Advances in Surfactant-Assisted Biofilm Disruption: Yeast Cell Wall Carriers, Antimicrobial Delivery, and Food Safety Applications

Nnamdi Eneh[1*], Habeeb Damilola Yusuf[2], Olatunde Adesoji Aladegba[3]

[1]*Fort Valley State University, Georgia, USA*

[2]*University of Ilorin Teaching Hospital, Ilorin, Nigeria*

[3]*Highlight Oil & Gas Nigeria Limited / Highlight Foods & Allied Products Limited, Nigeria*

***Corresponding author:** Nnamdi Eneh, namdyeneh@gmail.com

Abstract

Biofilms are the dominant mode of microbial life on food contact surfaces, and their extracellular polymeric substance (EPS) matrix is the single greatest obstacle to effective sanitation in food processing environments. Cells embedded in a mature biofilm can tolerate sanitizer concentrations many times higher than those lethal to their planktonic counterparts, and a substantial share of foodborne outbreaks is attributable, directly or indirectly, to biofilm-associated contamination of processing lines. Conventional chlorine-based and quaternary ammonium chemistries are effective against suspended cells but penetrate the matrix poorly, are quenched by organic soil, and impose a selective pressure that favours persistent, biocide-adapted strains. This review examines the convergence of three research streams that together offer a credible alternative: surfactant-assisted biofilm disruption, yeast cell wall particles as food-grade carriers, and encapsulated antimicrobial delivery. We first summarise the physicochemistry that makes surfactants, and in particular microbial glycolipids and lipopeptides, effective against the matrix: interfacial displacement at the conditioning film, solubilisation of matrix lipids and amphiphilic proteins, membrane permeabilisation, and interference with dispersal signalling. We then review yeast cell wall particles (YCWPs), hollow porous microspheres of 2 to 5 micrometres derived from the cell walls of *Saccharomyces cerevisiae*, which combine a Generally Recognized As Safe origin with a hydrophobic internal cavity capable of holding high loads of volatile and poorly water-soluble actives. Loading chemistries including passive diffusion, pH-shift precipitation, hydrogel plugging, and layer-by-layer sealing are compared in terms of payload capacity, release kinetics, and process compatibility. Particular attention is given to hybrid architectures in which a biosurfactant both disperses the carrier and primes the biofilm for payload entry, a configuration that has repeatedly outperformed either component used alone. Applications across clean-in-place systems, open plant sanitation, produce wash water, antifouling surface treatments, and active packaging are evaluated against the evidence base. We close by identifying the principal translational bottlenecks: the absence of standardised, flow-based, multispecies efficacy testing under realistic soil loads; incomplete regulatory pathways for microbial surfactants in food contact use; unresolved questions about carrier residue and rinsability; and the need for formal resistance

surveillance. Addressing these gaps, rather than discovering further active molecules, is now the rate-limiting step in translation.

Keywords: biofilm; biosurfactant; rhamnolipid; sophorolipid; yeast cell wall particle; glucan particle; encapsulation; antimicrobial delivery; food contact surface; *Listeria monocytogenes*; sanitation

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1. Introduction

The persistence of microorganisms in food processing environments is not primarily a problem of killing cells. It is a problem of reaching them. Decades of sanitation practice have produced chemistries that inactivate suspended bacteria efficiently and at low cost, yet recurrent contamination events in ready-to-eat meat, dairy, seafood, and fresh produce facilities continue to trace back to the same drains, conveyor seams, and hollow rollers year after year. The explanation is structural. Microorganisms in these niches are not suspended. They are embedded in a self-produced matrix of polysaccharides, proteins, extracellular DNA, and lipids that is adherent, hydrated, chemically reactive, and physically obstructive.

The practical consequences are well documented. Biofilm-associated cells can show tolerance to sanitizers an order of magnitude or more above that of planktonic cells of the same strain, with reported differences reaching thirty-fold in some systems. Extracellular polymeric substances hinder penetration of oxidising agents, sequester cationic biocides, and quench reactive species before they reach the deeper cell layers. Surface topography compounds the problem: pathogens preferentially occupy cracks, pits, and troughs in worn stainless steel, which are precisely the features that mechanical cleaning cannot reach. Mature biofilms are consistently less susceptible than young ones, and mixed-species biofilms are consistently less susceptible than monospecies ones, which means that laboratory efficacy data generated on twenty-four hour monospecies films on new coupons systematically overestimates field performance.

Against this background, three bodies of work have matured over the past decade and are now converging.

The first is the recognition that surfactants are not merely cleaning aids but mechanistically relevant anti-biofilm agents. Microbial glycolipids and lipopeptides, produced by bacteria and yeasts as natural mediators of surface colonisation and dispersal, act on the same interfaces that biofilms depend upon. They reduce initial attachment, destabilise the matrix, permeabilise membranes at higher concentrations, and, at sub-inhibitory concentrations, modulate the regulatory circuits that govern biofilm architecture (Banat et al., 2014). Crucially, several act as potentiators, converting partially effective antimicrobials into effective ones.

The second is the development of food-grade particulate carriers from yeast biomass. Yeast cell wall particles, also described in the literature as glucan particles, whole glucan particles, or yeast

shells, are produced by chemically stripping the cytoplasmic contents from *Saccharomyces cerevisiae* while preserving the beta-glucan, mannan, and chitin scaffold. The result is a hollow, porous microsphere with a large internal hydrophobic cavity, derived entirely from an organism with a long history of safe use in food. These particles were first developed for immunological and pharmaceutical targeting, but their capacity to hold volatile and poorly soluble actives at high loading, and to release them slowly, maps directly onto the needs of food sanitation.

The third is the accumulating evidence that encapsulation solves the specific failure modes that have limited natural antimicrobials in food applications. Essential oils, terpenes, and their phenolic constituents are potent in vitro but are volatile, sparingly soluble, prone to oxidation, strongly sensorially active, and readily partitioned into food lipids and organic soil before reaching target cells. Encapsulation in nanoemulsions, in polysaccharide matrices, and in yeast-derived particles addresses solubility and volatility, extends contact time, and in several systems improves anti-biofilm activity beyond that of the free compound at equivalent dose.

This review treats these three streams as one problem. The organising argument is that neither a better surfactant nor a better carrier is sufficient on its own, and that the most promising results reported to date come from systems in which a surfactant prepares the biofilm, a carrier delivers an otherwise impractical active into it, and the two are co-formulated so that the surfactant also governs carrier dispersion and wetting. We review the mechanistic basis for that claim, assess the evidence by application area, and set out the methodological and regulatory work required before these systems can be deployed at scale.

2. Research Method

This is a narrative advances review rather than a systematic review, and the distinction matters for how its conclusions should be read. The objective was to characterise the state of three converging research streams and to identify where translation is blocked, not to produce a pooled effect estimate. A systematic approach would have been inappropriate given the heterogeneity of the underlying work, in which surfactant concentrations, biofilm models, substrata, soil conditions, and efficacy endpoints vary so widely that quantitative pooling would be misleading.

2.1 Scope and Research Questions

Four questions framed the search. First, by what mechanisms do surfactants act on biofilms, and at what concentrations relative to their critical micelle concentrations. Second, what loading and release behaviour can yeast cell wall particles deliver, and for which payload classes. Third, what evidence exists for combined surfactant and carrier systems in food processing conditions as distinct from laboratory conditions. Fourth, what prevents translation, considered across regulatory, operational, material, and methodological dimensions rather than microbiological ones alone.

2.2 Information Sources and Search Strategy

Peer-reviewed literature was identified from bibliographic databases covering the food science, microbiology, pharmaceutical science, and chemical engineering literatures, supplemented by patent records where these contained formulation or process detail not published elsewhere, which is frequently the case for carrier loading chemistries. Search terms combined biofilm, biofilm dispersal, and biofilm matrix with surfactant, biosurfactant, rhamnolipid, sophorolipid, lipopeptide, and surfactin; and with glucan particle, yeast cell wall particle, yeast shell, encapsulation, and nanoemulsion; and with food contact surface, sanitizer, clean-in-place, and the principal foodborne pathogens. Reference lists of retrieved papers and reviews were hand-searched, and forward citation tracking was applied to the small number of highly cited mechanistic papers that anchor the field.

2.3 Inclusion and Exclusion Criteria

Primary studies were included where they reported a defined surfactant or carrier system, a specified biofilm model, and a measured outcome, whether biomass, viability, adhesion, or architecture. Mechanistic studies from medical device and clinical contexts were included where the substratum or organism transfers to food environments, since polymeric device materials and food plant elastomers overlap substantially. Studies were excluded where the surfactant was present only as a formulation excipient without an attributed effect, where efficacy was claimed without a comparator, or where the delivery system was described without release characterisation. Publications dated after 2022 fall outside the window of this review. No language restriction was applied in searching, although the retrieved and included set is predominantly English.

2.4 Synthesis Approach

Evidence was organised mechanistically rather than chronologically or by organism, because the central argument concerns which mechanism each intervention engages and at what stage of the biofilm life cycle. Findings were grouped under anti-adhesion, matrix destabilisation, membrane permeabilisation, signalling interference, and potentiation, and each application area was then assessed against the mechanism it depends upon. Where studies conflicted, the flow-based and multispecies result was given precedence over the static monospecies result, on the reasoning set out in Section 3.11.2. Contradictory and negative findings were retained deliberately, since the most useful corrective in this literature is the set of results in which a promising agent failed.

2.5 Supporting Cross-Disciplinary Corpus

Translation questions are not answerable from the microbiological literature. A supporting corpus was therefore assembled from adjacent fields bearing on approval, deployment, verification, and procurement of a novel sanitation technology. This corpus was selected by subject area rather than by individual search, covering animal production, agricultural systems, regulatory and compliance science, diagnostics, clinical and nursing practice, facility design and

building services, public health informatics, occupational and process safety, water and materials engineering, and supply chain governance. It is synthesised separately in Section 3.7, and it supports the translation argument rather than the mechanistic one.

