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Bacteriophage and Endolysin Therapy for Skin Dysbiosis, Mechanistic Insights, and Therapeutic Applications

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Skin dysbiosis, characterized by microbial imbalance and pathogen overgrowth, plays a central role in several common skin disorders, including acne vulgaris, atopic dermatitis, and chronic wound infections. Conventional broad-spectrum antibiotics often disrupt beneficial skin microbiota and contribute to antimicrobial resistance, including emergence of multidrug-resistant pathogens. These limitations have driven interest in precision antimicrobial strategies. Bacteriophages and phage-derived endolysins have emerged as promising alternatives due to their high specificity, potent bactericidal activity, and ability to disrupt biofilms while preserving commensal bacteria. This review outlines the mechanistic basis and therapeutic potential of phage and endolysin-based approaches for skin diseases. Lytic phages selectively infect and kill bacterial hosts through intracellular replication and cell lysis. In contrast, endolysins enzymatically degrade peptidoglycan, leading to rapid bacterial destruction. The study discusses disease-specific applications, including targeting pro-inflammatory *Cutibacterium acnes* phylotypes in acne vulgaris, selective reduction of *Staphylococcus aureus* colonization in atopic dermatitis, and disruption of polymicrobial biofilms involving methicillin-resistant *S. aureus* and *Pseudomonas aeruginosa* in chronic wounds. Preclinical studies, early human studies, and case reports suggest reduced pathogen burden and clinical improvement, supporting further clinical evaluation. Remaining challenges include formulation stability, host immune interactions, regulatory pathways, and biomarker-guided clinical trial design. Overall, phage and endolysin-based therapies represent precision, next-generation tools for restoring skin microbial balance in the era of antibiotic resistance.

Key Words: Acne vulgaris, Atopic dermatitis, Bacteriophages, Biofilms, Endolysins, Skin microbiome

INTRODUCTION

Human skin is a complex ecological interface in which host immunity interacts with a diverse microbial community to maintain barrier integrity and protect against pathogens. Disruption of this balance by inflammation, environmental stress, or antibiotic exposure can lead to microbial dysbiosis, which underlies several common dermatologic conditions, including acne vulgaris, atopic dermatitis (AD), and chronic wound infections[1]. Overgrowth of pathogenic bacteria, such as *C. acnes*, *S. aureus*, methicillin-resistant *S. aureus*, and *P. aeruginosa*, amplifies inflammation, impairs barrier function, and contributes to development of recurrent or treatment-resistant disease[2,3].

Systemic and topical antibiotics have long been central to management of skin infections and inflammatory dermatoses. However, increasing antimicrobial resistance, disruption of commensal microbiota, and limited efficacy against biofilm-

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associated bacteria have highlighted the need for more selective antimicrobial strategies[4]. Phages and phage-derived endolysins have therefore emerged as promising alternatives because they exhibit host-specific bacteriolytic activity, disrupt biofilms, and largely spare beneficial microbiota, making them particularly attractive for dermatologic applications[5]. Preclinical and early translational studies show that *C. acnes*-specific phages reduce inflammatory lesions in acne models. Staphylococcal endolysins improve outcomes associated with AD while preserving commensal *Staphylococcus* species. In chronic wounds, phages targeting *P. aeruginosa* effectively disrupt and degrade bacterial biofilms[6-8].

Advances in metagenomic sequencing have further revealed that skin virome, particularly phages, play a significant role in shaping microbial community structure. Phage populations' alterations observed in acne and AD suggest that rather than merely reflecting microbial imbalance, phage bacteria interactions may contribute directly to disease phenotypes[9]. These findings support the concept of phage-based therapeutics as precision tools capable of modulating dysbiotic microbial networks rather than indiscriminately eliminating skin bacteria.

This review integrates mechanistic insights, disease-specific evidence, and current therapeutic progress in phage and endolysin-based interventions for acne, AD, and chronic wound infections. It also highlights key opportunities and challenges for translating these biologics into routine dermatologic practice.

