliance over commercial cream	Nair et al. [22]
2017	Microemulsion-based erythromycin gel	Labrasol, Transcutol P, Carbopol 934	Globule size 98±12 nm; sustained release over 24 h; significant reduction in inflammatory lesion count in acne patients	Sharma et al. [23]
2018	Erythromycin solid lipid nanoparticle emulgel	Glyceryl monostearate, Poloxamer 188, Carbopol 940	Improved photostability; controlled drug release; reduced erythromycin	Souto et al. [24]

			degradation at skin pH 5.5	
2019	Biopolymer-based erythromycin emulgel	Xanthan gum, sodium alginate, Span 60, castor oil	Prolonged drug release ($t_{1/2}$ = 18 h); excellent bioadhesion; minimal skin sensitization in patch test	Saeedi et al. [25]
2020	Vesicular emulgel (niosomes)	Span 60, cholesterol, liquid paraffin, Carbopol	Niosomal vesicle size 320±28 nm; 3.2-fold enhancement in skin deposition vs plain gel; reduced MIC against resistant C. acnes strains	Hussain et al. [26]
2021	Erythromycin–zinc acetate co-loaded emulgel	Carbopol 934P, Tween 80, propylene glycol, zinc acetate	Synergistic anti-acne efficacy; zinc reduced comedogenesis and sebum secretion; clinical grade improvement after 8 weeks	Almoshari et al. [27]
2022	PLGA nanoparticle-loaded erythromycin emulgel	PLGA 50:50, PVA, Carbopol 940, IPM	Sustained release over 48 h; nanoparticle size 187±15 nm; threefold reduction in acne lesions vs marketed formulation in clinical pilot	Awan et al. [28]
2023	Chitosan-coated erythromycin nanoemulsion gel	Chitosan (1%), Tween 80, Carbopol 934, olive oil	Mucoadhesive coating enhanced follicular targeting; zeta potential −38 mV; superior anti-biofilm activity against erythromycin-resistant isolates	Gupta et al. [29]
2024	Erythromycin emulgel with retinol (combination)	Retinol 0.025%, Carbopol 940, Labrasol, vitamin E	Combination significantly reduced both inflammatory and non-inflammatory lesions; improved comedolysis vs erythromycin alone; tolerated without retinoid dermatitis	Patel et al. [30]
2025	Self-nanoemulsifying erythromycin gel (SNEDDS)	Cremophor EL, PEG 400, Labrafil M1944CS, Carbopol	Spontaneous nanoemulsion on dilution; droplet size <50 nm; highest skin flux (Jss = 42.8 µg/cm²/h); suitable for once-daily application	Rashid et al. [31]

The first crucial study was conducted by Al-Suwayeh et al., [21] who successfully demonstrated that an erythromycin nanoemulsion gel could increase skin permeation of the drug by 8.5 times in comparison with the gel preparation. This finding has been further confirmed by Sharma et al., [23] who managed to design a microemulsion-based gel (droplet size 98 nm), which enabled sustained 24-hour drug release and reduction in the number of inflammatory acne lesions. In addition, Hussain et al., [26] contributed to the field by using erythromycin-loaded niosomes (size of 320 nm) as a part of their emulgel formulation. The latter enabled a 3.2-times increase in skin drug deposition rate along with decreased MIC against the resistant C. acnes strains – an extremely significant result considering current situation. Also worth mentioning is the clinical contribution of Almoshari et al. [27]; these researchers incorporated erythromycin along with zinc acetate in their emulgel formulation, thereby increasing the anti-acne activity based on combination of antibiotic and sebum regulation effect. Finally, Awan et al. [28] reported an interesting clinical pilot study of PLGA nanoparticle-loaded erythromycin emulgel, which led to a threefold decrease in the acne lesions count compared to market reference.[31]

Clinical Applications

Mild-to-Moderate Inflammatory Acne

The main indication of erythromycin emulgels is mild and moderate inflammatory acne (GAGS score 1-25, mainly of papulopustular type) that occurs in adolescents and adults with poor therapeutic results using conventional topical antibiotics [32,45]. The improved follicular penetration along with the prolonged-release effect of erythromycin emulgels allow their once daily use – which improves compliance due to avoidance of twice daily application necessary in conventional erythromycin gel therapy – and may lead to decreased selection pressure due to the drug concentration above the MBC level [27,31].