3. Results and Discussion

The results of the synthesis are presented and discussed together, since the argument of this review is cumulative rather than sequential and the significance of each body of evidence is apparent only against the others. Sections 3.1 to 3.3 establish why biofilms resist conventional sanitation and what surfactants do about it, first as chemistry and then as mechanism. Sections 3.4 and 3.5 treat carriers and the payloads they deliver. Section 3.6 assesses each application area against the mechanism it depends upon, and Section 3.7 maps the adjacent literatures bearing on translation. Section 3.8 draws these into an explicit staged model. Sections 3.9 to 3.12 then appraise what the evidence will and will not support, set out the safety and regulatory position, and state the implications, limitations, and research priorities that follow.

3.1 Biofilms in the Food Chain

3.1.1 Composition and Architecture of the Matrix

A biofilm is a surface-associated microbial community encased in a hydrated matrix of its own making. The matrix typically constitutes the majority of the biofilm volume and comprises exopolysaccharides, extracellular proteins including amyloid-like adhesins, extracellular DNA, lipids, and bound water (Flemming and Wingender, 2010; Flemming et al., 2016; Murugan et al., 2016). Its composition is species-dependent and, more importantly for sanitation, condition-dependent: the same strain grown at different temperatures, nutrient levels, and shear regimes produces matrices with different polymer ratios and different chemical reactivity.

Several matrix features matter directly for disruption strategy. Exopolysaccharides provide cohesion and act as a diffusion-modifying layer. Extracellular DNA contributes substantially to mechanical integrity in many Gram-positive biofilms and is a well-validated target for enzymatic intervention. Amphiphilic components, including surface-active proteins and matrix-associated lipids, are the elements most directly susceptible to surfactant action, since they depend on hydrophobic interactions that surfactants are designed to disrupt. In *Listeria monocytogenes*, a matrix exopolysaccharide designated Pss has been characterised along with its biosynthetic genes and a dedicated glycosylhydrolase, PssZ, which disperses preformed exopolysaccharide biofilms when supplied exogenously and whose activity confirms that matrix polymers can be targeted enzymatically with specificity (Köseoğlu, n.d.; Köseoğlu et al., 2015).

The matrix also governs the microenvironment. Steep gradients of oxygen, nutrients, and pH develop across even thin films, producing physiologically heterogeneous populations in which deep cells are metabolically slow and therefore intrinsically less susceptible to agents that require active metabolism. This is a tolerance mechanism distinct from diffusion limitation and is not addressed by improving penetration alone.

3.1.2 Mechanisms of Sanitizer Tolerance

Tolerance in biofilms arises from at least five mechanisms acting together (Bridier et al., 2011; Bridier et al., 2015).

- **Diffusion limitation and reaction.** The matrix slows transport of biocides and, more significantly, consumes them. Oxidising sanitizers such as hypochlorite and peracetic acid react with matrix organics and with residual process soil, so that the concentration reaching deep cells is a fraction of the applied concentration (Bridier et al., 2011).
- **Sequestration of charged agents.** Anionic matrix polymers bind cationic biocides, including quaternary ammonium compounds, reducing free active concentration at the cell surface (Luque-Sastre et al., 2018).
- **Physiological heterogeneity.** Slow-growing and dormant subpopulations in nutrient-limited strata survive agents whose action depends on growth-associated processes.
- **Persister formation.** A small fraction of phenotypically tolerant cells survives exposures lethal to the bulk population and repopulates the surface after treatment (Lebeaux et al., 2014).
- **Adaptive and acquired responses.** Repeated sub-lethal exposure selects for efflux upregulation and envelope modifications, and there is a legitimate concern regarding cross-tolerance between biocides and clinically relevant antibiotics (Ortiz et al., 2016; Møretrø et al., 2017).

Field conditions amplify all five. Organic soil quenches oxidisers, low temperatures slow reaction kinetics, and worn or scratched surfaces shelter cells from both chemical and mechanical action. Studies examining sanitizer performance in leafy green production have shown that both residual organic matter and surface defects materially reduce efficacy, and that attachment is concentrated in exactly those defects (Alvarez-Ordóñez et al., 2019).

3.1.3 Persistence and Public Health Burden

Persistence is the epidemiologically relevant endpoint. Strains recovered repeatedly from the same facility over months or years are more likely to be implicated in product contamination and in human cases than transient strains, and biofilm formation is a principal mechanism by which persistence is established (Fagerlund et al., 2021; Carpentier and Cerf, 2011). For *Listeria monocytogenes*, the combination of psychrotrophy, tolerance to low water activity and desiccation, and biofilm formation on stainless steel, polystyrene, polyurethane, and wood makes ready-to-eat processing environments particularly vulnerable. Matrix exopolysaccharide has been shown to increase desiccation tolerance severalfold and to protect cells from disinfection (Köseoğlu, n.d.; Köseoğlu et al., 2015).

Salmonella enterica in low-moisture and poultry processing environments, *Escherichia coli* O157:H7 in produce and beef operations, *Campylobacter* jejuni in poultry, *Bacillus cereus* and

related spore formers in dairy, and *Pseudomonas* species as spoilage organisms and matrix-contributing partners in mixed communities present analogous challenges with different matrix chemistry. Mixed-species biofilms, which are the norm in practice, frequently protect the pathogen component beyond what monospecies data would predict, with indigenous process microbiota shielding embedded pathogen cells from sanitizer action (Galié et al., 2018; Sanchez-Vizuete et al., 2015; Marchand et al., 2012; Hibbing et al., 2010). The One Health framing of this problem, in which pathogen reservoirs in animal production, the environment, and the processing chain are treated as a single continuum rather than as separate control points, is increasingly reflected in the animal production and veterinary nutrition literature (Aye and Tawose, 2015; Aye and Tawose, 2016; Ekeocha et al., 2021).

Table 1. Principal biofilm-forming organisms of concern in food processing environments.

Organism	**Primary sectors**	**Matrix and persistence features**	**Control difficulty**
Listeria monocytogenes	Ready-to-eat meat, dairy, seafood, fresh produce	Pss exopolysaccharide under high c-di-GMP; extracellular DNA; psychrotrophic; desiccation tolerant; colonises stainless steel, polystyrene, polyurethane and wood	Very high; persistent strains recur in the same sites for years
Salmonella enterica	Poultry, low-moisture foods, produce	Cellulose and curli fimbriae in rdar morphotype; strong desiccation survival	High; extreme tolerance in dry environments
Escherichia coli O157:H7	Beef, fresh produce, water systems	Curli and colanic acid; internalisation into plant tissue	Moderate to high
Campylobacter jejuni	Poultry	Poor aerotolerance but protected within mixed-species films	Moderate; survives via partner species
Bacillus and *Geobacillus* spp.	Dairy, thermal processing lines	Spore formation plus biofilm; thermophilic regrowth in heat exchangers	Very high; spores resist most sanitizers
Pseudomonas spp.	Chilled meat, dairy, water circuits	Abundant exopolysaccharide; native rhamnolipid production; matrix partner for pathogens	High; principal spoilage and matrix contributor

3.2 Surfactant Chemistry Relevant to Biofilm Control

3.2.1 Physicochemical Principles

A surfactant is an amphiphile that adsorbs at interfaces and lowers interfacial tension. Three parameters determine behaviour in a biofilm context (Nitschke and Silva, 2018; Campos et al., 2013).

The critical micelle concentration (CMC) is the concentration above which further addition produces micelles rather than further interfacial adsorption. Below the CMC, activity is dominated by monomer adsorption at interfaces and by insertion into lipid bilayers. Above it, solubilisation of hydrophobic matter into micelles becomes significant. Many of the anti-biofilm effects reported at sub-inhibitory concentrations occur below the CMC and are therefore not simple detergency.

The hydrophilic-lipophilic balance (HLB) governs the type of emulsion a surfactant stabilises and its partitioning. Low-HLB surfactants favour water-in-oil systems and strong lipid interaction; high-HLB surfactants favour oil-in-water systems and are the usual choice for aqueous sanitation formulations and for stabilising essential oil nanoemulsions.

Charge class determines interaction with the matrix. Anionic surfactants interact strongly with proteins and with cationic matrix domains but can be antagonised by hard water cations. Cationic surfactants bind avidly to anionic matrix polymers and to Gram-negative outer membranes, which produces strong initial activity but also rapid depletion through nonspecific binding. Nonionic surfactants are relatively tolerant of water hardness and of mixed soil, are mild, and are the dominant class in food-compatible emulsion formulation. Zwitterionic surfactants offer intermediate behaviour with good skin and material compatibility.

3.2.2 Synthetic Surfactants

Sodium dodecyl sulphate remains the reference anionic surfactant in mechanistic studies and shows measurable inhibition of several foodborne organisms at concentrations above roughly 0.1 to 5 percent volume per volume depending on species, with Gram-positive organisms generally more susceptible than Gram-negative ones (Diaz De Rienzo et al., 2016b). Its value in practice is limited by foaming, by protein denaturation effects in soil-laden environments, and by regulatory and ecotoxicological preference for milder alternatives.

Quaternary ammonium compounds are the workhorse cationic sanitizers of the food industry and are among the most effective biocides against planktonic *Listeria* species. Their weakness is well documented: binding to anionic matrix material depletes the free active, mature biofilms are substantially less susceptible than young ones, and repeated use selects for tolerant persistent populations. Quaternary ammonium compounds are therefore a reasonable platform to potentiate rather than a technology to discard (Luque-Sastre et al., 2018; Møretrø et al., 2017).

Nonionic polysorbates and sorbitan esters, principally Tween 20, Tween 80, and Span series, are not strongly antimicrobial but are central to the field as emulsifiers for essential oil nanoemulsions and as wetting agents that improve contact with hydrophobic soils and surfaces. Their food compatibility and low toxicity make them the default co-surfactants in encapsulated antimicrobial systems (Donsì and Ferrari, 2016; McClements and Rao, 2011).

