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Review Article

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From Palm Kernel Lipids to Anti-Biofilm Antibiotic Adjuvants: Lauric Acid and Monolaurin for Membrane Disruption, MRSA Antibiotic Potentiation, and Local Infection Control—A Critical Review

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Abstract

Antimicrobial resistance and biofilm-associated tolerance jointly undermine the effectiveness of conventional anti-infective therapy. Lauric acid and its monoacylglycerol derivative glycerol monolaurate, commonly termed monolaurin, are membrane-active antimicrobial lipids that can be produced from lauric-rich palm kernel oil. Contemporary evidence shows that these compounds can disrupt microbial membranes, inhibit biofilm formation, affect virulence-related pathways, reduce survival of antibiotic-tolerant persister populations, and potentiate selected conventional antibiotics. Particularly important recent evidence demonstrates monolaurin activity against wound-derived Methicillin-Resistant *Staphylococcus Aureus* (MRSA) biofilms and synergistic interactions with β-lactam antibiotics. This critical qualitative review integrates source-specific palm-kernel evidence with molecule-specific antimicrobial, antibiofilm, and antibiotic-adjuvant evidence. It distinguishes genetically encoded resistance from biofilm tolerance and persistence and evaluates organism-specific responses, especially the greater challenge posed by Gram-negative outer membranes. Formulation strategies including liposomes, emulsions, hydrogels, and device-localized delivery are considered because therapeutically useful local concentrations may be more achievable than systemic exposure. Current evidence does not justify positioning monolaurin as a replacement antibiotic or assuming that antimicrobial findings obtained with coconut- or unspecified-source material automatically establish efficacy for palm-kernel-derived products. The most defensible development strategy is a standardized, pharmaceutical-grade palm-kernel-derived lauric-lipid platform designed for localized antibiofilm therapy and antibiotic potentiation, supported by rigorous susceptibility testing, tissue-safety assessment, resistance-evolution studies, pharmacokinetics, animal infection models, and controlled clinical trials.

Keywords: Palm kernel oil, Lauric acid, Monolaurin, Glycerol monolaurate, Antimicrobial resistance, Biofilm, MRSA, Antibiotic adjuvant, Membrane disruption, Wound infection

JEL Classification: I10, I12, I18, O32, Q16.

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Introduction

Antimicrobial Resistance (AMR) has become one of the defining biomedical challenges of the twenty-first century. The 2019 global AMR analysis estimated that bacterial resistance was directly attributable to approximately 1.27 million deaths and associated with substantially more deaths, while updated projections indicate that the cumulative burden could increase considerably through 2050 without improved prevention, diagnostics, stewardship, and treatment. Resistant *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and other high-priority pathogens remain major contributors to treatment failure and mortality. *S. aureus* is especially important because it combines extensive virulence potential, hospital and community transmission, biofilm formation, and resistance phenotypes such as methicillin resistance [1-4]. AMR, however, does not explain all antimicrobial treatment failure. Biofilm-associated infections introduce an additional layer of biological recalcitrance because microorganisms embedded within extracellular polymeric matrices occupy heterogeneous physiological states, experience nutrient and oxygen gradients, and can contain slowly growing or dormant subpopulations. These properties may drastically reduce antimicrobial susceptibility even when classical resistance determinants have not changed. Biofilm dispersal, metabolic heterogeneity, phenotypic tolerance, and persister formation therefore complicate the relationship between standard planktonic minimum inhibitory concentrations and therapeutic success *in vivo* [5-9].

This distinction is clinically important. Standard antimicrobial susceptibility testing remains predominantly planktonic, whereas chronic wound infections, implant-associated infections, catheter infections, and many oral or mucosal infections frequently involve structured microbial communities. A drug concentration that prevents visible growth of free-living cells may not eradicate microorganisms embedded in mature biofilms. This gap has stimulated interest in therapies that attack biofilm architecture, bacterial membranes, virulence systems, persister populations, or antibiotic penetration rather than seeking only an additional conventional bacteriostatic or bactericidal target [7,10-12]. Lauric acid and glycerol monolaurate, generally called monolaurin, offer an unusually interesting platform in this context. Lauric acid is a 12-carbon saturated medium-chain fatty acid with amphiphilic characteristics, while monolaurin is its monoacylglycerol derivative. Both have long been investigated for antimicrobial properties, particularly against Gram-positive bacteria and lipid-enveloped pathogens. Contemporary mechanistic reviews increasingly frame these compounds as membrane-active amphiphiles whose biological performance depends on chain length, self-assembly, concentration, lipid-bilayer composition, and physicochemical environment rather than as nonspecific "natural antimicrobials" [13-15].

For the palm-oil sector, the distinction between palm mesocarp oil and palm kernel oil is essential. Palm kernel oil has a substantially higher proportion of lauric lipids than ordinary palm oil and represents an industrially relevant raw material for medium-chain fatty acids and their derivatives. Contemporary compositional analysis confirms the distinctive fatty-acid profile of palm kernel oil, while direct experimental evidence demonstrates that palm kernel olein and stearin can be processed by enzymatic glycerolysis to yield purified monolaurin with measurable antibacterial activity [16,17]. The 2022 palm-kernel study is particularly important for the present review because it establishes a source-specific technological bridge rather than merely assuming that any lauric lipid could originate from palm kernel. *Ngatirah, et al.,* prepared monolaurin from blends of palm kernel olein and palm kernel stearin and verified the product by analytical characterization. The resulting material inhibited the tested *S. aureus*, *E. coli*, and *Bacillus subtilis* strains, although the experiments were not designed around resistant clinical isolates, mature biofilms, or antibiotic-adjuvant endpoints. It therefore provides evidence for palm kernel → monolaurin → antibacterial activity, but not yet for palm kernel → pharmaceutical monolaurin → MRSA biofilm eradication in patients [17].

A separate molecular evidence stream became especially relevant in 2024. Hassan Abd El-Ghany and colleagues demonstrated antimicrobial and antibiofilm activity of monolaurin against MRSA isolates recovered from wound infections. A related investigation involving *S. aureus* isolates found monolaurin MICs in the hundreds to thousands of micrograms per milliliter, morphological abnormalities after treatment, reduced *blaZ* expression, and extensive synergy with β-lactam antibiotics by fractional inhibitory concentration and time-kill analyses. These observations create a plausible role for monolaurin not only as an antimicrobial agent but also as an antibiotic potentiator capable of modifying the bacterial envelope or resistance-associated physiology [18,19]. The central translational question is therefore no longer whether lauric lipids have antimicrobial properties. The more useful question is whether a standardized palm-kernel-derived preparation can exploit membrane activity to suppress biofilms and increase the effectiveness of existing antibiotics without unacceptable tissue toxicity, microbiome disruption, or resistance evolution. This framing is especially relevant to localized infections, where high local concentrations could potentially be achieved through wound dressings, hydrogels, emulsions, coatings, or antimicrobial-lock-like strategies while limiting systemic exposure. Accordingly, this critical qualitative literature review evaluates five connected evidence domains: palm-kernel production and pharmaceutical identity, membrane-disruptive antimicrobial mechanisms, biofilm and persister-cell activity, antibiotic potentiation and potential resensitization, and formulation-dependent translational opportunities. A central principle throughout the review is that source-specific evidence and molecule-specific evidence must remain distinct. The fact that monolaurin can be produced from palm kernel does not automatically establish that every monolaurin

biofilm result applies to an uncharacterized palm-derived preparation, equivalence must be demonstrated analytically and pharmacologically.