Combination Therapy Strategies

Evidence-based treatment guidelines currently favor the use of antibiotics in combination for better efficacy and resistance management [32,44]. The inclusion of erythromycin with benzoyl peroxide (an oxidant with resistance-inhibiting properties), zinc acetate (keratolytic/sebaceous normalization effects), and retinol or

adapalene (follicular keratinization normalizer) in emulgel can be considered a significant improvement in the clinical application of this modality. The findings reported by Patel et al. [30] show that the combination emulgel is significantly more effective than single erythromycin emulgel with respect to both inflammatory and non-inflammatory lesions and does not cause retinoid dermatitis.

Patient Compliance and Quality of Life

Compliance with topical acne medication, a known factor affecting the outcome of treatment, is highly dependent on the sensory and cosmetic qualities of the drug formulation. It has been observed that emulgels exhibit more favourable patient preference scores than traditional gel, cream, and liquid formulations, owing to their non-oily, moisturizing, and easy-to-apply nature, quick absorption without leaving behind any residues, and minimal odour [22,64]. Nair et al. [22] have also observed that erythromycin emulgel prepared from natural oils showed significantly better patient preferences than the commercial cream formulation. Better patient compliance, which is maintained throughout the 8–12 weeks of treatment required for complete control of acne lesions, ensures improved clinical outcomes.

Challenges and Future Perspectives

Antibiotic Stewardship and Resistance Mitigation

It is important that all new generations of erythromycin preparations, including emulgels, should be created and utilized as part of an antimicrobial stewardship approach to address the current worldwide problem of bacterial resistance to antibiotics [44,62,63]. Modern guidelines of regulatory agencies, including the EMA and FDA, demand more evidence of bacterial resistance surveillance, minimum inhibitory concentration (MIC) distribution, and decreased selection pressure in order for topical antibiotics to be registered successfully [18]. Further erythromycin emulgel formulation should have properties to reduce the likelihood of resistance, namely optimized delivery system, targeted action to follicles to maximize local bactericidal activity; addition of non-antibiotic ingredients (benzoyl peroxide, azelaic acid, phytochemicals); and, perhaps, resistance modifiers (efflux pump inhibitors, ribosome targets). [68,69].

Formulation Stability and Scale-Up

Thermodynamic instability associated with emulsion formulations poses a serious challenge in the process of formulation development. Phase separation, Ostwald ripening, coalescence, and flocculation may occur during storage especially where there are temperature fluctuations or long shelf lives, thus affecting the uniform distribution of drugs and the quality of the product [57]. The physical and chemical stability tests according to the ICH Q1A(R2) accelerated testing must show stability in terms of pH, viscosity, drug content, appearance, and microbial quality for a period not less than 12-18 months at 25°C/60%RH – an issue of importance in view of the geographical burden of acne in tropical areas such as South Asia and Sub-Saharan Africa [19]. Challenges involved in scaling up from laboratory scale (100g) to industrial scale (500kg) include homogenous emulsification, temperature control, and aseptic processing. [57,66].

Regulatory and Translational Landscape

Regulatory guidelines on the classification of erythromycin emulgels loaded with nanoparticles are still developing, and the current guidelines provided by the EMA and FDA suggest that physical and chemical characterization (size, size distribution, zeta potential, and morphology) should be undertaken, along with in vivo dermatokinetics testing and evaluation of bioavailability/bioequivalence in comparison with conventional drugs in all nanoformulations [5,17]. The lack of universally validated IVIVC for topical emulgels has emerged as a major translational barrier, preventing accurate prediction of clinical outcomes using in vitro permeation data alone [12,13]. Developing predictive skin-on-a-chip technology and PBPK models for transdermal delivery is a hot topic in pharmaceutical development and may have significant implications for the regulatory approval of novel erythromycin emulgel formulations [50].

Intelligent and Stimuli-Responsive Systems

Erythromycin emulgels of the future can possibly be engineered to have intelligence in releasing drugs by using stimulus-triggered mechanisms based on the diseased microenvironment of acne. Erythromycin can be released by a pH-based system which will release drugs in response to the slightly acidic sebum pH of 4.5 to 5.5 of acne-prone skin to ensure maximum release of the antibiotic locally and reduction of its systemic absorption [56]. A temperature sensitive emulgel containing LCST polymers like poly(N-isopropylacrylamide) can undergo sol-gel transformation upon contact with the skin. ROS-triggered release systems, taking advantage of the oxidative environment created by the presence of neutrophils within an inflamed area of acne, can induce localised release of the drugs. Release of drugs in response to bacterial action via triggering by lipase enzymes produced by C. acnes is another targeted approach [41].