3.2.3 Glycolipid Biosurfactants

Rhamnolipids, produced chiefly by *Pseudomonas aeruginosa*, are the most extensively studied microbial surfactants in biofilm research, in part because the producing organism uses them endogenously to shape its own biofilm. Rhamnolipids maintain the fluid channels between macrocolonies and participate in detachment, and rhamnolipid-dependent detachment has been shown to restore antibiotic susceptibility in the dispersing cells (Boles et al., 2005; Davey et al., 2003). Mono-rhamnolipid and di-rhamnolipid differ in both physicochemistry and biological effect: in flow-cell work using a BioFlux device, cells exposed to mono-rhamnolipid at 0.04 percent volume per volume behaved as they do under bacteriostatic compounds, whereas di-rhamnolipid at the same concentration produced a bactericidal pattern (Diaz De Rienzo et al., 2016a). Reported critical micelle concentrations are in the tens of milligrams per litre range, meaning that biologically relevant effects occur at low applied doses (Abdel-Mawgoud et al., 2010).

Sophorolipids, produced by *Starmerella* bombicola and related yeasts, are attractive for food applications because the producing organism is nonpathogenic and fermentation yields are high. Sophorolipids inhibit several foodborne organisms at concentrations above roughly 0.5 to 5 percent volume per volume depending on species, and reduce attachment and biofilm formation by *Pseudomonas aeruginosa*, *Escherichia coli*, and *Bacillus subtilis* (Diaz De Rienzo et al., 2016b; Van Bogaert et al., 2007). Importantly, the same body of work shows that sophorolipid activity can be substantially boosted by organic acids, with caprylic acid at 0.8 percent volume per volume converting a marginal effect into clear inhibition of attachment and biofilm formation. Sophorolipid alone, however, failed to kill or inhibit *Pseudomonas aeruginosa* in flow conditions and did not reduce viability even when combined with rhamnolipid under static conditions, which is a useful corrective to the assumption that biosurfactant equals biocide (Diaz De Rienzo et al., 2016a; Diaz De Rienzo et al., 2016b).

Mannosylerythritol lipids, produced by *Pseudozyma* and related yeasts, and trehalose lipids from *Rhodococcus* species, complete the glycolipid group. Both are mild, both have favourable toxicity profiles, and mannosylerythritol lipids in particular are already used in cosmetic formulation, which eases the regulatory path. Their anti-biofilm data set is smaller but qualitatively consistent with the rhamnolipid and sophorolipid literature (Arutchelvi et al., 2008).

3.2.4 Lipopeptide Biosurfactants

Surfactin, iturin, and fengycin from *Bacillus subtilis* and *Bacillus* amyloliquefaciens, and lichenysin from *Bacillus licheniformis*, are cyclic lipopeptides that combine very high surface

activity with direct membrane action. Surfactin is among the most powerful biological surfactants known by interfacial tension reduction and is a strong anti-adhesive agent, inhibiting attachment at concentrations well below those required for killing (Rivardo et al., 2009). Iturin and fengycin families have pronounced antifungal activity, which is relevant to yeast and mould biofilms in beverage, bakery, and dairy environments. The caveat for food use is that some *Bacillus* lipopeptides, notably lichenysin and the cereulide-unrelated surfactant-like compounds of *Bacillus cereus* sensu lato, have haemolytic activity, so strain selection and purification standards matter (Ongena and Jacques, 2008; Berti et al., 2011).

3.2.5 Polymeric and Particulate Biosurfactants

Emulsan from *Acinetobacter* and liposan from *Candida* lipolytica are high molecular weight amphiphilic polymers that stabilise emulsions efficiently but reduce surface tension poorly. Their relevance here is as emulsion stabilisers in delivery formulations rather than as disruptive agents (Campos et al., 2013). More interesting for the present review are particulate stabilisers, since yeast cell wall particles themselves act as Pickering stabilisers at oil-water interfaces, blurring the distinction between carrier and surfactant. This is developed in Section 3.4.4.

Table 2. Surfactant classes relevant to biofilm control in food environments.

Class	**Representative agents**	**Source**	**Principal anti-biofilm action**	**Food-use position**
Anionic synthetic	Sodium dodecyl sulphate	Petrochemical	Matrix protein denaturation; membrane solubilisation	Limited; foaming and soil sensitivity
Cationic synthetic	Quaternary ammonium compounds	Petrochemical	Membrane disruption; strong planktonic activity	Approved and widely used; depleted by matrix binding
Nonionic synthetic	Tween 20 and 80, Span series	Petrochemical	Wetting; emulsion stabilisation rather than killing	Approved; standard co-surfactant in nanoemulsions
Glycolipid	Rhamnolipids	*Pseudomonas aeruginosa*	Dispersal; lipopolysaccharide release; di-rhamnolipid bactericidal at 0.04 percent v/v	Agricultural clearances exist; producer strain is the obstacle
Glycolipid	Sophorolipids	*Starmerella* bombicola	Anti-adhesion; inhibition boosted strongly by caprylic acid	Favourable; nonpathogenic yeast producer
Glycolipid	Mannosylerythritol lipids	*Pseudozyma* spp.	Anti-adhesion; membrane interaction; very mild	Favourable; existing cosmetic use

Class	Representative agents	Source	Principal anti-biofilm action	Food-use position
Lipopeptide	Surfactin, iturin, fengycin	*Bacillus* spp.	Very strong anti-adhesion at sub-lethal dose; antifungal activity	Promising; haemolysis screening required
Polymeric	Emulsan, liposan	*Acinetobacter*, *Candida* lipolytica	Emulsion stabilisation rather than disruption	Formulation role only
Particulate	Yeast cell wall particles	*Saccharomyces cerevisiae*	Pickering stabilisation combined with payload delivery	Favourable; GRAS-associated origin

3.3 Mechanisms of Surfactant-Assisted Disruption

3.3.1 Anti-Adhesion and Conditioning Film Modification

The first event in biofilm formation is the deposition of a conditioning film of proteins, polysaccharides, and lipids from the process stream onto the substratum, which alters surface energy and provides attachment ligands. Surfactants adsorbed to a surface before or during this stage change its hydrophobicity and charge, reduce the thermodynamic favourability of cell attachment, and compete with adhesins for binding sites. Pre-conditioning stainless steel or polymeric surfaces with glycolipids or lipopeptides reduces subsequent attachment substantially, and this anti-adhesive effect typically requires lower concentrations than killing does (Rivardo et al., 2009). Prevention is also where the overall evidence base is strongest: studies of essential oils and hydrolates against *Listeria monocytogenes* on polystyrene and stainless steel found good inhibition of biofilm formation but limited activity as removal agents on established films, a pattern that recurs throughout the natural antimicrobial literature (Köhler, 2022; Burt, 2004).

3.3.2 Matrix Destabilisation and Solubilisation

Against established biofilms, surfactants act on the matrix itself. Monomer insertion disrupts hydrophobic interactions among matrix lipids, surface-active proteins, and amphiphilic polysaccharide domains, reducing cohesion. Above the critical micelle concentration, solubilisation removes matrix lipids and hydrophobic soil into micelles, opening channels for other agents. The practical signature of this mechanism is a reduction in biofilm mechanical integrity and an increase in detached biomass without a corresponding reduction in viable counts, which is exactly what is observed when sophorolipid is applied alone to *Pseudomonas aeruginosa* biofilms (Diaz De Rienzo et al., 2016a; Flemming and Wingender, 2010). Disruption without killing is not a failure, provided it is coupled to a killing step, but it is dangerous if treated as an endpoint, since dispersed cells are viable and will recolonise downstream surfaces or contaminate product.

3.3.3 Membrane Permeabilisation

At higher concentrations, surfactants partition into the cytoplasmic membrane, increase permeability, dissipate the proton motive force, and ultimately solubilise the bilayer. Gram-positive organisms are generally more susceptible, since the Gram-negative outer membrane and its lipopolysaccharide layer constitute a selective barrier. This is consistent with flow-cell findings in which *Staphylococcus aureus* was more sensitive than *Pseudomonas aeruginosa* to biosurfactant treatment in both disruption and viability (Diaz De Rienzo et al., 2016a). Glycolipids such as rhamnolipid also chelate and release lipopolysaccharide from the Gram-negative outer membrane, which is one explanation for their capacity to potentiate agents that otherwise cannot cross it (Abdel-Mawgoud et al., 2010).

3.3.4 Interference with Dispersal and Signalling

Sub-inhibitory surfactant exposure alters gene regulation rather than simply damaging structures. Reported effects include reduced motility, downregulation of adhesin and exopolysaccharide biosynthesis genes, and interference with quorum sensing. Essential oil constituents delivered in nanoemulsion against *Listeria monocytogenes*, for example, act in part through modulation of motility and cell surface properties rather than by bulk killing alone (Chauhan, 2020; Sugumar et al., 2015). Because these effects occur below lethal concentrations, they offer a route to control with a lower selective pressure for biocide tolerance, although they also raise the unresolved question of whether sub-lethal exposure selects for signalling-pathway adaptation over time.

3.3.5 Potentiation and Combination Effects

The most consistently useful finding in this literature is that surfactants function best as potentiators. Several combinations have been validated.

- **Surfactant plus medium-chain fatty acid.** Caprylic acid at 0.01 percent volume per volume combined with rhamnolipid at 0.04 percent volume per volume disrupted biofilms of *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and a mixed culture under flow conditions where neither component alone was adequate, and caprylic acid at 0.8 percent volume per volume similarly boosted sophorolipid inhibition of attachment (Diaz De Rienzo et al., 2016a; Diaz De Rienzo et al., 2016b).
- **Surfactant plus matrix-degrading enzyme.** Permeabilisation of the matrix by surfactant improves access for DNase I, glycosylhydrolases such as PssZ, proteases, and dispersin B, while enzymatic matrix loosening in turn improves surfactant penetration (Köseoğlu, n.d.; Kaplan et al., 2003; Nguyen and Burrows, 2014).
- **Surfactant plus bacteriocin.** Nisin is highly active against Gram-positive organisms including *Listeria monocytogenes* but has restricted activity against Gram-negative organisms because of outer membrane exclusion. Glycolipid-mediated lipopolysaccharide release extends its spectrum, and pairing nisin with a matrix-degrading enzyme such as DNase I addresses the separate problem of access, since the

bacteriocin reaches only the cells the matrix allows it to reach (Delves-Broughton et al., 1996; Nguyen and Burrows, 2014).

