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Polysaccharide-based superwetting and hydrated antibacterial interfaces: evidence gaps, mechanisms, and translational criteria

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Highlights:

- This review covers polysaccharide coatings, membranes, fibers and hydrogels.
- Superwetting claims require a defined wetting metric; interfacial hydration requires separate evidence.
- Bacterial adhesion, killing and biofilm control require different assays.
- Wetting and antibacterial tests require batch-matched specimens under the same conditioning protocol.
- None of the representative studies directly linked retained wetting to antibacterial performance using matched specimens.

Abstract: Polysaccharide materials are often called superwetting antibacterial systems because they swell or have a low initial water contact angle. But these measurements do not show that the materials kill bacteria or control biofilms. This review looks at polysaccharide-based superwetting and hydrated interfaces, including coatings, polymer brushes, porous membranes, fibrous layers, hybrid interfaces, and selected hydrogels. Hydrophilic and hydrated systems are included to help compare how these interfaces work, but their inclusion does not mean they show superwetting behavior. We assessed studies in five separate categories: quantitative wetting, interfacial hydration, bacterial adhesion, bacterial viability and biofilm response. We also examined whether wetting and biological performance persisted after exposure to proteins, salts, flow, wear and sterilization. Among the representative systems audited in this review, none reported quantitative wetting, retained wetting after relevant conditioning, and an antibacterial endpoint using matched specimens from the same preparation batch, subjected to the same conditioning protocol, and evaluated against matched controls. Hydrated polysaccharide interfaces can reduce protein adsorption and bacterial attachment. Reported bactericidal effects involved cationic groups, released drugs, metal or oxide phases, or light-activated treatment; hydration alone was not established as the cause of killing. A combined material needs two measurements: retained hydration with reduced attachment, and active killing at a reported exposure.

Keywords: polysaccharide; superwetting interface; interfacial hydration; bacterial adhesion; antibacterial coating; biofilm control

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1. Introduction

Biomaterial infection starts with surface conditioning. Proteins adsorb within seconds after a device, dressing or scaffold contacts blood, exudate or tissue fluid. The adsorbed layer changes surface charge and receptor exposure. Bacteria then attach through hydrophobic, electrostatic and receptor-mediated interactions. Stable attachment is followed by cell growth, extracellular polymeric substance production and biofilm formation. This sequence drives infection on catheters, vascular devices, orthopaedic implants and chronic wounds [1–4].

Most antibacterial materials release an agent or have bacteria-killing groups fixed to their surface. Release systems may exhibit burst release, reservoir depletion and subtherapeutic late exposure. Contact active surfaces lose activity when proteins or dead cells mask the active groups. A high positive charge or hydrophobicity can also damage mammalian cells. A planktonic killing result cannot predict how long it will protect a surface. Antifouling coatings act earlier by limiting protein adsorption and bacterial attachment, but abrasion, dehydration and high inocula may compromise their protective performance and even lead to barrier failure [5,6].

Wetting changes how liquid contacts the material. High surface energy helps water spread, and pores and roughness draw liquid in through capillary action. Water-filled rough surfaces can also repel oil underwater. These measurements describe liquid behavior, not antimicrobial activity. Reduced bacterial adhesion requires fewer attached cells after a set wash or flow test. Antibacterial activity requires fewer surviving bacteria. Biofilm control requires changes in the number of living biofilm cells, biomass, thickness or matrix after a set period of biofilm growth [7–10].

Polysaccharides contain hydroxyl, carboxyl, amino, acetamido or sulfate groups that bind water and provide sites for chemical modification. They can form thin coatings or be processed into films, fibers and hydrogels. The stability of these hydrated interfaces depends on polymer chemistry, network integrity and exposure conditions. Salt can screen ionic groups, proteins can displace interfacial water, and weak networks can erode or detach. Surface hydration requires separate assessment because bulk swelling measures overall water uptake. Zwitterionic groups provide strong hydration, but their performance still depends on salt concentration, chain architecture and exposure time [11–13].

Earlier reviews have focused on hydrogel crosslinking, swelling, mechanics and hydration layer stabilization [14–18]. Here, we focus on a related but distinct question: whether the wetting behavior reported for polysaccharide interfaces is supported by evidence of antibacterial performance.

In the studies summarized in Table 1, we did not find a comparison that isolated the contribution of retained wetting to infection control using matched specimens exposed to the same conditioning protocol. We therefore distinguish measurements of wetting and hydration from tests of bacterial adhesion, viability and biofilm response. We also consider whether these properties are retained after exposure to conditions relevant to the intended application. Figure 1 illustrates the relationship between material design, interfacial measurements and antibacterial evaluation.