Literature Review: Conceptual and Theoretical Foundations

Resistance, Tolerance, Persistence, and Biofilm Recalcitrance

Genetic antimicrobial resistance refers to heritable characteristics that permit bacterial populations to grow or survive despite drug exposures that inhibit susceptible counterparts. Examples include target alteration, antibiotic inactivation, reduced permeability, acquisition of resistance genes, and active efflux. MRSA illustrates this clearly because β-lactam resistance is largely associated with acquisition of *mecA* or related determinants encoding low-affinity penicillin-binding proteins. Similar target-specific mechanisms operate alongside β-lactamase genes such as *blaZ*, membrane adaptation, and regulatory changes [4,20]. Antibiotic tolerance is conceptually different. A tolerant population may survive prolonged antimicrobial exposure without displaying the same increase in MIC expected from classical resistance. Persistence is an extreme form of phenotypic survival involving small subpopulations capable of withstanding otherwise lethal treatment and later repopulating once drug pressure is removed. Persistence can contribute to recurrent infection and may create ecological opportunities for genetic resistance to evolve, making therapies that kill metabolically inactive or membrane-vulnerable persisters especially attractive [6,9]. Biofilms incorporate both genetic and phenotypic mechanisms. Their extracellular matrix can delay or alter antimicrobial diffusion, while local pH, oxygen, nutrients, and waste products generate physiological heterogeneity. Cells in mature biofilms can display altered stress responses, membrane physiology, growth rates, quorum signaling, and gene expression. Consequently, the minimum biofilm inhibitory concentration and minimum biofilm eradication concentration may differ dramatically from planktonic MIC values, and no universally implemented clinical method yet captures these differences adequately [7,8,21].

Biofilm Lifecycle and Therapeutic Intervention Windows

Biofilm development is dynamic rather than binary. Initial reversible attachment to a surface is followed by more stable adhesion, cellular aggregation, matrix production, maturation into structured communities, and ultimately dispersal. Each stage presents different therapeutic vulnerabilities. Preventing attachment may require anti-adhesive or surface-active interventions, whereas mature biofilm eradication requires penetration, disruption of extracellular material, killing of physiologically heterogeneous cells, and control of released organisms [5,12]. This is relevant to lauric acid because subinhibitory concentrations need not act in the same manner as bactericidal concentrations. Kim et al. demonstrated that lauric acid and myristic acid could inhibit single- and polymicrobial biofilm formation involving *S. aureus*, *E. coli* O157:H7, and *Candida albicans* without simply suppressing all planktonic growth. Transcriptomic observations included reductions in *S. aureus hla and hld, E. coli csgAB, fimH* and *flhD,* and *C. albicans HWP1*, implying effects on virulence, attachment, motility, matrix-associated behavior, and fungal morphogenesis rather than only nonspecific killing [22]. The fungal component deserves attention because chronic wounds, oral communities, and device-associated biofilms can be polymicrobial. Medium-chain fatty acids can interfere with *Candida albicans* hyphal development and biofilm formation in ways that resemble aspects of farnesol-mediated quorum regulation. This broadens the possible value of lauric lipids but also complicates interpretation because bactericidal, antifungal, antivirulence, and biofilm-modulatory concentrations may differ substantially [22,23].

Lauric Acid and Monolaurin as Membrane-Active Amphiphiles

Lauric acid contains a hydrophobic hydrocarbon chain and a carboxylic-acid head group whose ionization depends on the physicochemical environment. Monolaurin retains the 12-carbon chain but replaces the free fatty-acid head group with a glycerol monoester. This difference affects solubility, charge state, aggregation, membrane partitioning, self-assembly, and biological interactions. Therefore, lauric acid and monolaurin should not be treated as interchangeable simply because one is derived chemically from the other [14,15]. The antimicrobial behavior of medium-chain fatty acids and monoglycerides is strongly associated with lipid-bilayer interaction. Their hydrophobic chains can partition into bacterial membranes, while their polar groups remain near lipid-water interfaces. Depending on concentration and membrane composition, this may promote bilayer disorder, altered permeability, membrane deformation, leakage of intracellular constituents, disruption of protein-lipid interactions, and loss of homeostatic control. The exact mechanism is not identical for every lipid, organism, or growth state, which explains why chain length and head-group chemistry can substantially change antimicrobial potency [14,15]. Direct membrane-model evidence reinforces this interpretation. Tan et al. examined medium-chain fatty acids and monoglycerides against tethered bilayers prepared from *E. coli*-derived lipids and documented compound-specific membrane-disruptive effects. Importantly, such model systems separate bilayer interaction from whole-cell phenomena such as active transport and metabolism. They also emphasize that activity observed against a simple membrane does not guarantee equivalent antibacterial activity against an intact Gram-negative bacterium surrounded by an outer membrane, lipopolysaccharide, porins, and envelope-maintenance systems [24]. Recent work with lauric-acid microemulsions against *S. aureus* further supports membrane disruption as an important mechanism and suggests potential interference with cell-wall physiology. Formulation-dependent studies such as this are useful because free hydrophobic fatty acids can behave differently from emulsified preparations in aqueous biological environments [25].

Gram-Positive Versus Gram-Negative Susceptibility

Gram-positive organisms such as *S. aureus* possess a thick peptidoglycan wall external to the cytoplasmic membrane but lack the lipopolysaccharide-rich outer membrane characteristic of Gram-negative bacteria. Hydrophobic antimicrobial lipids may therefore gain more direct access to the cytoplasmic membrane of susceptible Gram-positive organisms. This helps explain why *S. aureus* has featured prominently in contemporary monolaurin studies [13,18]. Gram-negative bacteria represent a more difficult target. Their outer membrane functions as a permeability barrier that excludes many hydrophobic or bulky molecules, even when intracellular targets remain pharmacologically vulnerable. Contemporary antibiotic-adjuvant research therefore actively seeks molecules capable of permeabilizing the Gram-negative outer membrane and restoring activity of compounds that would otherwise be excluded [26]. Dhanda et al. demonstrated the broader principle that relatively weak membrane perturbation can strongly potentiate antibiotics against multidrug-resistant Gram-negative organisms while minimizing the toxicity associated with aggressively membrane-lytic compounds. Their findings are not evidence for monolaurin itself, but they provide an important translational concept: a membrane-active molecule need not be a powerful stand-alone antibiotic to be clinically useful if it can safely increase access or efficacy of another antimicrobial [27].

Antibiotic Adjuvant Versus Antibiotic Replacement

An antibiotic replacement must independently achieve effective antimicrobial concentrations in infected tissue, eradicate clinically relevant pathogens, demonstrate an acceptable therapeutic index, and perform reliably in controlled clinical trials. An antibiotic adjuvant has a different role. It may increase permeability, inhibit resistance determinants, modify membrane properties, attenuate virulence, disrupt biofilms, or alter bacterial physiology so that an established antibiotic becomes more effective. This distinction is central to the proposed palm-kernel platform. Natural products and membrane-active small molecules are increasingly investigated as antibiotic sensitizers against MRSA. Contemporary evidence demonstrates that membrane fluidization or weak perturbation can restore β-lactam activity in resistant *S. aureus*, while natural-product combinations can reduce effective antibiotic concentrations or reverse resistance-associated phenotypes under experimental conditions [28,29]. The same principle applies to biofilms. Combination approaches pairing a biofilm-disruptive intervention with a conventional antibiotic frequently outperform either strategy alone because matrix disruption or dispersal without antimicrobial killing could release viable pathogens capable of colonizing new sites. Thus, the therapeutically attractive endpoint is simultaneous disruption and eradication rather than dispersion alone [10,11].