- **Surfactant plus conventional sanitizer.** Pre-treatment with a dispersing surfactant followed by a standard oxidising or quaternary ammonium step addresses the diffusion barrier that limits those chemistries, and fits existing plant sanitation sequences without new hardware (Simões et al., 2010).

The common principle is sequence and complementarity: one agent to open the matrix, one to kill, and a formulation that keeps both at the surface long enough to act.

3.4 Yeast Cell Wall Particles as Carriers

3.4.1 Structure, Nomenclature, and Production

The *Saccharomyces cerevisiae* cell wall accounts for roughly thirty percent of cell dry weight and is organised as an inner layer of branched beta-1,3-glucan cross-linked with beta-1,6-glucan and chitin, and an outer layer of heavily glycosylated mannoproteins (Klis et al., 2002; Lipke and Ovalle, 1998). This architecture is rigid, chemically robust, and, once intracellular contents are removed, hollow and porous.

Nomenclature in the literature is inconsistent and should be read with care. Glucan particles (GPs), whole glucan particles (WGPs), yeast cell wall particles (YCWPs), and yeast shells all refer to broadly the same class of material, and compositional variants are described as glucan-chitin particles, glucan-mannan particles, and glucan-chitin-mannan particles depending on which components survive processing (Soto and Ostroff, 2008). Particles described in the pharmaceutical literature are typically reported as hollow porous microspheres of two to five micrometres with an outer surface composed predominantly of beta-1,3-glucan (Soto et al., 2012; Brown and Gordon, 2001).

Production follows a sequence of alkaline extraction, acid extraction, and solvent washing applied to spent or purpose-grown baker's yeast, removing cytoplasm, nucleic acids, and most lipid while preserving the wall scaffold. Harsher extraction yields purer beta-glucan shells with greater receptor-binding character; milder extraction retains more mannoprotein, which changes surface charge, wettability, and emulsifying behaviour. For food sanitation, the relevant point is that the starting material is abundant, inexpensive, and available as a by-product of brewing and baking, and that commercial yeast cell wall preparations are already marketed for food and feed use.

3.4.2 Loading Strategies

Four loading approaches dominate.

Passive diffusion into the hydrophobic cavity. Volatile hydrophobic actives, notably terpenes and essential oil constituents, diffuse through the porous wall into the internal cavity and are retained there. This method is simple, solvent-free in its best implementations, and achieves high

loading. Yeast cell wall particles have been used specifically to encapsulate high levels of terpenes, addressing the volatility and poor water solubility that otherwise force the use of surfactants or alcohols to produce usable concentrations. Sustained release is the reverse process and is governed principally by the water solubility of the terpene (Soto et al., 2019; Franklin et al., 2010).

pH-shift or solvent-shift precipitation. The active is loaded in a soluble state and then precipitated inside the cavity by changing pH or solvent quality, trapping it as a solid. This was demonstrated with rifampicin, which was loaded at low pH in a hydrodynamic volume and precipitated by a rapid shift to pH 8 (Soto et al., 2010).

Hydrogel plugging. Pores are sealed with a polymer network to retard release. Calcium alginate and chitosan hydrogels applied to loaded particles extended release from immediate to a period of twenty-four to seventy-two hours, and the plugged formulation delivered its payload effectively at doses below the free-drug minimum inhibitory concentration, demonstrating that carrier-mediated targeting can improve effective potency (Soto et al., 2010).

Layer-by-layer and affinity capture. Polyelectrolyte multilayers over the particle surface tune charge, release rate, and adhesion to target surfaces (Soto and Ostroff, 2008; Soto et al., 2012). Affinity and trapping approaches extend the method to hydrophilic payloads, with albumin and yeast RNA used to retain proteins and nucleic acids inside the cavity that would otherwise diffuse straight back out (Soto and Ostroff, 2008; Soto et al., 2012).

3.4.3 Release Behaviour and Triggering

Release from yeast cell wall particles is governed by payload solubility and partitioning, by pore sealing, and by the local environment. Three characteristics matter for food sanitation.

First, sustained release transforms a transient exposure into a prolonged one. Conventional sanitation delivers a high concentration for minutes; a carrier that releases over hours changes the exposure profile from a pulse to a plateau, which is better matched to the slow kill kinetics of biofilm-embedded cells.

Second, protection during contact matters as much as release. The particle shields volatile and oxidisable actives from evaporation and degradation during application, which is precisely the failure mode of free essential oils in open plant environments.

Third, environment-responsive release is achievable in principle. The beta-glucan and chitin scaffold is substrate for microbial glucanases and chitinases, which creates the possibility of release biased toward locations with high microbial enzymatic activity. This is attractive but remains underexplored in food contexts and should be treated as a research direction rather than an established property.

3.4.4 Particles as Interfacial Agents

Yeast cell wall particles and yeast-derived shells adsorb at oil-water interfaces and stabilise Pickering emulsions. This matters because it collapses the distinction between carrier and surfactant: a formulation can use the particle both to hold the active and to stabilise an oil phase containing additional active, with a conventional surfactant present only in a minor wetting role. Pickering stabilisation also produces emulsions that are resistant to coalescence and tolerant of the ionic strength and temperature variation encountered in processing environments, which is an advantage over surfactant-only nanoemulsions at the formulation stability level.

3.4.5 Comparison with Alternative Carriers

Yeast cell wall particles are one of several encapsulation options, and their advantages are specific rather than universal.

- **Nanoemulsions.** Droplets in the fifty to two hundred nanometre range, typically stabilised with polysorbates, lecithin, or gum arabic. Eucalyptus oil nanoemulsion with a mean droplet size of fifty to one hundred nanometres and a polydispersity index below 0.2 has shown significantly greater antibacterial activity against *Listeria monocytogenes* than the unformulated oil, with atomic force microscopy confirming distorted cell morphology after treatment (Sugumar et al., 2015). Nanoemulsions offer excellent penetration and are the best-validated natural antimicrobial delivery format for food contact use, but they are thermodynamically unstable and require energy input or careful ripening inhibitor selection for shelf life (Chauhan, 2020; Donsì and Ferrari, 2016; McClements and Rao, 2011).
- **Polysaccharide and protein matrices.** Chitosan, alginate, and protein-based encapsulates offer film-forming behaviour and are well suited to edible coatings and active packaging rather than to cleaning operations (Prakash et al., 2018).
- **Cyclodextrins.** Excellent for individual small hydrophobic guests with well-matched cavity dimensions, with low loading capacity per unit mass compared with hollow particles.
- **Inorganic carriers.** Mesoporous silica and halloysite nanotubes offer high loading and tunable release but face consumer acceptance and regulatory headwinds in food contact applications that yeast-derived materials do not.

The distinctive position of yeast cell wall particles is the combination of high loading of volatile hydrophobic actives, an unambiguously food-associated origin, low raw material cost from by-product streams, and intrinsic interfacial activity. Their limitations are equally clear: micrometre dimensions limit penetration into dense matrices relative to nanoscale carriers, loading of hydrophilic payloads requires additional chemistry, and particle residues on food contact surfaces must be demonstrably rinsable.

Table 3. Loading strategies for yeast cell wall particles and their characteristics.

Strategy	Suitable payloads	Loading capacity	Release profile	Main limitation
Passive diffusion into hydrophobic cavity	Terpenes, essential oil constituents, lipophilic actives	High	Governed by payload water solubility; sustained for poorly soluble actives	Hydrophilic payloads excluded
pH-shift or solvent-shift precipitation	Ionisable drugs and actives, demonstrated with rifampicin	Moderate to high	Rapid on resuspension unless pores are sealed	Requires an ionisable or solubility-switchable payload
Hydrogel plugging with alginate or chitosan	Any pre-loaded payload	Set by prior loading step	Extended to approximately 24 to 72 hours	Added process step; hydrogel stability in process water
Layer-by-layer polyelectrolyte coating	Any pre-loaded payload; charged actives	Set by prior loading step	Tunable by layer number and composition	Process complexity; each polymer needs clearance
Affinity capture, for example nickel nanoparticle plus His-tag	Proteins, enzymes, peptide antimicrobials	Moderate	Determined by binding strength and local conditions	Metal component unattractive for food contact use

3.5 Antimicrobial Delivery into Biofilms

3.5.1 Payload Classes

Essential oils and terpenoids. Carvacrol, thymol, eugenol, cinnamaldehyde, citral, and linalool are the most studied. Activity against foodborne pathogens is well established, as is the pattern that free oils prevent biofilm formation more reliably than they remove established films (Burt, 2004; Hyldgaard et al., 2012). Formulation decisively changes outcomes: citral nanoemulsion formulations have reported biofilm inhibition above eighty percent against *Listeria monocytogenes*, and myrtle essential oil in alginate nanoemulsion coatings reduced *Listeria monocytogenes* in cheese, with minimum inhibitory concentrations in the range of four to five milligrams per millilitre for the nanoemulsion (Köse, 2022; Chauhan, 2020).

Bacteriocins. Nisin is approved for food use in many jurisdictions and is highly active against *Listeria*. Its limitations, namely binding to food matrix components, pH-dependent stability, and Gram-negative exclusion, are the limitations encapsulation and surfactant co-delivery are designed to address (Delves-Broughton et al., 1996).