SKIN MICROBIOME AND DISEASE-RELEVANT DYSBIOSIS

The skin microbiome is a highly organized ecosystem of bacteria, fungi, viruses, and phages occupying distinct anatomical niches. Sebaceous regions are dominated by *Cutibacterium* species, moist areas are enriched with *Staphylococcus* and *Corynebacterium*, and dry skin sites support greater microbial diversity[10]. This spatial distribution reflects metabolic specialization and continuous interactions between resident microbes and a host immune system. Under homeostatic conditions, commensal microorganisms contribute to barrier integrity, induce antimicrobial peptide production, and support immune tolerance[11].

Dysbiosis refers to disruptions in microbial composition, functional activity, or phage bacteria interactions that disturb this balance and promote disease. In acne vulgaris, inflammatory *C. acnes* phylotypes, particularly IA1 and IA2, become dominant within the pilosebaceous unit. These strains produce porphyrins, extracellular lipases, and biofilms that enhance oxidative stress and follicular inflammation[12]. Multilocus sequence typing analyses of Korean clinical isolates

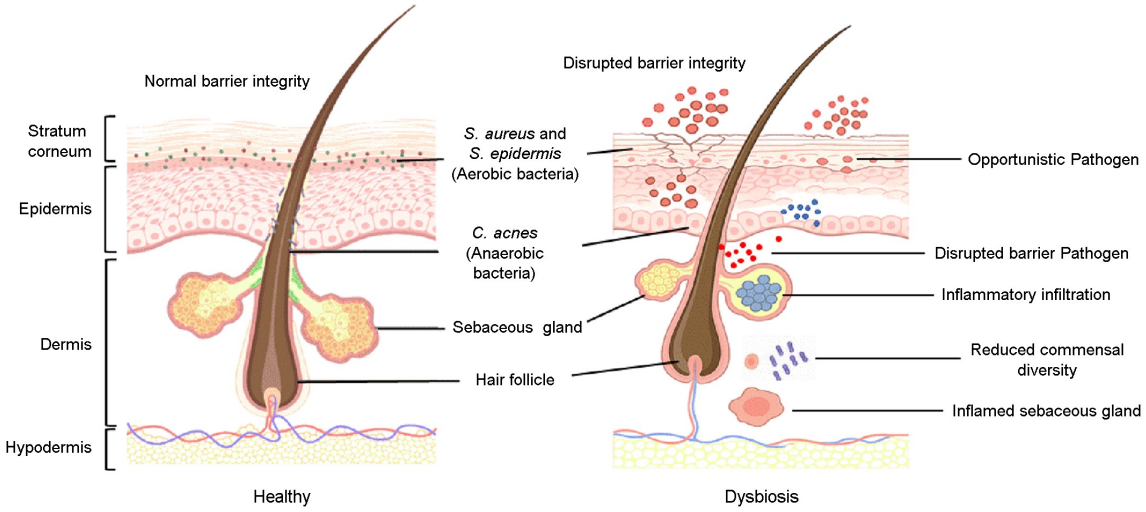

Fig. 1. Skin microbiome and disease-related dysbiosis. Schematic illustration of the human skin depicts microbial distribution and barrier status under homeostatic and dysbiotic conditions. In healthy skin, an intact epidermal barrier supports a balanced commensal microbiota, with *Staphylococcus epidermidis* and low-abundance *Staphylococcus aureus* predominating on the skin surface and *Cutibacterium acnes* localized within the pilosebaceous unit, contributing to barrier maintenance and immune homeostasis. In dysbiosis, epidermal barrier disruption facilitates opportunistic pathogen overgrowth and penetration, reduces commensal diversity, and promotes inflammatory cell infiltration and sebaceous gland inflammation, collectively promoting cutaneous inflammation and disease susceptibility. Created with BioRender.com.

further demonstrate marked strain-level diversity and emerging antibiotic resistance in *C. acnes*, emphasizing limitations of prolonged antibiotic therapy and the need for targeted alternatives[13].

AD displays a distinct dysbiotic pattern. Disease flares are associated with excessive colonization by *S. aureus* and a concurrent loss of protective commensal staphylococci. This imbalance promotes Th2-skewed immune responses, epidermal barrier dysfunction, and increased susceptibility to secondary infections. Recent metagenomic studies have also revealed pronounced alterations in AD patients' skin virome[3,14]. Changes in phage abundance and composition suggest that rather than merely reflecting inflammatory states, phage-bacterium interactions may actively influence microbial dominance and disease severity[15].