Method

This study was designed as a critical qualitative literature review rather than a systematic review or meta-analysis. A qualitative design was selected because the relevant evidence spans feedstock chemistry, enzymatic synthesis, lipid biophysics, microbiological susceptibility, biofilm biology, antibiotic-combination studies, formulation science, chronic-wound therapeutics, medical-device infection, and translational pharmacology. These domains contain substantially heterogeneous experimental systems and outcomes that are not appropriately reducible to a single pooled effect estimate. Narrative reviews can nevertheless achieve methodological rigor by clearly defining their purpose, evidence boundaries, search concepts, and interpretive framework [30]. The literature synthesis prioritized peer-reviewed articles published from 2020 through 2026. Search concepts included combinations of "palm kernel," "lauric acid," "monolaurin," "glycerol monolaurate," "MRSA," "antimicrobial resistance," "biofilm," "persister," "membrane disruption," "β-lactam synergy," "antibiotic potentiation," "wound biofilm," "device biofilm," "liposome," "hydrogel," and "antimicrobial lock." Literature searching was conceptually broad because the central research question requires integration of source-specific palm-kernel evidence and molecule-specific antimicrobial evidence rather than a narrow intervention comparison [31].

Evidence was synthesized thematically rather than chronologically. Thematic analysis was used to identify recurring mechanisms, areas of convergence, contradictions, and translational gaps across chemically, microbiologically, and clinically distinct literature. This strategy is consistent with qualitative-review methodologies in which heterogeneous findings are organized into higher-order explanatory themes rather than tabulated as if they were directly comparable clinical interventions [32]. Five evidence categories were distinguished. The first consisted of direct palm-kernel-derived lauric-lipid production and antimicrobial evidence. The second consisted of direct lauric acid or monolaurin antimicrobial, antibiofilm, persister, and antibiotic-combination studies where botanical source was different or unspecified. The third involved mechanistic membrane literature. The fourth comprised transferable antibiofilm and drug-delivery evidence. The fifth covered clinical contexts such as wound and medical-device biofilms. This hierarchy was applied to prevent molecular evidence from being presented as direct clinical proof. No PRISMA diagram is presented, no formal meta-analysis was conducted, and no pooled susceptibility estimate was calculated. These methodological choices are intentional because the aim is critical mechanistic and translational interpretation rather than exhaustive systematic evidence grading.

Results: Thematic Findings

Palm Kernel Provides a Credible Source-Specific Feedstock

Palm kernel oil is an industrially relevant source of lauric lipids and differs markedly in fatty-acid profile from palm mesocarp oil. Its high medium-chain saturated-fatty-acid content creates a rational feedstock for producing lauric acid and glycerol

monoesters. Contemporary compositional work confirms the importance of lauric acid within palm-kernel lipid fractions [16]. The most important direct source-specific study is that of Ngatirah et al., who employed enzymatic glycerolysis of palm kernel olein-stearin blends. Under optimized conditions, the researchers generated and purified monolaurin and confirmed product identity using spectroscopic methods. The purified material showed antimicrobial activity, with reported MIC values including 500 ppm for the tested *E. coli* strain, 500 ppm for *S. aureus*, and 100 ppm for *B. subtilis*. These experiments directly validate palm kernel as a monolaurin feedstock but do not establish pharmaceutical equivalence to monolaurin used in MRSA or clinical biofilm experiments [17]. Other synthesis research demonstrates that monolaurin production can be intensified through enzyme-catalyzed esterification in microreactors. Miao and Li reported rapid lauric-acid conversion and high monolaurin selectivity using immobilized lipase under optimized microreactor conditions. Such process technologies matter because a future antimicrobial product would require reproducible isomer composition, purity, throughput, and scalable processing rather than merely proof that monolaurin can be synthesized [33].

Figure 1 illustrates that source identity is one of the central conceptual challenges of the review. It separates the palm-kernel production chain from subsequent pharmacological claims and identifies the analytical checkpoints required before molecule-level antimicrobial evidence can legitimately be transferred to a palm-derived pharmaceutical product (Figure 1).

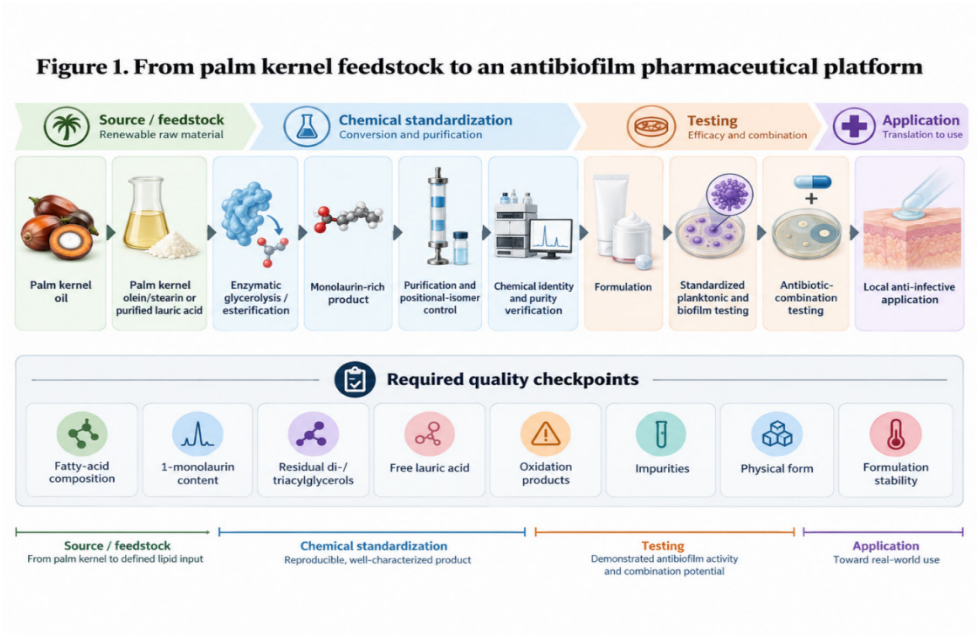

Figure 1: From palm kernel feedstock to an antibiofilm pharmaceutical platform.

The key message of Figure 1 is that botanical source should not be confused with pharmacological identity. If highly purified 1-monolaurin synthesized from palm-kernel lauric acid is chemically equivalent to purified monolaurin synthesized from another source, its intrinsic molecular activity should principally depend on structure, purity, physical state, and formulation rather than on the plant from which the carbon atoms originated. Consequently, source-comparative research should emphasize analytical equivalence, impurities, co-lipids, positional isomers, and formulation characteristics instead of assuming source-dependent pharmacology without evidence [17,33].

Monolaurin has Direct Activity Against Wound-Derived MRSA

The 2024 MRSA study by *Hassan Abd El-Ghany, et al.,* provides one of the strongest direct links between monolaurin and clinically relevant biofilm-forming resistant bacteria. The investigators examined MRSA isolates obtained from wound infections and demonstrated both antimicrobial and antibiofilm effects. Monolaurin inhibited biofilm formation and affected established biofilms, creating a more clinically relevant evidence base than experiments limited to planktonic reference strains [18]. The importance of this result is twofold. First, it suggests that monolaurin activity persists against bacteria already displaying a major clinically relevant resistance phenotype. Second, biofilm effects indicate that activity cannot be evaluated exclusively by planktonic MIC. These findings should nevertheless be interpreted within their experimental limits: *in vitro* efficacy does not establish that the required concentrations are tolerated in human wound tissue, remain active in wound exudate, penetrate polymicrobial matrices, or improve healing.