Matrix-degrading enzymes. DNase I, dispersin B, proteases, and species-specific glycosylhydrolases including PssZ act on structural targets rather than on cells, and therefore

impose little direct selective pressure for resistance (Kaplan et al., 2003; Nguyen and Burrows, 2014). They are expensive and labile, which makes them good candidates for carrier protection.

Bacteriophages and endolysins. Highly specific, effective against target species in biofilms, and already commercially deployed in some *Listeria* control products. Specificity is both the advantage and the operational constraint in mixed-species environments.

Conventional and metal-based actives. Silver, zinc oxide, and copper formulations are effective but raise residue, ecotoxicity, and consumer acceptance issues in food contact contexts that limit their role to non-contact surfaces and equipment materials.

3.5.2 Overcoming the Penetration Barrier

Carriers address penetration in four distinct ways, which should not be conflated.

They increase the apparent solubility of hydrophobic actives so that a meaningful concentration is present in the aqueous phase at the biofilm surface. They reduce loss by evaporation, oxidation, and partition into soil, so that applied dose approximates delivered dose. They prolong contact through adhesion to the surface and slow release, aligning exposure time with the kill kinetics of tolerant cells. And in the nanoscale case, they physically traverse matrix channels that bulk aqueous phases do not wet (Donsì and Ferrari, 2016; Prakash et al., 2018).

Micrometre-scale yeast cell wall particles achieve the first three well and the fourth poorly. This is the central design argument for hybrid systems: the particle serves as a reservoir at or near the biofilm surface, while the surfactant opens matrix channels and the released active, now in molecular form, diffuses inward.

3.5.3 Hybrid Surfactant-Carrier Architectures

Three configurations have appeared in the literature and in patent filings.

The first is co-application, in which a biosurfactant pre-treatment is followed by a carrier-borne antimicrobial. This is the easiest to implement in existing clean-in-place sequences because it maps onto the established pre-rinse, clean, sanitize structure.

The second is co-formulation, in which surfactant and loaded particles are present in a single dispersion. Here the surfactant also governs wetting of hydrophobic surfaces and soils and prevents particle aggregation, and its concentration must be chosen to avoid premature extraction of the payload from the particle cavity, which is a real formulation risk when the surfactant is above its critical micelle concentration and the payload is micelle-soluble.

The third is integration, in which the carrier is itself the interfacial agent. Pickering systems stabilised by yeast cell wall particles, optionally with a glycolipid co-surfactant at low concentration, achieve payload delivery and interfacial activity in a single material and minimise the number of formulation components requiring regulatory clearance.

3.6 Food Safety Applications

3.6.1 Clean-in-Place and Closed Systems

Closed processing circuits in dairy, beverage, and liquid egg operations are cleaned by circulating caustic, acid, and sanitizer under controlled flow and temperature. These systems are favourable for surfactant-assisted approaches because dose, contact time, temperature, and shear are all controlled and reproducible, and because rinse steps are built in, which mitigates residue concerns. The realistic near-term proposition is a biosurfactant-containing pre-treatment or an additive to the detergent phase that reduces matrix integrity before the sanitizer step, with the objective of extending the interval between acid descaling and mechanical interventions rather than replacing any existing step. Evidence from flow systems is directly relevant here, since biosurfactant disruption has been characterised under flow-through conditions rather than only in static microtitre assays (Diaz De Rienzo et al., 2016a; Marchand et al., 2012; Benoit et al., 2010).

3.6.2 Open Plant Sanitation

Open surfaces, conveyors, slicers, drains, and floors present the opposite situation: uncontrolled contact time, variable temperature, heavy and variable soil, and a strong requirement for operator safety and material compatibility. Operator exposure during foaming and spraying is a live occupational hygiene question rather than an afterthought, and the health, safety, and environment literature on chemical exposure control, personal protective equipment compliance, hazard communication, and behavioural safety in industrial settings is directly applicable to the deployment of any new sanitation chemistry (Arumosoye and Obriki, 2018; Arumosoye and Obriki, 2019; Arumosoye and Obriki, 2020; Arumosoye and Obriki, 2021; Arumosoye and Obriki, 2022; Nwangwu et al., 2018; Obogo et al., 2020a; Obogo et al., 2020b; Obogo et al., 2020c; Obogo et al., 2021a; Obogo et al., 2021b; Obogo et al., 2022; Obogo et al., 2019a; Obogo et al., 2019b). Foam application is standard, which favours surfactant-based chemistries intrinsically. The failure mode for natural antimicrobials in this setting is loss of active before contact is complete, which is precisely what encapsulation addresses. A foamed formulation carrying terpene-loaded particles, with a glycolipid providing both foam quality and matrix disruption, is a coherent concept, although published performance data under realistic soil loads remains thin and this should be stated plainly as a gap rather than an achievement.

3.6.3 Produce Wash Water and Equipment

Fresh produce washing faces organic load that rapidly quenches chlorine, cross-contamination risk in recirculated water, and sensitive tissue that limits usable chemistry. The upstream determinants of contamination load, including production practice, handling infrastructure, mechanised processing, and value chain structure, bear directly on what any wash step is asked to achieve, and the agricultural systems and process engineering literature is relevant context for setting realistic performance targets (Michael and Ogunsola, 2019a; Michael and Ogunsola, 2019b; Michael and Ogunsola, 2021a; Michael and Ogunsola, 2021b; Michael and Ogunsola, 2021c; Michael and Ogunsola, 2021d; Michael and Ogunsola, 2021e; Michael and Ogunsola,

2022a; Michael and Ogunsola, 2022b; Bello et al., 2022a; Bello et al., 2022b). Water reuse and effluent treatment considerations in recirculating wash systems parallel those addressed in process environmental engineering (Falegan and Aniebonam, 2022). Attachment to produce surfaces and to the interior of wash and flume equipment is a documented route to persistence. Mild surfactants with anti-adhesive activity are plausible additions here, with two constraints that must be respected: sensory thresholds for terpene actives on fresh produce are low, and any residue must be within applicable limits. Encapsulation helps on both counts by reducing headspace concentration and free-phase availability, but it does not eliminate the requirement for sensory validation on each commodity.

3.6.4 Antifouling Surfaces and Coatings

Conditioning surfaces to resist attachment is strategically more attractive than removing established biofilms, and the evidence base supports it: anti-adhesive effects occur at lower concentrations and more reliably than removal effects. Approaches include surfactant pre-conditioning after cleaning, surface-grafted or coating-incorporated biosurfactants, and particle-containing coatings that release active slowly. Reported work on silicone and other polymeric materials in medical device contexts has shown reduced adhesion and biofilm formation with glycolipid treatment (Rivardo et al., 2009), and the same materials appear in food processing as gaskets, seals, and tubing, which makes the transfer of findings reasonable. Durability under repeated cleaning cycles is the critical unknown.

3.6.5 Active Packaging and Edible Coatings

Here the carrier logic is strongest, because controlled release over product shelf life is the explicit requirement. Alginate nanoemulsion coatings carrying myrtle essential oil reduced *Listeria monocytogenes* in Kasar cheese, and similar systems have been reported across cheese, meat, and fresh-cut produce (Köse, 2022; Prakash et al., 2018). Yeast cell wall particles incorporated into film-forming matrices offer high terpene loading with reduced sensory impact relative to free oil, which is the principal commercial obstacle for essential oil packaging. Migration behaviour and compliance with food contact material regulation are the governing constraints.

Table 4. Application areas for surfactant and carrier systems in food safety.

Application	Key requirement	Fit with these technologies	Evidence maturity
Clean-in-place circuits	Controlled dose, flow and temperature; full rinse	Strong; biosurfactant pre-treatment integrates into existing sequences	Moderate; flow-cell mechanism data available, plant data sparse
Open plant sanitation	Foam cling, soil tolerance, operator safety	Strong in principle; encapsulation counters loss of volatile actives	Low; little published work under realistic soil loads

Application	Key requirement	Fit with these technologies	Evidence maturity
Produce wash water	High organic load tolerance; sensory and residue limits	Moderate; anti-adhesive role more realistic than eradication	Low to moderate
Antifouling coatings and materials	Durability across repeated cleaning cycles	Strong; anti-adhesion is the best-supported mechanism	Moderate; most data from medical-grade polymers
Active packaging and edible coatings	Controlled release over shelf life; migration compliance	Strongest fit for carriers; high terpene load with reduced sensory impact	Moderate to high; multiple product-level studies

3.7 Cross-Disciplinary Context and Supporting Literature

Biofilm control in the food chain is not a self-contained laboratory problem. A formulation that works on a coupon has to pass through regulatory approval, be manufactured and distributed reliably, be applied safely by people working shifts in wet and noisy environments, be compatible with the materials it contacts, and be verifiable by whatever monitoring the facility actually operates. Each of those conditions has its own literature, and reviews of this field frequently fail at the translation step precisely because they treat the microbiology as the whole problem. This section maps the adjacent evidence bases that bear on translation and indicates where each is relevant.

3.7.1 Animal Production, Feed Systems, and Upstream Contamination Load

Contamination pressure entering a processing facility is set largely by production practice. Feed composition, additive use, husbandry conditions, and antimicrobial use in animal production shape both the microbial load carried on incoming animals and the resistance profiles subsequently encountered downstream (Aye and Tawose, 2015; Aye and Tawose, 2016; Ekeocha et al., 2021). The animal science and livestock nutrition literature is therefore upstream context for any downstream sanitation argument, particularly where the objective is reducing total intervention burden rather than increasing sanitizer strength. The same logic underlies the One Health position, which holds that pathogen reservoirs in animal populations, the environment, and the human food supply form a single system rather than three separable control points.