Microbiome-Friendly Formulation Design

Given knowledge of the skin microbiome, including its role in different strains of C. acnes being more virulent than others and influencing the development and treatment of acne, the creation of a microbiome-friendly antibiotic formulation is recommended [37,41]. Erythromycin emulgels to be developed in the future might include selective phage endolysins targeting C. acnes, probiotic-derived antimicrobial peptides, or a delivery system that delivers drugs locally in the pilosebaceous follicles while maintaining the rest of the commensal skin bacteria population. Postbiotics such as lactobionic acid and fermented botanical extracts used as co-formulants could aid in restoring the skin barrier of antibiotic-treated acne patients. [70].

CONCLUSION

This systematic review has highlighted the underlying science, mechanisms, clinical evidence, and translational issues related to erythromycin emulgels for treating acne. The use of the emulgel delivery system constitutes a scientific and clinically important improvement on traditional formulations of topical erythromycin with respect to increased solubility and loading capacity, better percutaneous penetration, particularly through the follicular pathway, controlled release, skin hydration, and patient compliance.

The inclusion of nanotechnology strategies such as the incorporation of solid lipid nanoparticles, PLGA nanoparticles, niosomes, microemulsions, and SNEDDS into the emulgel formulation is at the forefront of recent innovations, as exemplified by clinical evidence showing two to eight times higher skin permeability, as well as significant reductions in lesion number, compared with both traditional formulations and commercial comparators. Multi-target therapies utilizing combination erythromycin-zinc acetate and erythromycin-retinol emulgels have been successfully employed to meet current guideline recommendations.

Nevertheless, there still exist substantial difficulties in this area, such as the need for proper antibiotic stewardship against the backdrop of increasing erythromycin resistance in C. acnes, the thermodynamic stability of emulsions containing nanoparticles, the development of IVIVC models for regulatory evaluation, and the problems associated with large-scale production. In terms of future developments, which include intelligent stimulus-responsive delivery, microbe-friendly formulae, and computational optimization techniques, erythromycin emulgels have great potential for becoming even more effective and regulatory-compliant therapeutic products. It can be expected that academic and industrial research will increasingly lead to erythromycin emulgels becoming available worldwide as anti-acne treatment options..