Membrane Disruption Provides a Plausible Mechanistic Foundation

Membrane interaction remains the most coherent unifying mechanism for lauric-lipid activity. Medium-chain fatty acids can alter permeability, destabilize lipid packing, and induce leakage. *Casillas-Vargas, et al.,*

emphasized that antibacterial fatty-acid activity depends strongly on molecular structure, chain length, unsaturation, concentration, and target-cell physiology. This complexity argues against describing lauric acid as a nonspecific detergent, its efficacy emerges from defined physicochemical interactions with biological membranes [14]. The recent persister study by *Seo, et al*., provides particularly important mechanistic evidence. Lauric acid showed the strongest activity among the examined medium-chain fatty acids against *S. aureus* persister-enriched populations, with killing associated with increased membrane permeability and ATP leakage rather than conventional metabolic targeting. Because persisters are relatively refractory to antibiotics that depend on active growth, membrane disruption may represent a valuable metabolism-independent vulnerability [34]. This finding supports a multi-hit model. Lauric lipids may directly reduce bacterial viability, weaken membrane homeostasis, increase vulnerability of dormant populations, and alter access of companion antibiotics. Importantly, however, membrane perturbation that is therapeutically useful against bacteria must remain sufficiently selective to avoid equivalent injury to keratinocytes, fibroblasts, erythrocytes, and other mammalian cells.

Figure 2 integrates the central mechanistic hypothesis of the manuscript. It depicts lauric acid and monolaurin not as conventional receptor-specific antibiotics but as membrane-active agents capable of affecting several interconnected determinants of biofilm survival and antibiotic response (Figure 2).

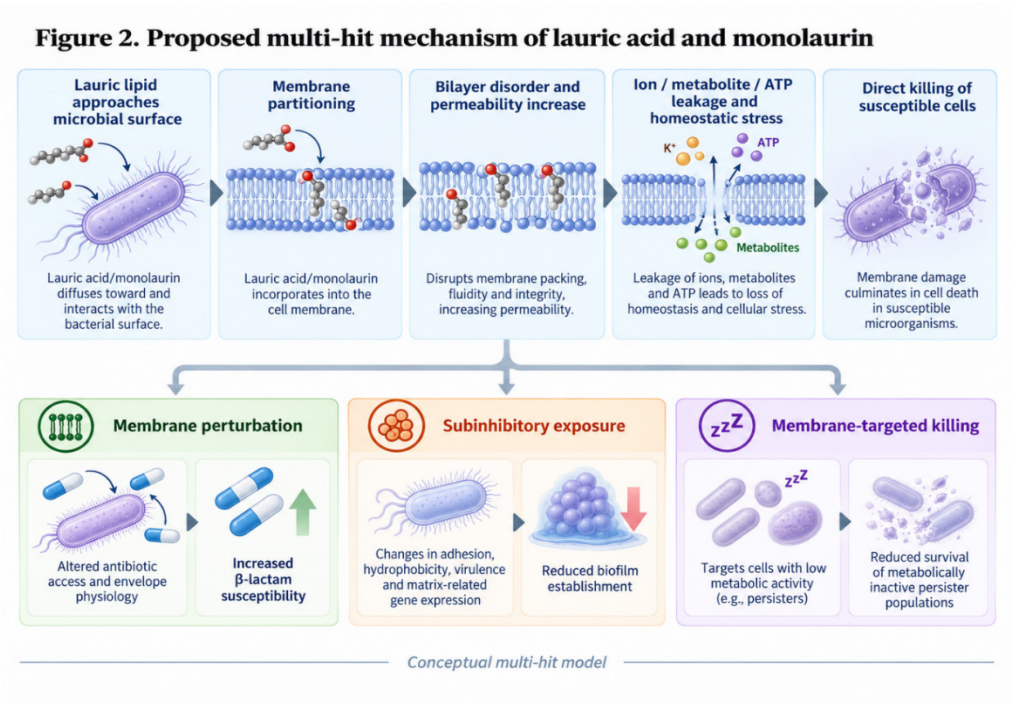

Figure 2: Proposed multi-hit mechanism of lauric acid and monolaurin.

Figure 2 deliberately separates experimentally supported effects from stronger causal claims that remain unproven. Membrane permeability and persister killing have been demonstrated for lauric acid, while monolaurin has produced morphological changes and antibiotic synergy in *S. aureus*. Lauric acid has also altered biofilm- and virulence-associated gene expression in polymicrobial models. The evidence does not yet establish that one molecular event explains all these effects, and future lipidomic, transcriptomic, membrane-potential, permeability, and resistant-mutant experiments will be needed to determine whether membrane disruption is the initiating mechanism or one component of a broader physiological response [19,22,34].

Biofilm Inhibition Includes Anti-Adhesion and Antivirulence Effects

Lauric acid appears capable of affecting biofilm biology at concentrations or conditions distinct from those required for direct growth inhibition. Kim et al. reported inhibition of single-, dual-, and three-species biofilms involving *S. aureus*, *E. coli* O157:H7, and C. albicans. The effects were accompanied by reduced microbial

surface hydrophobicity and modulation of genes involved in hemolysis, adhesion, motility, curli production, and fungal hyphal development [22]. Such findings fit broader contemporary research showing that natural compounds can interfere with *S. aureus* biofilms through diverse targets, including adhesion systems, quorum regulation, ica pathways, *agr, sarA*, microbial surface components recognizing adhesive matrix molecules, and virulence-factor expression. This literature does not validate lauric acid at each individual target, but it provides a mechanistic context for interpreting sub-MIC biofilm effects [12,35]. A critical point is that reduced biofilm biomass does not necessarily indicate microbial eradication. Crystal-violet-type biomass assays may detect changes in matrix or adhesion while viable bacterial populations persist. Future lauric-lipid experiments should therefore combine biomass measurement with viable counts, metabolic assays, confocal imaging, matrix quantification, and MBEC-like endpoints.

Monolaurin Can Potentiate β-Lactam Activity

The 2024 BMC Infectious Diseases study provides direct evidence supporting an antibiotic-adjuvant interpretation. Among 115 *S. aureus* isolates, monolaurin MICs ranged from approximately 250 to 2000 μg/mL. The study detected *blaZ* in a large proportion of isolates and observed significant reductions in *blaZ* expression after monolaurin exposure. Checkerboard/FIC and time-kill experiments demonstrated strong synergy with β-lactam antibiotics, with high proportions of tested combinations classified as synergistic [19]. These results provide more than evidence of additive killing. Reduced β-lactam MICs, time-kill synergy, morphological alterations, and changes in a resistance-associated gene collectively suggest that monolaurin can modify the physiological context in which β-lactams act. However, the term resensitization should be reserved for combinations that move a resistant phenotype into a clinically meaningful susceptible range under standardized interpretive criteria. Experimental synergy alone does not necessarily mean that a patient infection has become clinically susceptible. The broader MRSA literature supports the biological plausibility of membrane-based resensitization. Membrane adaptation can interact with β-lactam susceptibility, and experimental membrane fluidizers have restored β-lactam effectiveness against MRSA. Natural-product sensitizers are likewise being explored as resistance-modifying agents rather than replacement antibiotics [20,28,29]. Complementary 2025 evidence further supports an adjuvant mechanism: lauric acid potentiated ciprofloxacin against a MepA-expressing *S. aureus* strain, increased membrane permeability, and reduced mepA expression even though it lacked direct antibacterial activity in that model [36].