Chronic wounds present another form of severe dysbiosis. Stable polymicrobial biofilms containing MRSA, *P. aeruginosa*, *enterococci*, and anaerobic bacteria characterize such lesions[16]. Biofilm-associated extracellular matrices limit antibiotic penetration, impair immune clearance, and sustain chronic inflammation, ultimately delaying tissue repair.

Together, these findings establish dysbiosis as a central driver of skin disease. Defining microbial and viral community shifts across acne, AD, and chronic wounds provides a critical foundation for precision therapeutics. In this context, phages and endolysins offer targeted strategies to eliminate pathogens while preserving the skin's broader microbial ecosystem[17]. Fig. 1 illustrates commensal microbes' spatial organization in healthy skin and characteristic shifts observed during dysbiosis across major skin diseases.

MECHANISMS OF PHAGES AND ENDOLYSINS IN SKIN DISEASE

Phages exert therapeutic effects through precise bacterial

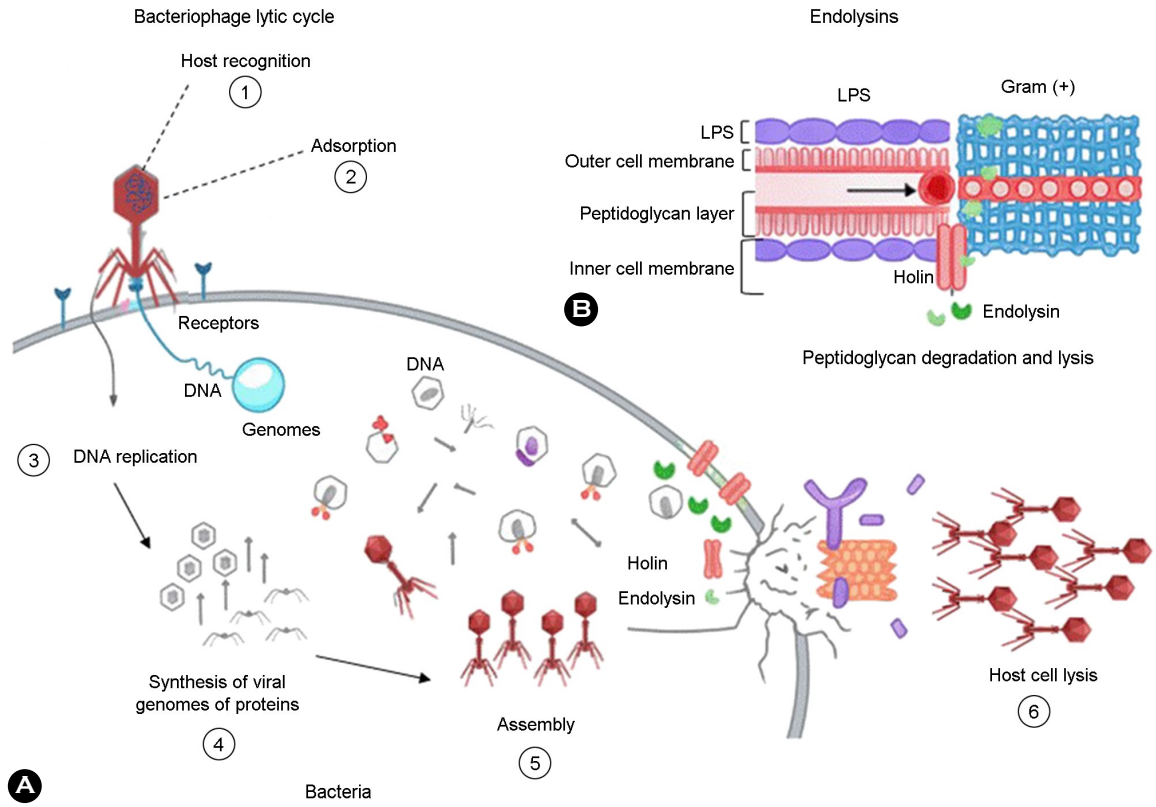

Fig. 2. Mechanistic actions of phages and endolysins on skin-associated bacterial pathogens. (A) Lytic phages recognize and adsorb specific bacterial surface receptors, inject their genomic material, replicate intracellularly, and assemble progeny virions. Phage-encoded holins permeabilize the inner membrane, enabling endolysins to access and degrade the peptidoglycan layer, resulting in host cell lysis and release of mature phage particles. (B) Endolysins mediate rapid bacterial killing by cleaving peptidoglycan, leading to cell wall disruption and osmotic lysis, particularly in Gram-positive skin-associated pathogens. Created with BioRender.com.