Literature scope. We searched Europe PMC for studies combining polysaccharides with terms related to wetting, interfaces, infection and material formats. The search was last updated on 8 August 2026, and DOI metadata for selected records were checked against Crossref. Search terms included chitosan, cellulose, nanocellulose, alginate, hyaluronic acid, dextran, starch, pullulan and carrageenan. We prioritized studies published between January 2021 and August 2026, while retaining earlier articles

that established relevant principles of hydration, biofilm formation and polysaccharide materials. Original studies were selected with attention to the reported material composition, wetting or hydration measurements, bacterial strain, adhesion or viability outcomes, and biological safety. This is a focused narrative review rather than a systematic review; the studies in Table 1 were selected for comparison and do not constitute an exhaustive survey of the field.

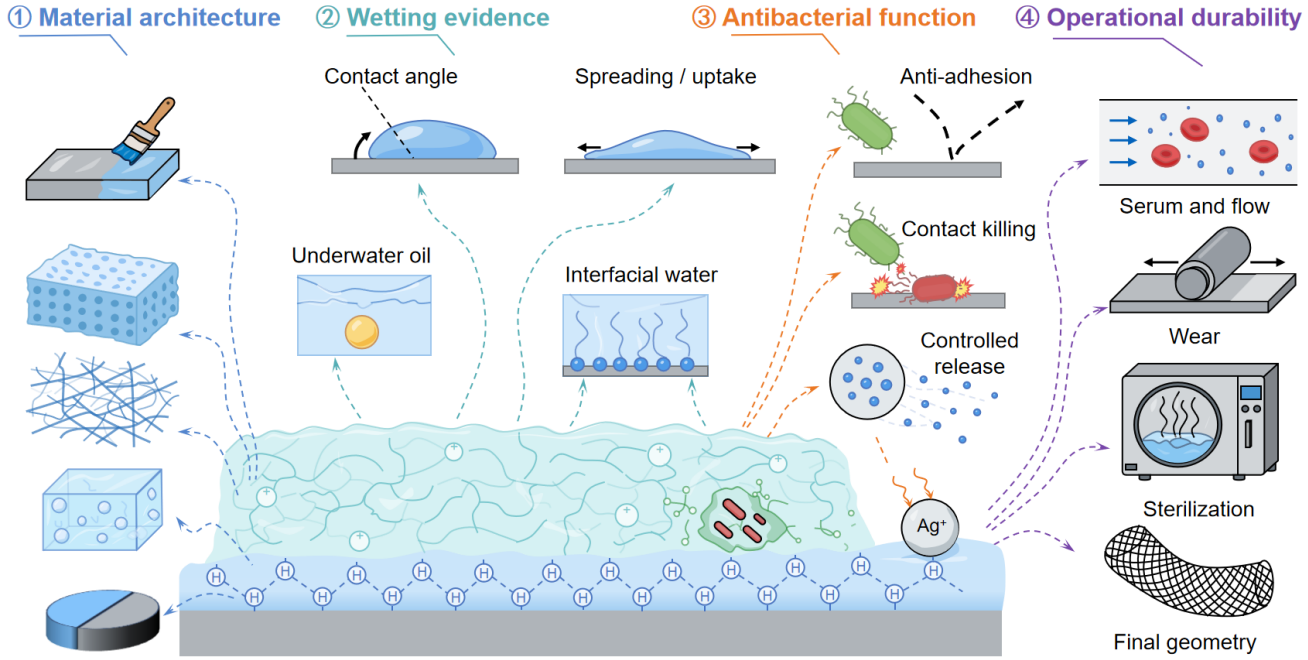


Figure 1. Design-to-validation framework for polysaccharide-based superwetting and hydrated antibacterial interfaces. Representative material architectures include surface coatings, porous monoliths, fibrous membranes, hydrogels, and layered or Janus composites. Their wetting characteristics should be evaluated using complementary evidence, including contact angle, spreading or liquid uptake, underwater oil repellency, and interfacial water retention. Antibacterial performance may arise from hydration-mediated anti-adhesion, contact-active killing, or the controlled release of antibacterial agents such as Ag^+. A low contact angle alone does not demonstrate antibacterial activity. Practical translation further requires the retention of interfacial function in complex biological fluids and under continuous flow, mechanical wear, sterilization, storage, and the geometry of the final device or dressing. Green bacteria represent viable cells, whereas red bacteria represent killed or membrane-damaged cells. This Figure was created by our team using BioGDP software.

This review is organized around one central question: what evidence connects a retained superwetting or hydrated interfacial state to the relevant antibacterial outcome, while distinguishing that contribution from independent active mechanisms under intended-use conditions? The five evidence domains are evaluated as linked evidence for answering this question rather than as interchangeable outcomes.