Persister Killing may Differentiate Lauric Acid from Many Conventional Antibiotics

A particularly promising development is the demonstration that medium-chain fatty acids can reduce survival of *S. aureus* persisters generated after exposure to ciprofloxacin, oxacillin, or tobramycin. Lauric acid was active at lower concentrations than shorter-chain comparators in the study by Seo et al., and activity correlated with membrane permeability. This result is notable because persister cells often survive through metabolic quiescence, making them poorly susceptible to drugs targeting cell division, protein synthesis, or metabolic pathways [34]. The implication is not that lauric acid is universally "persister-proof." Instead, it suggests a mechanistic advantage of targeting a physical cellular structure that remains essential regardless of growth state. Whether the same effect occurs in mature wound biofilms, where extracellular matrix and tissue components can sequester lipid molecules, requires direct investigation.

Gram-Negative Efficacy is a Boundary Condition Rather than a Universal Property

The palm-kernel monolaurin study reported activity against its tested *E. coli* strain, and lauric acid has demonstrated antibiofilm effects involving *E. coli* O157:H7. Nevertheless, Gram-negative bacteria should remain a distinct translational category. The outer membrane can substantially reduce access of hydrophobic molecules to the cytoplasmic membrane, and species-specific susceptibility varies widely [17,22,24]. One possible strategy is combination with safe outer-membrane permeabilizers. Contemporary adjuvant research shows that weakly perturbing compounds can increase uptake of otherwise ineffective antibiotics against Gram-negative organisms. This concept could eventually be extended to lauric-lipid formulations, but direct evidence is currently insufficient, and such combinations would require careful toxicity assessment [26,27].

Figure 3 illustrates organism-specific envelope architecture as one of the main reasons broad-spectrum claims concerning lauric lipids would currently be premature. The comparison highlights the additional outer-membrane barrier that can restrict access of hydrophobic lauric lipids to the cytoplasmic membrane of Gram-negative organisms (Figure 3).

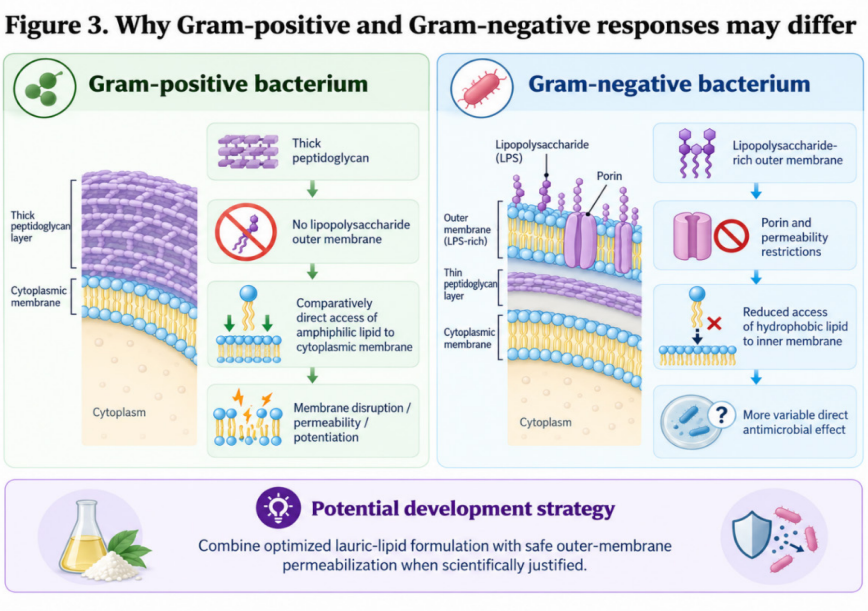

Figure 3: Why Gram-positive and Gram-negative responses may differ.

The Figure illustrates why the article does not treat activity against MRSA as proof of equivalent activity against *Pseudomonas, Acinetobacter*, or Enterobacterales. The Gram-negative outer membrane is itself a major intrinsic resistance mechanism. Although lauric acid and monolaurin can interact with bacterial lipid systems, access to those systems is constrained by envelope architecture. Organism-specific MIC, MBIC, MBEC, and combination testing is therefore indispensable.

Formulation can Amplify Antibiofilm Performance

Hydrophobic antimicrobial lipids present formulation challenges in aqueous biological systems. Effective free concentrations may be reduced by precipitation, phase separation, adsorption to proteins, binding to wound exudate components, or incorporation into non-target lipid structures. Formulation therefore determines not merely convenience but the concentration of biologically available lipid at the microbial surface. Bharathi et al. provided direct evidence that liposomal delivery can dramatically alter fatty-acid antibiofilm activity. Lecithin-fatty-acid liposomes strongly enhanced activity against polymicrobial biofilms and disrupted preformed *S. aureus* and *C. albicans* biofilms more effectively than free fatty acids. The study reported roughly two orders of magnitude enhancement for selected antibiofilm endpoints, demonstrating that carrier architecture can convert a moderately active lipid into a substantially stronger biofilm intervention [37]. This finding is especially relevant to palm-kernel development. Instead of asking only whether purified palm monolaurin has an acceptable MIC, pharmaceutical research should ask whether emulsification, liposomal incorporation, nanoparticles, hydrogels, or surface coatings can maintain a high effective local concentration and prolong contact with biofilm while reducing mammalian-cell exposure.

Chronic Wounds are the Most Compelling First Clinical Application

Chronic wounds provide perhaps the most realistic translational environment because biofilms are common, MRSA and other resistant pathogens are clinically important, topical access is feasible, and systemic pharmacokinetics need not be the first hurdle. A 2025 meta-analysis estimated biofilm prevalence at approximately 68% across included chronic-wound studies, with *S. aureus* and *P. aeruginosa* among the commonly detected organisms, although substantial heterogeneity remained [38]. Contemporary wound reviews emphasize that biofilms contribute to prolonged inflammation, immune evasion, delayed healing, and reduced antimicrobial effectiveness. Existing management typically relies on combinations of debridement, wound-bed preparation, antimicrobial dressings, antiseptics, systemic antibiotics where clinically indicated, and correction of underlying vascular or metabolic factors rather than a single "biofilm drug" [39-42]. Clinical management literature likewise emphasizes early, multimodal biofilm control using debridement, cleansing, and antimicrobial dressings because established wound biofilms increase antimicrobial tolerance and sustain chronic inflammation [43]. Recent *S. aureus* biofilm-model research also shows that biofilm-associated microenvironments can reshape immune-cell metabolism and impair bacterial clearance, supporting the use of host-relevant models when evaluating adjunctive agents [44].

The wound microbiome also complicates the therapeutic objective. Chronic wounds can contain diverse bacterial and fungal communities whose composition influences inflammation, healing, and response to treatment. Broad membrane-active therapy could theoretically reduce pathogens while also disrupting commensal communities, so future formulations should measure microbiome-level effects rather than interpreting maximal microbial killing as universally beneficial [45]. Hydrogels represent a particularly attractive platform. They can maintain moisture, incorporate lipophilic agents through emulsified or nanoparticle phases, provide sustained local release, and remain in direct contact with the wound. Contemporary reviews demonstrate

rapid development of antibacterial and antibiofilm hydrogels, including stimuli-responsive and combination systems, but clinical translation continues to require stronger biocompatibility, manufacturing, and outcome evidence [46-48]. Lipid nanoparticles similarly have potential to improve solubilization, local retention, controlled release, and wound compatibility. Their growing use in antimicrobial wound research provides a transferable formulation framework for palm-kernel lauric lipids [49,50].