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targeting, efficient lytic activity, and minimal disruption of commensal microbiota. The phage life cycle begins with recognition and binding to specific bacterial surface receptors that determine host specificity. In skin-associated pathogens, these receptors include lipoteichoic acids on *S. aureus*, cell wall-associated surface structures on *C. acnes*, and type IV pili on *P. aeruginosa*, which serve as essential adsorption receptors for phage PA1Ø[6]. After attachment, phages inject their genetic material into the host cell, thus leading to takeover of bacterial metabolism, intracellular replication, and eventual host lysis. Newly released virions then infect neighboring bacteria, allowing localized amplification at the infection site[18,19]. Fig. 2 summarizes the lytic phage life cycle's key steps and phage-derived endolysins' bacteriolytic action against skin-associated pathogens.

Endolysins represent a complementary antimicrobial strategy. These phage-derived enzymes directly cleave peptidoglycan, leading to rapid bacterial lysis. Their activity is particularly effective against Gram-positive organisms and does not require specific surface receptors or active bacterial growth. This allows endolysins to bypass several biofilm-associated resistance mechanisms. CHAP-domain endolysins display strong lytic activity against *S. aureus* and related pathogens. They remain stable across broad pH and temperature ranges and retain function in complex biological environments, making them suitable for topical dermatologic use[20,21]. In *in-vitro* MRSA biofilm assays, phage SAP-26 shows potent antibiofilm activity and synergizes with rifampicin, whereas its derived endolysin LysSAP26 displays strong bacteriolytic activity, supporting potential translational relevance of SAP-26-based phage and endolysin strategies for chronic wound infection models[22,23].

Beyond killing bacteria directly, phages and endolysins offer important ecological advantages. Their narrow host range enables preservation of beneficial commensals, such as *S. epidermidis*, contributing to immune regulation and barrier repair. Phages can also penetrate mature biofilms through enzymatic degradation of extracellular matrices or replication within deeper biofilm layers, overcoming conventional antibiotics' significant limitation[24]. In acne models, lytic *C. acnes* phages demonstrate strain-selective killing and reduce inflammatory cytokines' production, suggesting both antimicrobial and immunomodulatory effects[25].

Collectively, these mechanisms highlight phage and endolysin-based therapies' suitability for skin diseases. Their precision, antibiofilm activity, and microbiome compatibility position them as next-generation biologics for correcting dysbiosis while minimizing collateral damage[17]. Table 1 provides a comparative overview of disease-specific targets, therapeutic agents, mechanisms of action, and key outcomes for phage- and endolysin-based interventions across major skin diseases.

1. Bacteriophage and endolysin therapy for acne vulgaris

Acne vulgaris arises from complex interplay of follicular

Table 1. Applications of phages and endolysin therapy in major skin diseases

Skin disease	Target pathogens	Therapeutic agent	Mechanism of action	Preclinical and mechanistic outcomes	References
Acne vulgaris	*Cutibacterium acnes* (inflammatory phylotypes)	*C. acnes*-specific lytic phages and phage-derived endolysins	Phages selectively infect and lyse *C. acnes* within the pilosebaceous unit. Endolysins enzymatically degrade peptidoglycan, targeting planktonic cells and biofilm-associated bacteria.	Reduced *C. acnes* burden, disruption of biofilms, and attenuation of proinflammatory cytokine responses.	7, 27
Atopic dermatitis	*Staphylococcus aureus*	*S. aureus*-specific phages and staphylococcal endolysins (e.g., Staphefekt SA.100)	Endolysins selectively cleave *S. aureus* peptidoglycan while sparing commensal staphylococci, thereby limiting pathogen-driven immune activation.	Decreased *S. aureus* colonization, associated with improved barrier-related markers, and reduced Th2-associated inflammation.	8, 34
Chronic wounds	MRSA, *Pseudomonas aeruginosa* (polymicrobial biofilms)	Lytic phages (e.g., PA1Ø, SAP-26) and phage-derived endolysins (e.g., LysGH15, LysSAP26)	Phages lyse biofilm-embedded bacteria through infection and replication, whereas endolysins enzymatically degrade peptidoglycan, leading to rapid killing of Gram-positive pathogens and biofilm destabilization.	Demonstrated reduction of bacterial burden and disruption of mature biofilms in *in vitro* and preclinical infection models, supporting further evaluation in chronic wound settings.	6, 22, 23, 40, 50