2. Measurement criteria for superwetting and hydrated antibacterial interfaces

2.1. Hydrophilicity, superhydrophilicity and underwater superoleophobicity

A water contact angle (WCA) is interpretable only when droplet volume, acquisition time, surface condition and test geometry are reported. Angles below 90° indicate hydrophilicity. For consistency in this review, superhydrophilicity is assigned when the apparent water contact angle is ≤ 10° under a defined acquisition time, or when independent time-resolved imaging demonstrates complete lateral spreading to an equivalent near-zero angle. This classification is applied only when the measured response is not dominated by liquid penetration into the material. Published conventions include WCA < 10° [19] and the stricter WCA < 5° or complete spreading [20]. The ≤ 10° boundary is retained here as a review-specific operational convention rather than a universal standard. Report the measured angle and acquisition time so that the classification can be checked against the stated convention [14,21]. These literature conventions describe classification practices, not a harmonized pass/fail standard for polysaccharide antibacterial interfaces. Values near a boundary should be reported with measurement uncertainty rather than assigned to a category from a rounded mean alone.

On porous, fibrous or strongly absorbent materials, disappearance of the external droplet or an apparent decrease to 0° is not by itself evidence of superhydrophilicity. The same observation can result from capillary uptake into the internal pore volume. Surface spreading and absorption must therefore be resolved separately before a superhydrophilic state is assigned.

For underwater wetting, this review uses an underwater oil contact angle of ≥ 150° as the operational criterion for underwater superoleophobicity on a prehydrated surface; the inclusive boundary is specified because published definitions also use > 150° [22]. The oil identity, droplet volume, immersion or prehydration time, acquisition time and hydrostatic condition should be reported. Oil adhesion force or sliding behavior provides additional evidence when low oil adhesion is part of the claim.

The terms used here refer to different measurements. Hydrophilicity is based on water wetting. Superhydrophilicity is assigned using the stated apparent-angle or independently verified spreading criterion, with acquisition time reported and uptake resolved. Underwater superoleophobicity describes an oil droplet on a water-conditioned surface. “Superwetting” is used as an umbrella term for extreme wetting states that meet the operational criteria defined above, rather than as an independent measurement or a synonym for hydrophilicity or interfacial hydration. None of these tests measures protein adsorption or bacterial behavior. Hydration-based antifouling requires reduced adsorption under biological conditioning. Reduced bacterial adhesion requires fewer attached cells after a defined wash. Killing requires a viability assay, while biofilm control requires a surface-associated community assay.

2.2. Dynamic spreading, capillary absorption and interfacial hydration

Contact-angle measurements should be paired with hydration or adsorption measurements. For porous or fibrous materials, separately record the surface liquid-film footprint, the subsurface wetted region and the residual external droplet volume from initial contact to equilibrium or droplet disappearance. Include an evaporation control when evaporative loss is appreciable. Lateral film expansion with limited external volume loss supports spreading, provided swelling and substrate deformation are also resolved. Volume loss beyond evaporation, accompanied by internal wicking or independently determined absorbed mass,

supports capillary uptake. When both processes occur, report their respective kinetics. Report the temporal and spatial resolution and the uptake detection limit. If these limits prevent the two processes from being distinguished, report droplet disappearance with unresolved contributions from spreading and uptake. Apparent angles on absorbing substrates should be compared at matched relative absorbed volumes, rather than by acquisition time alone [23].

Useful methods include bound water analysis, quartz crystal microbalance with dissipation (QCM-D), differential scanning calorimetry, interfacial spectroscopy and wet state mass loss. A membrane with nanoparticle capture and hydrothermal crosslinking linked reinforced hydration to fouling under dynamic exposure [24]. Advancing and receding angles also require reported droplet volume and acquisition rate [21]. For soft films, QCM-D data require a viscoelastic model because the measured coupled mass includes water [25].

Equilibrium swelling measures total water uptake but does not separate free and bound water. Differential scanning calorimetry, low-field nuclear magnetic resonance, vibrational spectroscopy and QCM-D can probe confined water and hydrated film behavior. Salt screening can shift water near zwitterionic chains toward bulk-like dynamics [12]. Mixed organic foulants also change hydration according to polymer composition and amphiphilicity [13]. Repeat wetting and adsorption after biological conditioning.

2.3. Distinguishing anti-adhesion, killing and biofilm control

A material can perform well in one assay and fail in another. Cationic chitosan may be hydrophilic and bactericidal but still adsorb anionic proteins and retain dead cells. Neutral dextran can reduce attachment without killing bacteria. Porous bacterial cellulose can show rapid droplet loss through surface spreading, capillary uptake or both, yet shelter bacteria inside low shear pores. A drug releasing gel can kill bacteria without meeting a superhydrophilic threshold. Each claim should specify the affected bacterial process and the duration of the observed effect.