Device-Associated Biofilms Provide a Second Localized Opportunity

Medical devices create artificial surfaces on which microorganisms can adhere and form persistent communities protected from both antimicrobials and host immunity. Catheter-related infection exemplifies the problem because the device surface can sustain repeated bloodstream seeding and frequently requires removal when infection cannot be controlled. Recent reviews emphasize *S. aureus* and *P. aeruginosa* colonization, surface adhesion mechanisms, quorum signaling, and the development of antimicrobial or anti-adhesive coatings [51,52]. A lauric-lipid coating or localized reservoir is therefore conceptually attractive because it might act directly at the colonization interface rather than relying on systemic distribution. However, the essential requirements differ from wound treatment: a device coating must remain durable, biocompatible, stable during sterilization, non-thrombogenic where relevant, and active for clinically useful periods without promoting material degradation. Antimicrobial lock therapy provides an important clinical precedent for maintaining high local antimicrobial concentrations within catheter lumens. A 2025 scoping review documented widespread use of lock strategies to prevent or treat catheter-associated infection, often alongside systemic therapy [53]. Clinical studies likewise illustrate that localized antimicrobial exposure can support catheter salvage in selected settings [54]. These studies do not involve monolaurin but strengthen the translational logic of testing non-antibiotic antibiofilm agents in localized device environments.

Oral and Polymicrobial Biofilms Represent Promising but Complex Targets

Oral biofilms contain highly structured multispecies communities in which bacterial and fungal interactions can influence adhesion, acid production, inflammation, and antimicrobial tolerance. The demonstrated activity of lauric acid against mixed *S. aureus-E. coli*-Candida biofilms and the antifungal effects of medium-chain fatty acids against *C. albicans* provide proof that lauric-lipid biology can extend beyond single-species bacterial systems [22,23]. Translation to oral care would nevertheless require careful microbiome selectivity. The oral microbiota contains numerous beneficial or commensal organisms, and chronic indiscriminate membrane-active exposure could alter ecological balance. Applications such as short-contact mouth rinses, periodontal gels, denture coatings, or device surfaces may therefore be more realistic than chronic broad-spectrum microbiome suppression.

Figure 4 maps the lauric-lipid mechanism onto the biofilm lifecycle and illustrates why treatment timing may determine whether the primary effect is prevention, structural weakening, potentiation of antibiotics, or eradication of residual tolerant cells. It also distinguishes interventions aimed at preventing attachment from those intended to weaken mature biofilms, target persisters, or augment antibiotic activity during dispersal (Figure 4).

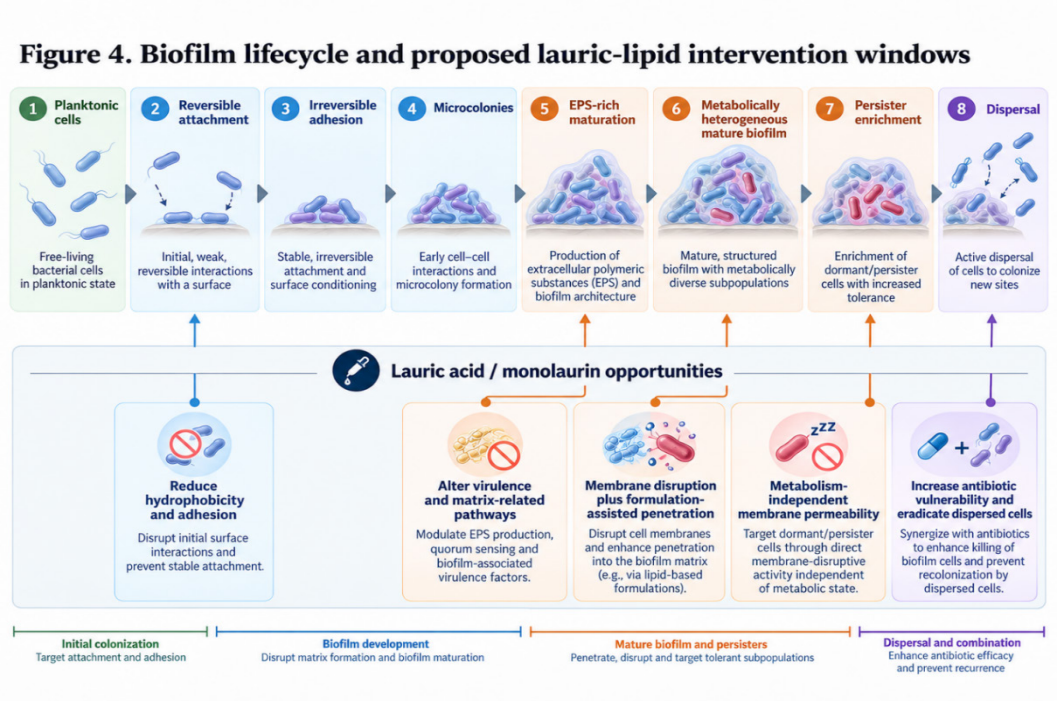

Figure 4: Biofilm lifecycle and proposed lauric-lipid intervention windows.

The framework argues against treating "antibiofilm activity" as a single outcome. A compound that prevents adhesion may be highly useful as a device coating but ineffective against a mature infected wound. Conversely, a formulation capable of killing persisters may be more valuable after debridement or during antibiotic treatment than for long-term prophylactic use. Development programs should therefore specify the intended biofilm stage rather than relying on one generic crystal-violet assay [5,7,11].

Discussion and Analysis

The Most Defensible Identity is "Antibiofilm Antibiotic Adjuvant"

The evidence synthesized here does not yet justify positioning monolaurin as a replacement antibiotic. Effective *in vitro* concentrations can be relatively high, organismal susceptibility is heterogeneous, Gram-negative activity is less predictable, standardized biofilm breakpoints do not exist, and controlled human efficacy trials are essentially absent. These limitations are substantial. The antibiofilm antibiotic-adjuvant identity is better aligned with the evidence. Monolaurin directly inhibits MRSA and its biofilms, potentiates β-lactams, and alters resistance-associated physiology. Lauric acid reduces polymicrobial biofilm formation and can kill antibiotic-surviving *S. aureus* persisters through membrane permeability. Together, these findings suggest complementary actions that could make conventional antibiotics work better rather than replacing them [18,19,22,34]. This positioning also aligns with broader antimicrobial-development trends. The escalating difficulty of developing entirely new antibiotics has renewed interest in adjuvants that restore existing drugs, increase permeability, neutralize resistance determinants, or disrupt biofilms. β-Lactamase inhibitors are the clinically established archetype, but membrane-targeted potentiators represent an expanding experimental class [4,26,27,29].

Palm-Kernel Origin Must be Demonstrated, Not Rhetorically Assumed

A central risk in developing the topic is a source-attribution error. Much of the monolaurin literature discusses coconut-derived compounds or does not specify the original lipid feedstock. It would therefore be scientifically incorrect to cite an unspecified monolaurin MRSA experiment and describe it as direct evidence for "palm-kernel-derived monolaurin." The correct translational chain has two independently supported components. First, palm kernel can be converted into chemically characterized monolaurin with antibacterial activity. Second, purified monolaurin as a molecular entity can inhibit MRSA biofilms and synergize with β-lactams. What remains missing is the bridging experiment: pharmaceutical-grade palm-kernel-derived monolaurin compared head-to-head with analytically equivalent monolaurin from other sources using resistant clinical isolates, mature biofilms, human-cell safety assays, and *in vivo* infection models. A well-designed source-comparison experiment should normalize for 1-monolaurin concentration rather than comparing equal masses of incompletely characterized preparations. Residual free fatty acids, diacylglycerols, triacylglycerols, positional isomers, oxidation products, surfactants, and formulation excipients should be quantified. If biological differences remain after such normalization, source-related compositional effects could then be investigated meaningfully.