hyperkeratinization, excess sebum production, microbial dysbiosis, and cutaneous inflammation. A key microbial feature of acne is the shift in *C. acnes* populations from a diverse community toward dominance of inflammatory phylotypes, particularly IA1 and IA2. These strains produce porphyrins, extracellular lipases, and biofilms that intensify oxidative stress, promote inflammation, and disrupt follicular barrier function[7,12]. Multilocus sequence typing studies of Korean clinical isolates further reveal pronounced strain-level heterogeneity and increasing resistance to commonly used antibiotics. These findings highlight long-term tetracycline and macrolide therapy's limitations and underscore the need for targeted alternatives[13,26].

C. acnes specific phages have emerged as promising precision therapeutics for acne treatment because they exhibit strong lytic activity against acne-associated strains and display highly conserved genomes, suggesting favorable safety profiles and low risk of horizontal gene transfer[27,28]. In preclinical acne models, lytic phages' administration reduces bacterial burden and attenuates inflammatory responses. Murine studies demonstrate decreased neutrophil infiltration and reduced inflammatory lesion size following intralesional phage treatment, supporting antimicrobial activity and suggesting downstream immunomodulatory effects in preclinical models[29]. Importantly, phage specificity enables selective elimination of pathogenic *C. acnes* while preserving beneficial cutaneous commensals contributing to skin homeostasis.

Phage-derived endolysins provide an additional therapeutic strategy. These enzymes rapidly degrade peptidoglycan upon contact and do not depend on bacterial metabolic activity. Recombinant and engineered endolysins derived from *C. acnes* phages show enhanced stability and broad activity across inflammatory subtypes. They also maintain compatibility with lipid-rich skin environments, making them suitable candidates for topical acne formulations[30].

Despite encouraging preclinical evidence, several translational challenges remain. The pilosebaceous unit's anaerobic and lipid-density environment can limit phage stability and tissue penetration. To address this and to enhance follicular targeting and sustained release, recent studies have explored delivery approaches including microencapsulation, liposomal carriers, hydrogels, and microneedle-assisted systems[31]. Additionally, individual phages' narrow host range may necessitate use of personalized phage panels or cocktails to ensure diverse clinical strains' coverage[19].

Overall, phage and endolysin-based therapies are becoming precision tools for restoring microbial balance, disrupting biofilms, and reducing inflammation in acne vulgaris. For successful clinical translation, continued advances in formulation technologies, engineered lysins, and strain-level diagnostics are critical[32].

2. Bacteriophage and endolysin therapy in atopic dermatitis (AD)

AD is a chronic inflammatory skin disease marked by epidermal barrier dysfunction, immune dysregulation, and pronounced microbial dysbiosis. A hallmark of AD is excessive colonization by *S. aureus*, closely correlated with disease severity. By releasing proteases, toxins, and superantigens, this pathogen promotes Th2-skewed immune responses, pruritus, and barrier damage[3]. In parallel, protective commensal staphylococci, such as *S. epidermidis* and *S. hominis*, are markedly reduced. Loss of these beneficial species weakens antimicrobial defense and facilitates pathogen dominance[33]. This shift from a diverse microbial ecosystem to *S. aureus*-driven dysbiosis represents a central therapeutic AD target.

To correct this imbalance, phages and phage-derived endolysins provide precision-based strategies. Staphylococcal endolysins, particularly those containing CHAP catalytic domains, rapidly cleave peptidoglycans with high specificity. These enzymes demonstrate potent lytic activity against *S. aureus*, including methicillin-resistant strains, while largely sparing commensal bacteria that support immune homeostasis[21,23]. Clinical studies evaluating the topical endolysin staphefekt SA.100 have shown reductions in *S. aureus* colonization and improvements in eczema severity scores reported in small clinical studies and case series. Importantly, during prolonged use, these benefits were observed without evidence of resistance development or disruption of beneficial skin microbiota[34].