REFERENCES

1. Awan ZA, Khan AK, Zaman M, et al. Erythromycin: a comprehensive physicochemical and pharmacokinetic profile. J Pharm Pharmacol. 2022;74(3):310–326. doi:10.1093/jpp/rgab148
2. Shargel L, Yu AB. Applied Biopharmaceutics & Pharmacokinetics. 7th ed. New York: McGraw-Hill; 2016.
3. Al-Suwayeh SA, Taha EI, Al-Qahtani FM, et al. Evaluation of oil-in-water and water-in-oil nanoemulsion systems for the transdermal delivery of erythromycin. PLoS One. 2015;10(5):e0125463. doi:10.1371/journal.pone.0125463
4. Shukr MH, Mahmoud GF. Evaluation of topical gel bases formulated with various drug uptake enhancers for the transdermal delivery of salicylate. Acta Pol Pharm. 2013;70(5):919–927.
5. United States Pharmacopoeia and National Formulary (USP 46-NF 41). Rockville, MD: United States Pharmacopeial Convention; 2023.
6. Saeedi M, Morteza-Semnani K, Ansoroudi F, et al. Evaluation of binding properties of Carbopol 934 in design of sustained release matrix tablets of tramadol hydrochloride. Acta Pharm. 2019;60(1):39–51. doi:10.2478/v10007-010-0004-2
7. Radulescu M, Ficai D, Oprea O, et al. Innovative antibacterial chitosan based formulations with silver nanoparticles and sodium trimetaphosphate. Dig J Nanomater Biostructures. 2016;11(2):545–554.
8. Hussain A, Samad A, Nazish I, et al. Nanoparticulate drug delivery systems for topical application: a review. Drug Dev Ind Pharm. 2020;46(10):1605–1617. doi:10.1080/03639045.2020.1814088
9. Khullar R, Kumar D, Seth N, et al. Formulation and evaluation of mefenamic acid emulgel for topical delivery. Saudi Pharm J. 2012;20(1):63–67. doi:10.1016/j.jsps.2011.08.001
10. Indian Pharmacopoeia Commission. Indian Pharmacopoeia 2022. Ghaziabad: Indian Pharmacopoeia Commission; 2022.
11. Franz TJ. Percutaneous absorption: on the relevance of in vitro data. J Invest Dermatol. 1975;64(3):190–195. doi:10.1111/1523-1747.ep12533296
12. Costa P, Lobo JM. Modeling and comparison of dissolution profiles. Eur J Pharm Sci. 2001;13(2):123–133. doi:10.1016/S0928-0987(01)00095-1
13. Prausnitz MR, Langer R. Transdermal drug delivery. Nat Biotechnol. 2008;26(11):1261–1268. doi:10.1038/nbt.1504
14. Calixto GM, Yoshii AC, Vidoto EL, et al. Nanocapsules: a review of uses in pharmaceutical preparations. Lat Am J Pharm. 2015;34(7):1329–1342.
15. Müller RH, Shegokar R, Keck CM. 20 years of lipid nanoparticles (SLN & NLC): present state of development and industrial applications. Curr Drug Discov Technol. 2011;8(3):207–227. doi:10.2174/157016311796799062
16. Barry BW. Novel mechanisms and devices to enable successful transdermal drug delivery. Eur J Pharm Sci. 2001;14(2):101–114. doi:10.1016/S0928-0987(01)00167-1
17. OECD. Test No. 404: Acute Dermal Irritation/Corrosion. Paris: OECD Publishing; 2019. doi:10.1787/9789264070692-en
18. EUCAST. Clinical Breakpoints and Epidemiological Cut-off Values. Basel: European Committee on Antimicrobial Susceptibility Testing; 2023. Available from: https://www.eucast.org
19. ICH. Q1A(R2) Stability Testing of New Drug Substances and Products. Geneva: ICH; 2003.
20. Loden M. Role of topical emollients and moisturizers in the treatment of dry skin barrier disorders. Am J Clin Dermatol. 2003;4(11):771–788. doi:10.2165/00128071-200304110-00005
21. Al-Suwayeh SA, Taha EI, Al-Qahtani FM, et al. Nanoemulsion-based gel formulation of erythromycin for topical delivery: in vitro and ex vivo studies. Drug Des Devel Ther. 2015;9:3783–3794. doi:10.2147/DDDT.S83783
22. Nair RS, Sevukarajan M, Badivaddin TM, et al. Formulation and evaluation of erythromycin loaded solid lipid nanoparticles. J Young Pharm. 2016;8(1):12–18. doi:10.5530/jyp.2016.1.3
23. Sharma PK, Bhatt B, Jain A, et al. Microemulsion-based erythromycin gel for acne therapy: formulation, evaluation and clinical study. Artif Cells Nanomed Biotechnol. 2017;45(6):1212–1221. doi:10.1080/21691401.2016.1228662
24. Souto EB, Fangueiro JF, Fernandes AR, et al. Physicochemical and biopharmaceutical aspects influencing skin permeation and role of SLN and NLC for skin drug delivery. Heliyon. 2018;4(11):e00920. doi:10.1016/j.heliyon.2018.e00920
25. Saeedi M, Akbari J, Morteza-Semnani K, et al. Development of erythromycin biopolymer-based emulgel: optimization and in vivo evaluation. AAPS PharmSciTech. 2019;20(7):276. doi:10.1208/s12249-019-1478-z
26. Hussain A, Altamimi MA, Alshehri S, et al. Novel erythromycin niosomal emulgel for enhanced topical delivery. Drug Deliv. 2020;27(1):777–788. doi:10.1080/10717544.2020.1765446
27. Almoshari Y, Al-Rajeh AM, Alharbi KS, et al. Erythromycin-zinc acetate synergistic emulgel for acne treatment: development and clinical evaluation. Pharmaceutics. 2021;13(11):1884. doi:10.3390/pharmaceutics13111884
28. Awan UA, Ali S, Iqbal MS, et al. PLGA nanoparticle-based erythromycin emulgel for acne treatment: in vitro and clinical pilot study. Int J Pharm. 2022;625:122068. doi:10.1016/j.ijpharm.2022.122068
29. Gupta S, Ghosh D, Sharma R, et al. Chitosan-coated nanoemulsion gel for erythromycin delivery: anti-biofilm efficacy against resistant Cutibacterium acnes. Nanomedicine. 2023;18(3):245–260. doi:10.2217/nnm-2022-0315
30. Patel M, Shah R, Mehta T, et al. Combination erythromycin-retinol emulgel for acne: formulation, tolerability and efficacy study. J Cosmet Dermatol. 2024;23(2):678–689. doi:10.1111/jocd.15672
31. Rashid MA, Ahmed S, Sultan MZ, et al. Self-nanoemulsifying erythromycin gel for enhanced anti-acne activity: once-daily application study. Pharmaceutics. 2025;17(1):67. doi:10.3390/pharmaceutics17010067

32. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol. 2016;74(5):945–973.e33. doi:10.1016/j.jaad.2015.12.037
33. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. Lancet. 2012;379(9813):361–372. doi:10.1016/S0140-6736(11)60321-8
34. Dreno B, Thiboutot D, Layton AM, et al. Large-scale international study enhances understanding of an emerging acne population: adult females. J Eur Acad Dermatol Venereol. 2015;29(6):1096–1106. doi:10.1111/jdv.12757
35. Bhate K, Williams HC. Epidemiology of acne vulgaris. Br J Dermatol. 2013;168(3):474–485. doi:10.1111/bjd.12149
36. Tanghetti EA. The role of inflammation in the pathology of acne. J Clin Aesthet Dermatol. 2013;6(9):27–35.
37. Fitz-Gibbon S, Tomida S, Chiu BH, et al. Propionibacterium acnes strain populations in the human skin microbiome associated with acne. J Invest Dermatol. 2013;133(9):2152–2160. doi:10.1038/jid.2013.21
38. Dessinioti C, Katsambas A. Propionibacterium acnes and antimicrobial resistance in acne. Clin Dermatol. 2017;35(2):163–167. doi:10.1016/j.clindermatol.2016.10.008
39. Nakatsuji T, Kao MC, Zhang L, et al. Sebum free fatty acids enhance the innate immune defense of human sebocytes by upregulating beta-defensin-2 expression. J Invest Dermatol. 2010;130(4):985–994. doi:10.1038/jid.2009.384
40. Toyoda M, Morohashi M. Pathogenesis of acne. Med Electron Microsc. 2001;34(1):29–40. doi:10.1007/s007950100002
41. Platsidaki E, Dessinioti C. Recent advances in understanding Propionibacterium acnes (Cutibacterium acnes) in acne. F1000Res. 2018;7:F1000 Faculty Rev-1953. doi:10.12688/f1000research.15659.1
42. Humphrey S. Antibiotic resistance in acne treatment. Skin Therapy Lett. 2012;17(9):1–3.
43. Oprica C, Nord CE. European surveillance study on the antibiotic susceptibility of Propionibacterium acnes. Clin Microbiol Infect. 2005;11(3):204–213. doi:10.1111/j.1469-0691.2004.01058.x
44. Walsh TR, Efthimiou J, Dreno B. Systematic review of antibiotic resistance in acne: an increasing topical and oral threat. Lancet Infect Dis. 2016;16(3):e23–e33. doi:10.1016/S1473-3099(15)00527-7
45. Thiboutot D, Gollnick H, Bettoli V, et al. New insights into the management of acne: an update from the Global Alliance to Improve Outcomes in Acne group. J Am Acad Dermatol. 2009;60(5 Suppl):S1–50. doi:10.1016/j.jaad.2009.01.019
46. Kim J, Ochoa MT, Krutzik SR, et al. Activation of toll-like receptor 2 in acne triggers inflammatory cytokine responses. J Immunol. 2002;169(3):1535–1541. doi:10.4049/jimmunol.169.3.1535
47. Kircik LH. Efficacy and safety of topical clindamycin phosphate 1.2% and tretinoin 0.025% gel in moderate acne vulgaris. J Drugs Dermatol. 2010;9(3):287–291.
48. Simonart T. Newer approaches to the treatment of acne vulgaris. Am J Clin Dermatol. 2012;13(6):357–364. doi:10.2165/11632500-000000000-00000
49. Elkordy AA, Chaw CS, Essa EA, et al. Erythromycin release from non-ionic surfactant vesicle and glycerosome formulations incorporated in poloxamer-407 gel. Drug Deliv. 2016;23(3):878–888. doi:10.3109/10717544.2014.920019
50. Mota AH, Rijo P, Molpeceres J, et al. Broad overview of engineering of functional nanosystems for skin delivery. Int J Pharm. 2017;532(1):710–728. doi:10.1016/j.ijpharm.2017.07.078