Membrane Disruption May Generate a Multi-Hit Therapeutic Effect

Membrane-active compounds are attractive because the bacterial membrane is simultaneously a permeability barrier, an energetic interface, a scaffold for proteins, and a determinant of antibiotic susceptibility. Perturbation can therefore have consequences extending far beyond immediate leakage. For lauric acid and monolaurin, the available evidence supports at least four potentially connected outcomes: direct membrane-associated killing, reduction of persister survival, modulation of biofilm/virulence physiology, and antibiotic potentiation. This creates a multi-hit hypothesis in which modest membrane perturbation may create a pharmacologically useful state even when the lipid concentration alone is not sufficient for complete bacterial eradication. This possibility is consistent with broader work showing that membrane fluidization or weak permeabilization can restore antibiotic susceptibility without requiring catastrophic lysis. *Podoll, et al.,* demonstrated β-lactam resensitization of MRSA using a small-molecule membrane fluidizer, whereas Dhanda et al. showed that mild perturbation can produce very large antibiotic-potentiation effects in Gram-negative superbugs. These studies strengthen the conceptual framework but should not be interpreted as direct mechanistic proof for monolaurin [27,28].

Synergy and Resensitization Should not be Conflated

The monolaurin-β-lactam findings are compelling but terminology matters. Checkerboard synergy means that the combined inhibitory concentrations produce a favorable fractional inhibitory concentration index. Time-kill synergy adds evidence that combined treatment produces enhanced reductions in viable cells. Neither criterion automatically establishes restored clinical susceptibility according to standardized breakpoint systems. "Resensitization" should therefore be reserved for conditions in which a resistant isolate crosses a clinically meaningful susceptibility threshold or regains a robust phenotype consistent with effective therapy. Future studies should report baseline resistance mechanisms, standardized MICs, combination MICs, susceptibility categories, population-analysis profiles, time-kill kinetics, and resistance emergence. Genetic deletion or overexpression of candidate determinants such as *blaZ*, mecA, and envelope-regulatory systems could then establish causal pathways.

Local Therapy is more Realistic than Immediate Systemic Development

Systemic development would create challenging pharmacological questions. Orally or intravenously administered lauric lipids would encounter absorption, metabolism, protein

binding, lipoprotein transport, tissue distribution, and host lipid-processing pathways. The antimicrobial concentrations needed *in vitro* may not translate into safe and persistent free concentrations at infected sites. Localized therapy offers a fundamentally different pharmacokinetic problem. In a wound, periodontal pocket, catheter lumen, device coating, or skin surface, high local concentrations can potentially be achieved while systemic exposure remains limited. The drug can also contact biofilm directly and can be combined with debridement or local antibiotic therapy. The extensive development of wound hydrogels, lipid nanoparticles, and antimicrobial-lock strategies provides practical precedents. Hydrogels can control release, maintain moisture, and incorporate lipophilic phases, while lipid nanoparticles can improve drug dispersion and persistence. Catheter-lock therapy demonstrates the clinical utility of deliberately maintaining very high antimicrobial concentrations within a confined device space [46,49,50,53].

Safety Cannot be Inferred from Food Use

Lauric acid and monolaurin occur in food-related contexts, but dietary exposure does not establish the safety of concentrated pharmaceutical exposure to wounded tissue, mucosa, implanted devices, or systemic circulation. Membrane-disruptive activity is therapeutically useful only within a selective window. Future studies should therefore determine cytotoxicity against keratinocytes, fibroblasts, endothelial cells, erythrocytes, and immune cells at concentrations that inhibit planktonic bacteria, prevent biofilms, eradicate mature biofilms, and potentiate antibiotics. Wound-relevant studies should assess epithelial migration, fibroblast proliferation, collagen formation, inflammatory responses, and re-epithelialization rather than relying only on short-term viability assays. This is especially important because modern wound care increasingly seeks agents that simultaneously reduce microbial burden and support tissue repair. Reviews of chronic-wound biofilms and antibacterial hydrogels repeatedly emphasize biocompatibility as a major translational requirement [40,42,47].

Microbiome Effects Require Explicit Investigation

A membrane-active antimicrobial may be less selective at the species level than a receptor-specific antibiotic. That could be advantageous for polymicrobial infected wounds but detrimental to healthy skin or oral ecosystems. The wound microbiome is increasingly recognized as a potential biomarker and therapeutic determinant, not merely a collection of pathogens. Different microbial communities can influence inflammation and healing trajectories, and repeated nonspecific antimicrobial exposure may alter ecological recovery. Consequently, future monolaurin research should incorporate community-level sequencing or culture-based microbiome analysis alongside pathogen counts [45]. The goal should not be indiscriminate sterilization of every colonized surface. A clinically successful local formulation should suppress pathogens and pathogenic biofilm states while preserving host tissue and, ideally, allowing recovery toward a healthier microbial community.

Resistance Evolution is Unknown and Should not be Assumed Impossible

Natural or membrane-active compounds are sometimes promoted as "resistance-proof." Such claims are scientifically unsafe. Bacteria can adapt membrane lipid composition, surface charge, envelope stress responses, efflux, metabolic states, and biofilm structure. Repeated sublethal exposure to lauric lipids could select adaptive phenotypes even if classical target-site mutation is less straightforward. Serial-passage studies should therefore measure changes in MIC, MBC, MBIC, MBEC, membrane composition, cross-resistance to host antimicrobial peptides, and susceptibility to conventional antibiotics. Whole-genome sequencing of evolved populations could identify adaptive pathways. Importantly, combination therapy may either slow resistance by lowering bacterial burden or accelerate selection if one agent is persistently underdosed.

Standardized Antibiofilm Susceptibility Testing is a Prerequisite for Translation

Biofilm studies remain methodologically heterogeneous. Static microtiter biofilms, colony biofilms, flow cells, Calgary-type devices, wound-like media, and ex vivo tissue systems produce different matrix architectures and physiological states. Lipid antimicrobials add further complications because apparent activity may depend on solvent, emulsifier, adsorption to plastic, serum proteins, ionic strength, and pH.

Coenye has emphasized that current clinical microbiology still lacks standardized biofilm AST equivalent to planktonic susceptibility frameworks. Consequently, future lauric-lipid studies should report solvent controls, actual soluble or dispersed concentrations, MIC/MBC, MBIC/MBEC, time-kill data, biomass, viable counts, microscopy, and relevant formulation properties [7]. For antibiotic-combination research, checkerboard assays should be complemented by time-kill experiments because FIC values alone may vary with methodology. Mature biofilm combinations should additionally determine whether treatment reduces viable biofilm burden rather than merely preventing new attachment.

A Bench-To-Bedside Development Sequence

The first development stage should be analytical standardization. A pharmaceutical candidate should specify the exact percentage of 1-monolaurin, free lauric acid, other monoacylglycerols, diacylglycerols, triglycerides, water, oxidation products, and excipients. Palm-kernel provenance should be traceable, but chemical composition should remain the principal quality criterion. The second stage should establish microbiological reproducibility across reference strains and clinically relevant resistant isolates. MRSA should be a priority because direct monolaurin evidence already exists. MSSA, vancomycin-intermediate phenotypes, coagulase-negative staphylococci, *Enterococcus, P. aeruginosa, A. baumannii*, and representative Enterobacterales should then define spectrum boundaries.