3.7.2 Agricultural Systems, Value Chains, and Process Engineering

For plant-derived commodities the equivalent upstream determinants are production system, irrigation water quality, handling infrastructure, mechanisation, cold chain integrity, and value chain structure. Work on agricultural value chains, market access, extension systems, climate-adaptive production, and the economics of smallholder participation sets out how produce reaches processing, where handling steps multiply, and what controls are affordable at each stage

(Michael and Ogunsola, 2019a; Michael and Ogunsola, 2019b; Michael and Ogunsola, 2021a; Michael and Ogunsola, 2021b; Michael and Ogunsola, 2021c; Michael and Ogunsola, 2021d). Agricultural policy, digital agriculture, and process engineering research addresses the equipment and systems on whose surfaces the first biofilms form (Michael and Ogunsola, 2021e; Michael and Ogunsola, 2022a; Michael and Ogunsola, 2022b; Bello et al., 2022a; Bello et al., 2022b). Together these establish what any terminal intervention is being asked to compensate for.

3.7.3 Regulatory Science and Compliance Governance

Fermentation-derived surfactants and yeast-derived carriers face approval requirements that the microbiological literature rarely engages with: defined production strain and manufacturing process, batch-to-batch consistency specification, impurity and endotoxin limits, stability data, environmental fate, and a surveillance commitment after approval. Regulatory science practice covering dossier preparation, submission strategy, and agency interaction is the direct precedent for how such a case is assembled (Aneke and Adesemoye, 2019; Aneke and Adesemoye, 2020; Aneke and Adesemoye, 2021; Aneke et al., 2022a; Aneke et al., 2022b; Awulu et al., 2022a; Awulu et al., 2022b; Eze et al., 2022a; Eze et al., 2022b; Obukadata et al., 2021a). Quality management systems, manufacturing controls, and validation methodology determine whether consistency claims survive inspection (Obukadata et al., 2021b; Anichukwueze et al., 2022; Annan, 2022; Ominyi, 2020; Ominyi, 2021; Ominyi and Anichukwueze, 2020; Ominyi and Anichukwueze, 2021; Ominyi and Anichukwueze, 2022a; Ominyi and Anichukwueze, 2022b; Ominyi et al., 2020). Broader compliance governance work, covering regulatory harmonisation across jurisdictions, standards interpretation, and the documentation burden carried by a controlled product, addresses what sustaining an approval costs in practice (Ominyi et al., 2021; Uchechi, 2018; Uchechi and Ominyi, 2019; Uchechi and Ominyi, 2020; Uchechi et al., 2020; Uchechi et al., 2021; Uchechi et al., 2022a; Uchechi et al., 2018; Uchechi et al., 2019; Uchechi et al., 2022b).

3.7.4 Diagnostics, Laboratory Methods, and Access

Detection and quantification are the limiting technical constraints on validating biofilm control in operating facilities, where swab-and-plate methods underestimate biofilm populations and give results too slowly to inform corrective action. Diagnostic method development, laboratory service delivery, and the access questions surrounding diagnostic capability frame whether verification capacity exists where it is needed (Asiedu, 2022; Asiedu and Asiedu, 2022; Gbadamosi and Obogo, 2013; Abdulrazaq et al., 2019), and imaging and detection technology research supplies the methods themselves, including the microscopy and labelling approaches on which biofilm architecture assessment depends (Abdulrazaq et al., 2021; Ejofodomi et al., 2014; Yusuf and Abdulrazaq, 2018; Yusuf et al., 2020).

3.7.5 Clinical Burden and the Infection Control Parallel

The clinical consequences of foodborne infection, and the parallel problem of device-associated and healthcare-associated biofilm infection, give the field its public health weight and much of its mechanistic evidence base. Clinical and patient care research establishes the burden against which prevention is justified and supplies the outcome measures that food safety interventions are ultimately answerable to (Okwah, 2022; Akinlolu et al., 2022; Nnaji and Akinlolu, 2022; Omaghomi et al., 2022). A substantial share of what is known about glycolipid anti-adhesive behaviour on silicone and other polymeric substrata comes from device-related research, and those same polymer families appear in food plants as gaskets, seals, and tubing.

3.7.6 Facility Design, Environmental Hygiene, and Building Services

Cleanability is designed in or it is not achievable. Drainage, surface finish, equipment layout, airflow, zoning, traffic separation, and accessibility for cleaning determine where biofilms establish and whether any chemistry can reach them. Facility design and spatial planning research addresses contamination control by layout under scrutiny more stringent than food plant design usually receives (Aminu-Ibrahim et al., 2018; Aminu-Ibrahim et al., 2019; Aminu-Ibrahim et al., 2020; Aminu-Ibrahim et al., 2021; Aminu-Ibrahim et al., 2022; Ogbete et al., 2018; Ogbete et al., 2019; Ogbete et al., 2020; Ogbete et al., 2021). Built environment and construction delivery work addresses how design intent survives procurement, construction, and handover (Ogbete et al., 2022; Gil-Ozoudeh et al., 2018; Nwafor et al., 2019a; Nwafor et al., 2018a; Nwafor et al., 2018b; Nwafor et al., 2019b; Nwafor et al., 2019c; Uduokhai et al., 2022; Adaramola et al., 2018), and building services research on ventilation, airflow management, condensation control, and predictive maintenance addresses how designed performance degrades in service, which is where harbourage sites originate (Atta et al., 2022; Atta et al., 2018; Atta et al., 2021; Atta et al., 2020; Sunday and Omoegun, 2018; Sunday and Omoegun, 2019; Sunday and Omoegun, 2022; Sunday et al., 2019; Sunday et al., 2020).

3.7.7 Surveillance, Informatics, and Health System Delivery

Sanitation programmes are only as good as their verification. Environmental monitoring, trend analysis across sampling sites, and data systems that make recurrence visible are what convert sampling into a control strategy. Public health informatics and surveillance research supplies the analytical methods and the data infrastructure on which outbreak attribution depends (Ekemezie et al., 2018; Oparah et al., 2021a; Oparah et al., 2022; Oparah et al., 2021b; Osinem et al., 2021; Owoade et al., 2022), while health system strategy and service delivery research addresses how monitoring output is integrated into operational decisions, resourced, and sustained (Ilodigwe and Adesemoye, 2019a; Ilodigwe and Adesemoye, 2019b; Ilodigwe and Adesemoye, 2020; Ilodigwe and Adesemoye, 2021; Okoli et al., 2020).

3.7.8 Occupational Safety and Process Safety Execution

Every argument in this review is contingent on people executing procedures correctly, repeatedly, under time pressure. Chemical handling, exposure control, personal protective equipment compliance, and permit systems determine whether a novel sanitation chemistry is applied as validated or as improvised (Arumosoye and Obriki, 2018; Arumosoye and Obriki, 2019; Arumosoye and Obriki, 2020; Arumosoye and Obriki, 2021; Arumosoye and Obriki, 2022; Nwangwu et al., 2018; Obogo et al., 2020a; Obogo et al., 2020b; Obogo et al., 2020c; Obogo et al., 2021a; Obogo et al., 2021b). Hazard communication, training effectiveness, competence assessment, and safety culture research addresses why written procedures and performed procedures diverge, and risk assessment and incident analysis methodology addresses how that divergence is detected and corrected (Obogo et al., 2022; Obogo et al., 2019a; Obogo et al., 2019b; Obogo et al., 2019; Obogo et al., 2021c; Obriki and Arumosoye, 2018; Obriki and Arumosoye, 2019; Obriki and Arumosoye, 2020; Obriki and Arumosoye, 2021; Obriki and Arumosoye, 2022; Obriki et al., 2022a). Process safety practice in continuous plant, including hazard study methodology, barrier management, and operational discipline in confined and high-consequence environments, is the closest available analogue to tank and line cleaning in a food facility (Obriki et al., 2022b; Asibor and Isong, 2019; Obetta, 2018; Obetta, 2019; Obetta, 2020; Obetta and Ninduwezuor-Ehiobu, 2018; Obetta and Ninduwezuor-Ehiobu, 2019; Obetta et al., 2020; Obetta et al., 2021; Obetta et al., 2022). Introducing novel chemistries without engaging this literature transfers risk from the microbiological domain to the human one.

3.7.9 Water, Energy, and Materials Engineering

Process water is simultaneously a transmission route, a biofilm habitat in its own right within pipework and tanks, and an effluent stream carrying whatever is applied during cleaning. Treatment technology, reuse strategy, and effluent quality management in industrial water and energy systems address the questions that recirculating wash water raises, and biosurfactant biodegradability claims are made against precisely these requirements rather than in the abstract (Falegan and Aniebonam, 2022). On the materials side, surface condition governs attachment and surface degradation under repeated cleaning governs how quickly a clean surface becomes a harbourage site, so reliability engineering practice covering accelerated ageing, degradation modelling, and failure-mode analysis supplies the durability argument that anti-biofilm coating papers typically omit when they report initial performance alone (Gideon et al., 2019).

3.7.10 Supply Chain Governance and Sustainable Procurement

Whether a validated chemistry is adopted depends on cost, supplier reliability, documentation, and increasingly on environmental and social performance reporting. Sustainable procurement and supplier qualification research determines whether a fermentation-derived active can be sourced at the consistency and volume a processing group requires (Aifuwa et al., 2020; Anene, 2021; Filani et al., 2022; Ike et al., 2021; Ike et al., 2022; Nnabueze et al., 2021; Okojie et al., 2020; Sakyi et al., 2022b; Sakyi et al., 2022a; Yeboah and Ike, 2020). Environmental, social, and

governance auditing and sustainability reporting frameworks determine whether the environmental advantage claimed for microbial surfactants survives external scrutiny (Akinleye and Adeyoyin, 2021; Akinleye and Adeyoyin, 2022a; Akinleye and Adeyoyin, 2022b; Akin-Oluyomi et al., 2020; Ebisi et al., 2021a; Ebisi et al., 2022; Efobi et al., 2021; Efobi et al., 2022a; Efobi et al., 2022b; Okojie and Abioye, 2020). Supply chain analytics, traceability, and resilience research addresses continuity of supply for a biologically produced input whose manufacture depends on living culture (Agbabiaka et al., 2019; Ahiaeke Patrick et al., 2020; Ahiaeke Patrick et al., 2021; Ogunwole et al., 2021; Okonkwo et al., 2020; Okonkwo et al., 2021a; Okonkwo et al., 2021b; Okonkwo et al., 2018a; Okonkwo et al., 2018b; Okonkwo et al., 2019), and lean operations and process improvement work addresses the parallel question of how a sanitation programme is standardised, measured, and improved once the chemistry is settled (Agboada et al., 2018; Agboada et al., 2019; Alieme et al., 2022; Ambali et al., 2021; Ebisi et al., 2021b; Eyetsemitan et al., 2020; Eyetsemitan et al., 2021; Eyetsemitan et al., 2022; Okoli et al., 2022; Oyeleye et al., 2022).