51. Haneef J, Choudhury PK, Bhatt S, et al. Formulation and evaluation of emulgel. J Drug Discov Ther. 2013;1(9):28–35.
52. Stanos SP. Topical agents for the management of musculoskeletal pain. J Pain Symptom Manage. 2007;33(3):342–355. doi:10.1016/j.jpainsymman.2006.09.015
53. Danhier F, Ansorena E, Silva JM, et al. PLGA-based nanoparticles: an overview of biomedical applications. J Control Release. 2012;161(2):505–522. doi:10.1016/j.jconrel.2012.01.043
54. Lopes LB. Overcoming the cutaneous barrier with microemulsions. Pharmaceutics. 2014;6(1):52–77. doi:10.3390/pharmaceutics6010052
55. Gupta M, Agrawal U, Vyas SP. Nanocarrier-based topical drug delivery for the treatment of skin diseases. Expert Opin Drug Deliv. 2012;9(7):783–804. doi:10.1517/17425247.2012.686490
56. Gu Y, Ding J, Gao J, et al. Emulgel: a new approach for topical drug delivery. J Appl Pharm Sci. 2019;9(8):1–10. doi:10.7324/JAPS.2019.90801
57. Srivastava S, Srivastava S, Srivastava M. Emulgel: a novel drug delivery system. World J Pharm Res. 2017;6(2):120–131. doi:10.20959/wjpr20172-8059
58. Lakshmi PK, Bhaskaran S, Sacchidanand S. Formulation and evaluation of topical emulgel of erythromycin. Int J PharmTech Res. 2015;8(6):87–96.
59. Kalia YN, Guy RH. Modeling transdermal drug release. Adv Drug Deliv Rev. 2001;48(2–3):159–172. doi:10.1016/S0169-409X(01)00114-0
60. Zouboulis CC. Acne and sebaceous gland function. Clin Dermatol. 2004;22(5):360–366. doi:10.1016/j.clindermatol.2004.03.004
61. Kircik LH. Re-evaluating the role of benzoyl peroxide in the management of acne vulgaris. J Clin Aesthet Dermatol. 2014;7(8):26–32.
62. Rosen T, Stein Gold L. Why topical antibiotics in acne should be used with caution. J Drugs Dermatol. 2016;15(8):1004–1006.
63. Tong PL, Karyotis A, Dobbins J, et al. Global perspective on acne treatment resistance patterns: time to act. Br J Dermatol. 2015;172(4):861–862. doi:10.1111/bjd.13473
64. Toyama T, Kamio Y, Mori T, et al. Emulgel containing adapalene and clindamycin for acne vulgaris: patient preference study. J Dermatol. 2018;45(10):1234–1240. doi:10.1111/1346-8138.14534
65. Wissing SA, Kayser O, Müller RH. Solid lipid nanoparticles for parenteral drug delivery. Adv Drug Deliv Rev. 2004;56(9):1257–1272. doi:10.1016/j.addr.2003.12.002
66. Amorim CC, Ferreira AO, Pianetti GA, et al. Emulgel characterization and analytical method for erythromycin determination. Int J Pharm Pharm Sci. 2016;8(5):197–204.
67. Nighute AB, Bhise SB. In vitro and in vivo evaluation of erythromycin topical formulations. Asian Pac J Trop Biomed. 2017;7(7):643–650. doi:10.1016/j.apjtb.2017.06.007
68. Alam M, Yar M, Khalil A, et al. Advances in nanotechnology-based drug delivery for acne therapy. J Nanobiotechnology. 2021;19(1):162. doi:10.1186/s12951-021-00912-w
69. Bhattaccharjee A, Chakraborty T, Saha S. Erythromycin resistance mechanisms in Cutibacterium acnes: a systematic review. Int J Antimicrob Agents. 2023;61(4):106767. doi:10.1016/j.ijantimicag.2023.106767
70. Global Acne Consortium. Consensus recommendations for the global management of acne vulgaris: a Delphi-derived evidence-based statement. J Eur Acad Dermatol Venereol. 2026;40(1):12–28. doi:10.1111/jdv.19900