Lytic phages also show therapeutic promise in AD. *S. aureus* phages can penetrate biofilms, replicate at infection sites, and selectively reduce pathogen burden. Their capacity to degrade extracellular biofilm matrices provides a clear advantage over conventional antibiotics that often show limited efficacy against biofilm-associated bacteria in AD lesions[24]. In preclinical models, phage treatment reduces skin inflammation, lowers bacterial load, and enhances pathways associated with barrier repair, suggesting coordinated antimicrobial and immunomodulatory effects[25].

Recent metagenomic analyses further highlight skin virome's role in AD. Significant alterations in phage abundance and diversity have been reported, with numerous viral genomes fluctuating in comparison to those found in healthy skin[15]. These findings suggest that rather than merely reflecting inflammation, phage-bacterial interactions may actively shape disease severity.

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Key translational challenges remain, including formulation stability on inflamed skin and strain heterogeneity among *S. aureus* isolates. Advances in engineered lysins, patient-specific phage cocktails, and combination approaches with moisturizers or anti-inflammatory agents may help overcome these barriers[35,36]. Collectively, phage- and endolysin-based therapies represent next-generation tools for restoring microbial balance and improving clinical AD outcomes. However, large randomized controlled trials remain limited, and standardized endpoints for microbiome-directed therapies are still evolving.

3. Phage and endolysin therapy for chronic wounds and polymicrobial skin infections

Chronic wounds represent one of the most challenging settings for antimicrobial intervention. Diabetic foot ulcers, venous leg ulcers, and pressure injuries commonly harbor dense polymicrobial biofilms composed of *S. aureus* (including MRSA), *P. aeruginosa*, enterococci, and obligate anaerobes. Biofilm-associated bacteria can tolerate antibiotic concentrations up to 1,000 times higher than those required to kill planktonic cells, evade host immune clearance, and sustain chronic inflammation, impairing tissue repair and delaying wound healing[37,38]. Standard treatments, such as debridement and broad-spectrum antibiotics, often yield inconsistent outcomes and further contribute to antimicrobial resistance.

In this context, phage therapy offers several advantages. Lytic phages can infect bacteria embedded within biofilms and replicate locally at the infection site. The *P. aeruginosa* phage PA1Ø is a well-characterized example that utilizes type IV pili as its bacterial receptor and efficiently lyses biofilm-associated cells[6]. Biofilm-focused experimental studies have

Table 2. Major skin pathogens and representative phages or endolysins under preclinical investigation

Skin disease	Target pathogen	Therapeutic agent	Key mechanism	Study type	Outcome	References
Atopic dermatitis	*Staphylococcus aureus*	SaGU1 (lytic phage)	Selective adsorption and lytic replication leading to bacterial cell lysis	*In vitro* (clinical *S. aureus* isolates from AD patients; host range and stability assays)	Demonstrated selective lytic activity against *S. aureus* isolates from patients with atopic dermatitis.	51
Atopic dermatitis	*Staphylococcus aureus*	Staphefekt SA.100 (endolysin)	Enzymatic cleavage of *S. aureus* peptidoglycan	Human case reports and clinical studies	Reduced *S. aureus* colonization and improvement of disease signs	8, 34
Acne vulgaris	*Cutibacterium acnes*	*C. acnes* phages (e.g., P1, P10, P14)	Highly specific lytic infection of *C. acnes*	*In vitro* characterization	Broad lytic activity against clinical isolates	27
Acne vulgaris	*Cutibacterium acnes*	CAP10-3 endolysin	Enzymatic degradation of peptidoglycans	*In vitro* assays	Demonstrated antibacterial activity against *C. acnes*	52
Chronic wounds / mixed biofilms	*Pseudomonas aeruginosa*	PA1Ø (lytic phage)	Type IV pili-dependent adsorption and lytic replication	*In vitro* and biofilm-focused studies	Effective biofilm disruption and bacterial killing	6, 39
Chronic wounds / MRSA biofilms	MRSA (*S. aureus*)	SAP-26 (lytic phage)	Biofilm penetration and phage-mediated lysis; enhanced activity with rifampicin	*In vitro* MRSA biofilm assay	Strong antibiofilm activity and synergy with rifampicin	22
Chronic wounds / Gram-positive pathogens	MRSA, MDR *S. aureus*	LysSAP26 (endolysin)	Enzymatic peptidoglycan degradation	*In vitro* antibacterial assays; *in vivo* systemic infection model	Potent bacteriolytic activity against planktonic and biofilm-associated bacteria	23

Evidence level reflects the experimental system used (*in vitro*, animal models, or human reports); no agent listed has yet received regulatory approval for dermatologic indications

demonstrated that PA1Ø reduces bacterial burden and disrupts biofilm architecture, supporting its translational relevance for chronic wound management[39].