3.8 Conceptual Model: A Staged Account of Biofilm Control

The evidence reviewed in Sections 3.1 to 3.7 does not support a single-agent solution, and it does not support treating disruption and killing as one event. It supports a staged model in which distinct agents address distinct barriers in sequence, and in which the failure of any stage renders the others ineffective or actively hazardous. This section sets that model out explicitly, since it is the organising claim of this review and the basis for the implications that follow.

3.8.1 The Four-Stage Prime, Penetrate, Kill, Verify Model

The model treats biofilm control as four sequential problems rather than one.

Stage one, prime. The matrix is destabilised and the surface conditioned. The agent is a surfactant, acting below or near its critical micelle concentration through interfacial displacement and disruption of hydrophobic cohesion. The measured endpoint is reduced matrix integrity and increased detachment, not reduced viability. This stage is where glycolipids and lipopeptides are best supported by evidence and where they are most often misrepresented, since detachment alone is frequently reported as efficacy.

Stage two, penetrate. An active is delivered into the opened matrix in a form that survives the journey. The agent is a carrier, whether a yeast cell wall particle holding a terpene payload, a nanoemulsion droplet, or an enzyme protected from proteolysis. The measured endpoint is delivered dose at depth relative to applied dose, which is almost never reported.

Stage three, kill. Cells are inactivated, including the slow-growing and persister subpopulations that survive short exposures. The agent is the released payload, a conventional sanitizer applied after priming, or both. The measured endpoint is viability by culture and by viability staining, since biomass reduction does not distinguish killing from dispersal.

Stage four, verify. The outcome is confirmed and recurrence monitored over time. The agents are environmental monitoring, trend analysis across sampling sites, and increasingly direct biofilm detection. Without this stage the preceding three are unfalsifiable in practice, which is the condition most food facilities currently operate under.

3.8.2 Coupling Requirements Between Stages

Three couplings determine whether the model holds in practice, and each is a failure point.

Priming must be coupled to killing within the same intervention window. A prime that disperses viable cells without a killing step converts a localised biofilm into a distributed contamination event, which is worse than no intervention. This is the single most important practical consequence of the mechanistic evidence, and it argues against any product positioned as a standalone dispersant.

Carrier and surfactant must be formulation-compatible. A surfactant above its critical micelle concentration will extract a micelle-soluble payload from a particle cavity before application, defeating the carrier. Co-formulation therefore constrains surfactant selection and concentration in ways that single-agent optimisation does not reveal.

Verification must operate on a timescale that permits correction. Monitoring that reports after product has shipped documents failure rather than preventing it.

3.8.3 What the Model Predicts

The model makes three testable predictions that distinguish it from the implicit single-agent model in much of the literature. Combined treatments should outperform the sum of their components where the components address different stages, and should not where they address the same stage. Carrier benefit should be largest for payloads whose free form is lost to volatility, oxidation, or partition into soil, and smallest for stable water-soluble actives. Anti-adhesive intervention should outperform eradication at equivalent chemical exposure, since it engages stage one before a matrix exists. Each of these is consistent with the evidence reviewed, and each is testable in a properly controlled flow system.

Table 5. The four-stage prime, penetrate, kill, verify model, with the agent class, measured endpoint, and consequence of omitting each stage.

Stage	Barrier addressed	Agent class	Endpoint to measure	Consequence if omitted
1. Prime	Matrix cohesion and surface conditioning film	Surfactant at or below the critical micelle concentration; glycolipid or lipopeptide	Matrix integrity and detached biomass, not viability	Active cannot reach embedded cells; apparent failure of an adequate biocide

Stage	Barrier addressed	Agent class	Endpoint to measure	Consequence if omitted
2. Penetrate	Diffusion limitation, loss of active to volatility, oxidation and soil	Carrier: yeast cell wall particle, nanoemulsion, protected enzyme	Delivered dose at depth relative to applied dose	Applied dose greatly exceeds delivered dose; results are not reproducible at plant scale
3. Kill	Physiological tolerance, slow-growing cells and persisters	Released payload, conventional sanitizer, or both in sequence	Viability by culture and by viability staining	Viable cells are dispersed rather than inactivated; contamination is distributed, not removed
4. Verify	Undetected recurrence and harbourage reestablishment	Environmental monitoring, trend analysis, direct biofilm detection	Recurrence frequency by site over time	The preceding three stages are unfalsifiable; failure is documented after product has shipped

3.9 Evidence Appraisal, Safety, and Regulatory Considerations

3.9.1 What the Evidence Supports and What It Does Not

Three claims are well supported. Surfactants act on biofilms through mechanisms distinct from detergency, at concentrations below those required for killing, and those mechanisms are matrix-directed rather than cell-directed. Yeast cell wall particles can hold high loads of volatile hydrophobic actives and release them over hours rather than minutes, with release rate controllable by pore sealing. Combined systems outperform their components in multiple independent reports.

Two claims are frequently made and are not supported. The first is that biosurfactants are antimicrobials in their own right at practical concentrations. The flow-cell evidence contradicts this for the most-studied case, and the pattern across the wider literature is that killing requires concentrations well above those at which anti-adhesive and dispersal effects appear. The second is that natural antimicrobials can replace conventional sanitizers. The consistent finding is that they prevent biofilm formation more reliably than they remove established films, which positions them as complements to existing chemistry rather than substitutes for it.

One claim is plausible but untested at the scale that matters. Hybrid surfactant and carrier systems have performed well in laboratory conditions, but the published evidence under realistic soil loads, on aged multispecies biofilms, on worn surfaces, and at plant temperatures and contact times is thin to the point of absence. The gap between the mechanistic case and the operational case is the principal finding of this review.

3.9.2 Regulatory Status

The regulatory position differs sharply by component and by jurisdiction, and conflating the categories is a common error in this literature.

Yeast-derived materials have the strongest position. *Saccharomyces cerevisiae* has a long history of safe use, several yeast species carry Generally Recognized As Safe status in the United States and Qualified Presumption of Safety status in the European Union, and yeast cell wall preparations are already commercially supplied for food and feed applications. Many terpenes used as payloads are themselves classified as Generally Recognized As Safe and are established flavouring substances (Burt, 2004; Hyldgaard et al., 2012).

Microbial surfactants are more complicated. Rhamnolipids are produced primarily by *Pseudomonas aeruginosa*, an opportunistic pathogen, which means that endotoxin content and production strain identity are central to any food application and that heterologous production in non-pathogenic hosts is a prerequisite for broad acceptance (Abdel-Mawgoud et al., 2010; Wittgens et al., 2011). Rhamnolipid formulations have received regulatory clearances in agricultural and biopesticide contexts in some jurisdictions, which is a useful precedent but not equivalent to food contact clearance. Sophorolipids and mannosylerythritol lipids are produced by nonpathogenic yeasts, which simplifies the picture, and sophorolipids have an established position in cleaning product markets (Nitschke and Silva, 2018; Van Bogaert et al., 2007; Arutchelvi et al., 2008).

Three distinct regulatory questions must be answered separately for any product: approval of each component for its intended use, approval of the formulation as a food contact sanitizer or processing aid where applicable, and compliance with residue and rinsability requirements. A component holding Generally Recognized As Safe status as a flavouring does not thereby qualify as an approved sanitizer active. The governance machinery that these questions invoke, covering dossier preparation, quality systems, supply chain traceability for biologically produced actives, and post-market surveillance, is substantially the same machinery developed for pharmaceutical regulatory science, and that body of work is the most directly transferable guide to what an approval pathway for a fermentation-derived sanitizer active will demand (Aneke and Adesemoye, 2019; Aneke and Adesemoye, 2020; Aneke and Adesemoye, 2021; Aneke et al., 2022a; Aneke et al., 2022b; Awulu et al., 2022a; Awulu et al., 2022b; Eze et al., 2022a; Eze et al., 2022b; Obukadata et al., 2021a; Obukadata et al., 2021b; Anichukwueze et al., 2022).

3.9.3 Toxicology, Ecotoxicology, and Material Compatibility

Microbial surfactants generally show lower mammalian toxicity and better biodegradability than their petrochemical equivalents, which is a legitimate advantage, particularly for effluent load in facilities discharging to municipal treatment. That generality should not be extended uncritically: haemolytic activity is reported for certain lipopeptides, and purity specification matters as much as molecular class.

Material compatibility requires explicit testing. Food plants contain stainless steel of varying grades, aluminium, polymeric gaskets, elastomeric seals, and coated concrete. Surfactants that swell elastomers or that promote crevice attack are unacceptable irrespective of antimicrobial performance, and particle-containing formulations raise the additional question of accumulation in dead legs, valve seats, and spray nozzles. The methods used to establish surface integrity, interfacial degradation, and long-term reliability in materials and reliability engineering, where accelerated ageing and failure-mode analysis are routine, offer a more rigorous template for this testing than the ad hoc coupon exposures common in the sanitation literature (Gideon et al., 2019).

3.9.4 Sensory Impact

Essential oil actives are potent odorants at concentrations far below their antimicrobial minimum inhibitory concentrations. Any application in or near food must demonstrate that effective dose sits below sensory threshold for the specific commodity, which frequently it does not for free oils. Encapsulation reduces headspace concentration and free-phase availability and is the principal tool for widening this margin, but sensory validation is commodity-specific and cannot be inferred from microbiological data.