The third stage should incorporate biofilm and persister pharmacology. Prevention of attachment, mature-biofilm killing, MBEC, persister survival, biofilm gene expression, matrix composition, and dispersal should be quantified separately. Studies should use wound-like media and polymicrobial systems as the program advances. The fourth stage should screen antibiotic combinations. β-Lactams deserve priority because direct synergy has already been demonstrated, but rational combinations could also examine glycopeptides, lipopeptides, aminoglycosides, fluoroquinolones, and topical agents. The objective should be to identify combinations that reduce both lipid and antibiotic exposure while maintaining robust killing. The fifth stage should optimize formulation according to intended clinical use. Wound hydrogels might favor sustained release and moist healing, liposomes might enhance biofilm penetration, oral gels might require taste and mucosal-safety optimization, and catheter coatings would need long-term surface stability. Formulation should therefore follow the clinical indication rather than precede it. The sixth stage should establish host safety and microbiome selectivity. Three-dimensional skin models, keratinocytes, fibroblasts, erythrocytes, mucosal models, and representative commensal communities should be included before animal efficacy experiments.

The seventh stage should use ex vivo and *in vivo* infection models. Porcine skin and wound models could be particularly informative because their tissue architecture is more clinically relevant than simple microtiter assays. Device models should incorporate physiologically realistic flow and conditioning films. The eighth stage should quantify local pharmacokinetics and pharmacodynamics. For a wound product, this could include free monolaurin concentration in wound fluid, tissue penetration, residence time, bacterial load, biofilm biomarkers, and healing endpoints. Unlike conventional systemic PK, the relevant question may be how long the compound remains above an effective local biofilm concentration. Finally, early clinical development should prioritize safety, tolerability, local exposure, microbial endpoints, and antibiotic-sparing potential before attempting large efficacy trials. These early trials should establish whether local exposure and microbiological response justify progression to larger efficacy studies.

Figure 5 summarizes the proposed translational pathway. It is deliberately structured as an evidence-gated roadmap: advancement should occur only after each preceding uncertainty—chemical identity, biological activity, biofilm efficacy, tissue safety, formulation performance, and *in vivo* exposure—has been resolved adequately (Figure 5).

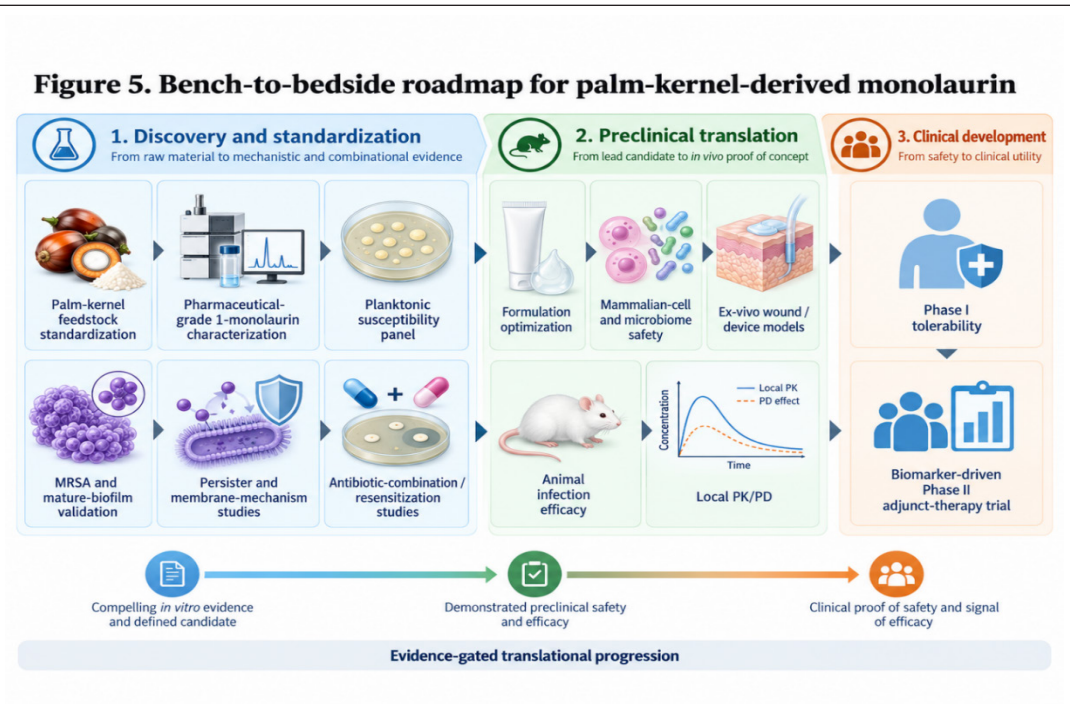

Figure 5: Bench-to-bedside roadmap for palm-kernel-derived monolaurin.

The roadmap intentionally positions clinical efficacy late in the development sequence. Current evidence is strong enough to justify further research but not to bypass fundamental pharmaceutical questions. The field first needs a reproducible palm-derived active ingredient and evidence that its biological performance is equivalent to the monolaurin used in the strongest MRSA studies. Formulation, safety, local exposure, and clinically relevant biofilm models must then demonstrate that promising *in vitro* concentrations can be translated into a viable therapeutic window.

Conclusion

Palm kernel oil provides a credible industrial feedstock for lauric acid and monolaurin, and contemporary research establishes that purified monolaurin can be synthesized directly from palm-kernel fractions with antibacterial activity. Independent biomedical evidence further shows that monolaurin can inhibit wound-derived MRSA, interfere with biofilm formation and established biofilms, and potentiate selected β-lactam antibiotics. Lauric acid adds complementary evidence through polymicrobial antibiofilm effects, virulence-related modulation, and membrane-mediated killing of antibiotic-tolerant *S. aureus* persisters. These findings support a mechanistically coherent development concept centered on microbial membrane perturbation. Rather than functioning through a single classical antibiotic target, lauric lipids may produce a multi-hit effect involving permeability changes, direct killing, reduced adhesion and virulence, persister vulnerability, and enhanced antibiotic activity. Their amphiphilic nature also makes formulation a central determinant of performance. The evidence does not yet justify describing palm-kernel-derived monolaurin as a clinically validated anti-MRSA treatment or a replacement antibiotic. The strongest MRSA and β-lactam-synergy studies establish molecule-level efficacy rather than direct source-specific efficacy for pharmaceutical palm-kernel material. Gram-negative susceptibility remains more uncertain because of the outer-membrane barrier, and human tissue tolerance, microbiome consequences, resistance evolution, local pharmacokinetics, and clinical efficacy are insufficiently characterized.

The most realistic near-term translation is therefore localized therapy. Chronic infected wounds, skin and soft-tissue infections, oral biofilms, catheter lumens, and antimicrobial device coatings allow direct contact with biofilm and potentially high local concentrations while limiting systemic exposure. Liposomes, emulsions, lipid nanoparticles, hydrogels, and coatings could further improve dispersion, retention, penetration, and controlled release. The most defensible scientific positioning is consequently palm-kernel-derived monolaurin as a localized membrane-active antibiofilm and antibiotic-adjuvant platform rather than a replacement antibiotic. Progress toward clinical use should depend on pharmaceutical-grade standardization, source-equivalence studies, standardized planktonic and biofilm susceptibility testing, rigorous antibiotic-combination experiments, host-cell and microbiome safety, resistance-evolution studies, formulation optimization, animal infection models, local pharmacokinetic/pharmacodynamic measurements, and controlled human trials.

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None.

Conflict of Interest

None.

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