Endolysins provide a complementary strategy against Gram-positive wound pathogens. The staphylococcal endolysin LysSAP26, derived from phage SAP-26, exhibits potent *in vitro* lytic activity against MRSA and other clinically relevant pathogens in planktonic and biofilm-associated states[23]. In contrast, the phage SAP-26 has been shown to display strong antibiofilm activity and marked synergistic effects when combined with rifampicin in *in-vitro* MRSA biofilm assays, resulting in substantial reductions in viable biofilm-associated bacteria compared with antibiotic treatment alone[22]. Other CHAP-domain endolysins also exhibit broad activity against Gram-positive wound isolates and remain stable across a range of pH conditions, supporting their incorporation into topical hydrogels and wound dressings[40].

An additional advantage of phage-based therapy is localized self-amplification. Applied phages replicate only in the presence of susceptible bacteria, increasing their concentration specifically at infected sites while minimizing systemic exposure and off-target effects on commensal skin microbiota[41]. This targeted activity may contribute to microbial rebalancing and reduced inflammatory signaling within chronic wounds.

Despite these benefits, several translational challenges remain. Effective penetration into mature biofilms, strain-level variability among clinical isolates, and integration with existing wound care protocols must be addressed to optimize therapeutic outcomes. Emerging formulation strategies, including alginate dressings, hydrogel encapsulation, and nanoparticle-based delivery systems, show promise in overcoming these barriers[31]. Collectively, phages and endolysins represent precision-based therapeutics with significant potential for treating chronic wounds dominated by antibiotic-resistant and biofilm-forming pathogens, warranting further evaluation in clinically relevant wound infection models (Table 2).

DISCUSSION

Phage- and endolysin-based therapeutics represent a promising paradigm shift in management of dysbiosis-driven skin diseases, offering mechanistically distinct advantages over conventional antimicrobial strategies. One of their most significant strengths lies in their high specificity. Lytic bacteriophages selectively target pathogenic species such as *C. acnes*, *S. aureus*, and *P. aeruginosa* while sparing commensal microorganisms essential for maintaining skin barrier function and immune homeostasis[11]. This targeted activity contrasts sharply with broad-spectrum topical and systemic antibiotics, which frequently disrupt microbial diversity, exacerbate dysbiosis, and contribute to disease recurrence and antimicrobial resistance.

Another major advantage of phage- and endolysin-based therapeutics is their efficacy against biofilms, a key factor underlying chronic skin infections and nonhealing wounds' persistence. Biofilm matrices restrict antibiotic penetration and protect bacteria from host immune responses. Multiple lytic phages, including PA1Ø and the staphylococcal phage SAP-26, have demonstrated in experimental models the ability to disrupt established biofilms and eliminate bacteria embedded within mature biofilm structures[6,22]. Endolysins are particularly effective against Gram-positive pathogens because they induce rapid bacterial lysis independent of metabolic state. This growth-phase independence enhances their activity against stationary-phase cells and antibiotic-tolerant populations, including MRSA[40].

Phages further possess unique capacity for localized self-amplification. Following topical or local administration, phages replicate exclusively in susceptible bacterial hosts' presence, leading to increased local concentration at infection sites while minimizing systemic exposure and off-target effects on the resident skin microbiota[18]. This self-limiting pharmacodynamic property may reduce dosing frequency and support sustained antimicrobial activity without cumulative toxicity.