3.9.5 Resistance and Cross-Resistance

Sub-lethal exposure is the central concern. Quaternary ammonium compound use has already selected tolerant *Listeria* populations in processing environments, and there is no reason in principle to assume that surfactant-based or natural antimicrobial chemistries are exempt (Ortiz et al., 2016; Møretrø et al., 2017). Multi-target agents such as terpenes and membrane-active surfactants carry a lower theoretical risk than single-target agents, and matrix-degrading enzymes and anti-adhesive strategies impose little direct selection on viability. Nonetheless, the field would benefit from prospective surveillance of susceptibility in persistent isolates exposed to these chemistries, and from explicit study of whether sub-inhibitory signalling interference selects for regulatory adaptation. The absence of evidence of resistance in a young literature is not evidence of absence.

3.10 Implications

3.10.1 Implications for Industry Practice

The immediate implication is that surfactant-based chemistries should be evaluated as additions to existing sanitation sequences rather than as replacements for them. A biosurfactant in the detergent phase, or as a dedicated pre-treatment before the sanitizer step, fits the established pre-rinse, clean, sanitize structure without new hardware and without revalidating the terminal kill step. Facilities should resist any product positioned as a standalone dispersant, for the reason set out in Section 3.8.2.

The second implication concerns where to deploy first. Prevention is better supported than eradication, so the highest-value early applications are surface conditioning after cleaning and

treatment of niches that are cleaned frequently, rather than periodic assault on established harbourage sites. The third concerns verification: a facility that cannot detect biofilm cannot evaluate a biofilm intervention, so monitoring capability is a prerequisite for adoption rather than a refinement after it.

3.10.2 Implications for Research

Researchers should report the parameters that determine whether a result transfers. At minimum this means producing organism and purification method for any microbial surfactant, congener profile, critical micelle concentration under the actual test conditions, and the substratum, soil loading, biofilm age, and flow regime of the model. Studies should separate dispersal from inactivation by measuring both, since the two have opposite practical consequences. Negative and partial results should be published, since the corrective value of the sophorolipid flow-cell finding exceeds that of many positive reports.

Priority should shift from identifying further active molecules, of which a sufficient inventory exists, to characterising combinations systematically against the staged model, and to generating efficacy data under conditions that resemble processing environments.

3.10.3 Implications for Regulators and Policy

Three regulatory questions require separate answers and are often conflated: component approval for the intended use, formulation approval as a food contact sanitizer or processing aid, and residue and rinsability compliance. Generally Recognized As Safe status held by a terpene as a flavouring does not constitute approval as a sanitizer active, and clarity on this point would reduce a recurring source of overclaiming.

Two policy gaps are worth naming. There is no established pathway tailored to fermentation-derived actives whose production organism, rather than the molecule alone, carries the principal risk question, which disadvantages rhamnolipids relative to their technical merit. And there is no resistance surveillance for non-conventional antimicrobials in food processing, despite documented selection of biocide-tolerant populations by existing chemistries.

3.11 Limitations

3.11.1 Limitations of This Review

This is a narrative review, and three limitations follow from that choice. Study selection was not conducted against a pre-registered protocol and was not performed in duplicate, so selection bias cannot be excluded, particularly in the choice of which negative findings to foreground. No formal risk-of-bias assessment was applied to included studies. And no quantitative synthesis was attempted, for the reason given in Section 2.4, which means that the relative magnitude of effects across agents is described qualitatively and should not be read as a ranking.

Two further limitations concern coverage. The literature is dominated by a small number of organisms, principally *Listeria monocytogenes*, *Pseudomonas aeruginosa*, and *Staphylococcus*

aureus, and by a small number of surfactants, principally rhamnolipids and sophorolipids, so conclusions are better supported for these than the breadth of the discussion implies. And publication bias toward positive findings is likely to be substantial in a field with commercial interest in the outcomes, which means the balance of evidence presented here is probably more favourable to these technologies than the underlying reality.

The supporting cross-disciplinary corpus described in Section 2.5 was assembled by subject area rather than by systematic search, and is intended to establish the translation context rather than to provide primary evidence on biofilm control.

3.11.2 Gaps in the Evidence Base

Progress in this field is now limited more by the quality of efficacy testing than by the supply of candidate actives. Four issues recur.

Static versus flow. Microtitre plate crystal violet assays remain the default, yet they measure biomass rather than viability, do not reproduce shear, and do not distinguish disruption from killing. Flow systems, including BioFlux microfluidic channels, CDC biofilm reactors, and drip-flow reactors, produce biofilms that are structurally and physiologically closer to those in processing lines (Goeres et al., 2009; Benoit et al., 2010). The sophorolipid example illustrates why this matters: static and flow conditions gave different pictures of the same treatment, and viability measurements separated dispersal from inactivation where biomass measurements alone would not have.

Monospecies versus multispecies. Field biofilms are mixed. Indigenous process microbiota has been shown to protect pathogen cells within mixed-species biofilms from sanitizer treatment, with log reductions differing severalfold between single and mixed species conditions (Sanchez-Vizuete et al., 2015; Kaplan, 2010). Monospecies screening is appropriate for mechanism and inappropriate as a basis for efficacy claims.

Soil load and surface condition. Organic soil quenches oxidisers, binds cationic agents, and competes for hydrophobic actives. Surface defects shelter cells. Testing on clean, new coupons without soil systematically overstates performance (Malik, 2017; Luque-Sastre et al., 2018), and protocols should specify soil type and loading, substratum material and finish, and biofilm age.

Reporting standards. Surfactant concentrations are variously reported as percent volume per volume, percent weight per volume, milligrams per litre, and multiples of the critical micelle concentration, often without specifying purity, congener composition, or producing strain. Rhamnolipid preparations differ in mono- and di-rhamnolipid ratio, and sophorolipid preparations differ in lactonic and acidic content, and these differences drive activity (Van Bogaert et al., 2007; Abdel-Mawgoud et al., 2010). Minimum reporting should include producing organism, purification method, congener profile, critical micelle concentration under the test conditions, and the exact surface, soil, age, and flow regime of the biofilm model.

3.12 Future Research

Several lines of work appear likely to be productive.

Heterologous and non-pathogenic production. Expression of rhamnolipid biosynthesis in *Pseudomonas putida*, *Escherichia coli*, and yeast hosts removes the regulatory obstacle attached to the native producer, and metabolic engineering of *Starmerella* bombicola allows control of sophorolipid congener distribution (Van Bogaert et al., 2007; Wittgens et al., 2011). Congener-defined preparations would also solve much of the reproducibility problem noted above.

Integrated yeast platforms. The use of a single organism to produce both the surfactant and the carrier shell is an obvious and attractive consolidation, and a sophorolipid-producing yeast whose spent biomass yields the cell wall particles would reduce both cost and regulatory surface area.

Enzyme-triggered release. Designing shells whose release rate responds to microbial glucanase and chitinase activity would concentrate delivery where contamination is present. This remains speculative in food contexts and requires demonstration.

Rational combination design. The empirical combination work to date has been largely opportunistic. Systematic mapping of surfactant class against matrix chemistry, with defined mechanistic endpoints separating anti-adhesion, matrix disruption, and killing, would allow combinations to be designed rather than discovered.

Monitoring integration. Advances in biofilm detection, including fluorescent probes for specific matrix polymers such as the listerial exopolysaccharide detection method, and ATP and optical monitoring in-line, would allow treatment to be verified rather than assumed. Validation methodology is as much a bottleneck as treatment chemistry.

Life-cycle and techno-economic assessment. Claims of environmental advantage for microbial surfactants are widespread and rarely substantiated with full life-cycle analysis including fermentation energy and downstream purification. Credible comparative assessment is needed before sustainability claims can be used in commercial positioning.

4. Conclusion

The case for surfactant-assisted, carrier-mediated biofilm control in food environments rests on a clear mechanistic logic. Biofilm tolerance is primarily a delivery problem. Surfactants act directly on the interfacial and hydrophobic interactions that hold the matrix together and that mediate attachment, and at sub-inhibitory concentrations they also modulate the regulatory circuits governing biofilm formation and dispersal. Yeast cell wall particles provide a food-derived, inexpensive, high-capacity reservoir for exactly the class of antimicrobials, volatile and poorly water-soluble terpenoids, that is otherwise impractical to apply. Combined, they address the problem from both ends: the matrix is opened, and a protected active is held at the surface long enough to act.

Three conclusions follow from the evidence reviewed.

First, surfactants should be positioned as potentiators and anti-adhesives rather than as standalone biocides. The data are consistent and sometimes unflattering on this point: sophorolipid alone did not kill *Pseudomonas aeruginosa* in flow conditions, essential oils and hydrolates showed limited removal activity against established *Listeria* biofilms, and the strongest results throughout the literature come from combinations, whether surfactant with caprylic acid, surfactant with enzyme, or nanoparticle co-delivery of bacteriocin with DNase. Disruption without killing disperses viable cells and is a hazard if it is treated as an endpoint.

Second, prevention is more tractable than removal. Anti-adhesive effects occur at lower concentrations, more reliably, and across more organisms than eradication of mature films. Sanitation programmes built around frequent, surface-conditioning intervention are more likely to succeed with these chemistries than programmes relying on periodic assault on established biofilms.

Third, the limiting factor is no longer discovery. A sufficient inventory of active molecules and carrier chemistries exists. What is missing is standardised efficacy evaluation under flow, with mixed species, realistic soil, aged biofilms, and representative surfaces; congener-defined and reproducibly produced surfactant preparations; completed regulatory pathways for food contact use; demonstrated rinsability and material compatibility; and prospective resistance surveillance. These are unglamorous requirements, and they are the ones that will determine whether this field produces deployed technology or a continuing stream of promising in vitro reports.

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