Despite these advantages, several limitations and translational challenges must be addressed. Many phages exhibit a relatively narrow host range, potentially limiting their efficacy against genetically diverse clinical isolates of *S. aureus* or *C. acnes*. This challenge may be mitigated using rationally designed phage cocktails, strain-matched therapeutic approaches, or adaptive phage formulations[19]. Formulation stability also remains a concern because phages and endolysins can be sensitive to environmental factors such as pH, temperature, desiccation, UV exposure, and lipid-rich skin environments[42]. Moreover, regulatory frameworks governing phage-based therapeutics are still evolving, and standardized guidelines across jurisdictions for manufacturing, quality control, genomic safety screening, and clinical evaluation remain limited[43].

Emergence of bacterial resistance to phages or endolysins represents another important consideration. However, resistance mechanisms differ fundamentally from those associated with antibiotics and might develop more slowly. Importantly, phages retain the ability to coevolve with bacterial populations under selective pressure, potentially restoring therapeutic efficacy *in vivo* even when resistance is observed *in-vitro*[44]. Combination strategies involving phage cocktails, periodic reformulation, or coadministration with antibiotics or endo-

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lysins may further suppress resistance development.

At this writing, technological and conceptual advances are rapidly expanding phage- and endolysin-based dermatological interventions' therapeutic potential. One key direction is personalized phage therapy, enabled by rapid pathogen sequencing, phage susceptibility profiling, and curated phage libraries. This approach is particularly relevant for diseases such as acne vulgaris and atopic dermatitis, in which strain-level diversity and variable phage sensitivity limit uniform treatment strategies' effectiveness[36]. Indeed, integration of artificial intelligence-assisted host-range prediction tools may further accelerate clinical implementation.

Advances in phage and endolysin engineering are also reshaping the field. Genetically modified phages can be designed to broaden the host range, enhance lytic activity, or interfere with bacterial virulence and quorum-sensing pathways[36]. Some engineered phages are being explored as delivery platforms for anti-inflammatory or immunomodulatory molecules, offering dual antimicrobial and host-directed therapeutic effects[45]. In parallel, engineered endolysins with optimized catalytic domains, enhanced stability, and improved tissue penetration have demonstrated superior activity against drug-resistant Gram-positive pathogens in preclinical studies.

Innovations in drug delivery systems are expected to enhance dermatologic applications further. Microneedle-based platforms allow targeted delivery into pilosebaceous units for acne treatment, whereas liposomes, hydrogels, and polymer-based nanoparticles improve stability and enable sustained release on the skin's surface[46,47]. In chronic wounds, alginate dressings and hydrogel matrices provide a moisture-rich microenvironment that supports phage viability and facilitates biofilm penetration[48].

Beyond direct pathogen eradication, phages are increasingly recognized as tools for microbiome engineering. Selective depletion of disease-driving taxa may promote ecological rebalancing rather than indiscriminate microbial suppression. Skin virome studies demonstrating correlations between phage community dynamics and disease activity in AD support this concept[15,49]. Combining phage therapy with microbiome-supportive interventions, such as probiotics or barrier repair strategies, may further enhance therapeutic durability and clinical outcomes.

In sum, although scientific, regulatory, and formulation challenges remain, precision targeting, antibiofilm activity, microbiome-sparing properties, and the expanding technological toolkit associated with phage- and endolysin-based therapeutics position them as highly promising next-generation approaches for precision dermatologic care.

CONCLUSION

Microbial dysbiosis and antibiotic-resistant pathogens increasingly drive such skin diseases as acne vulgaris, AD, and chronic wound infections. Conventional antimicrobial therapies often lack specificity, disrupt beneficial skin microbiota, and show limited efficacy against biofilm-associated bacteria. This review highlights phages and phage-derived endolysins as next-generation, precision-based therapeutics that address these limitations. Phages and endolysins selectively eliminate pathogenic bacteria, penetrate and disrupt biofilms, and preserve commensal microorganisms essential for skin barrier integrity and immune balance. By integrating mechanistic insights with disease-specific evidence, this work demonstrates how phage-based strategies can move dermatologic therapy beyond broad microbial suppression toward targeted microbiome modulation. Advances in phage engineering, endolysin optimization, and topical delivery systems further strengthen their translational potential. Importantly, these biologics offer a promising, scalable investigational approach. Collectively, this study positions phage and endolysin-based approaches as promising investigational tools with the potential to improve management of dysbiosis-driven skin diseases through precision, safety, and ecological restoration.

CONFLICT OF INTEREST

The Conflict of Interest statement is correct and no changes are required.

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