Biofilm prevention and biofilm disruption require different experiments. Prevention starts before attachment and follows matrix development. Disruption begins with a mature biofilm. A 24 h planktonic colony count supports neither claim. Relevant measurements include attached cells after washing, viable biofilm cells, biomass, thickness and extracellular polymeric substance at multiple times [26].

Biofilm methods measure different properties and require method-specific interpretation. Crystal violet includes dead cells in the biomass signal. LIVE/DEAD dyes report membrane permeability, not reproductive viability. Colony-forming unit (CFU) recovery depends on sonication or scraping efficiency. Test eradication by regrowth in fresh medium, biofilm depth imaging and clinically relevant isolates or mixed species.

2.4. Minimum evidence required for a superwetting antibacterial claim

The measurement must match the material. Nonporous coatings require static, advancing and receding angles plus hysteresis. Absorbent gels and fibrous mats require spreading time together with wicking distance, residual droplet volume or absorbed mass. Water filled surfaces can be assessed by underwater oil angle and oil adhesion force. These measurements must be repeated after exposure to saline, serum or artificial urine and after the relevant deformation or abrasion.

Controls must isolate the proposed mechanism. Hydration studies need a chemistry-matched surface with lower retained hydration. Contact-killing studies need a nonbactericidal matrix control and controls for leaching and no-contact exposure; compare charge, hydrophobicity and accessible group density to identify remaining confounders. Release studies need unloaded matrix and free agent controls. Light-activated studies need dark, light only and temperature-matched controls. Biofilm disruption must start from a preformed biofilm.

A low contact angle can establish wetting but not antibacterial causality. The minimum evidence comprises the intended wetting measurement, relevant conditioning and a mechanism-specific bacterial endpoint on matched material batches.

3. Architectures of polysaccharide-based superwetting and hydrated materials

Interfacial presentation often matters more than the polysaccharide name. Soluble chitosan, a grafted chitosan brush and quaternized chitosan inside a hydrogel expose different charge densities and chain mobilities. Never-dried bacterial cellulose retains a different pore structure from a dried and rehydrated membrane. Calcium alginate changes after ion exchange, and methacrylation changes hyaluronic acid. Report molecular mass, degree of substitution, crosslinker ratio, solids content, hydration history and surface composition.

Polysaccharides also serve different functions. Chitosan and cationized pullulan can damage bacterial membranes. Cellulose and nanocellulose reinforce water-retaining structures. Alginate manages fluid, hyaluronic acid supplies lubrication, and oxidized dextran or pullulan supports dynamic covalent bonding. Carrageenan and starch provide lower-cost gel matrices. No single polymer optimizes hydration, wet strength, tissue adhesion and killing. Assign each component one stated role and one matching measurement. For architecture-level comparison, link that role to the component's location at the exposed interface.

3.1. Surface-grafted coatings and polymer brushes

Chemical modification changes surface hydration and retention. Carboxymethylation adds anionic groups, oxidation adds aldehydes, quaternization fixes cationic charge and methacrylation enables photopolymerization. Sulfobetaine, carboxybetaine, phosphorylcholine and N-oxide groups form strongly hydrated ionic domains. Covalent grafting generally resists flow and friction better than physisorption. A scalable zwitterionic treatment for implantable devices shows that thin antifouling layers can be manufactured when graft density, coverage and curing are controlled [27].

Coating design involves a balance between exposed charge and interfacial hydration. A zwitterionic carboxymethyl chitosan coating reduced fibrinogen adsorption, platelet attachment and biofilm formation on blood-contacting devices [28]. N-oxide brushes provide a nonpolysaccharide hydration benchmark [29]. Quaternized chitosan with tannic acid and chitosan with dextran add contact activity and dynamic bonding [30,31]. Increasing cationic substitution also changes the balance between exposed charge and the surrounding hydrated domains. Charge, antibacterial dose and coating retention after sterilization must be measured together.

3.2. Porous membranes and nanofibrous interfaces

Bacterial cellulose can retain water within a nanofiber network and show underwater oil repellence. Oil and water separation studies provide wetting benchmarks but are not used here as evidence of biomedical antibacterial performance [32,33]. Silver, TiO_2, ZnO, selenium and glucose-responsive nanoreactors can be incorporated into porous polysaccharide structures. In these composites, cellulose controls water transport and structure while the added phase occupies a distinct functional domain [33–36].

Porosity increases water storage and capillary uptake. The apparent wetting response therefore depends on pore size, orientation, connectivity and the extent of liquid penetration into the internal pore space. Evaluate porosity with both wetting and liquid uptake measurements that distinguish surface spreading from capillary absorption.

Fibrous barriers provide permeability and high surface area. Regenerative scaffolds must also admit host cells and nutrients. A guided bone regeneration membrane separated the barrier and regenerative functions into different structural regions [37]. The relevant structural target is a connected water-transport pathway without loss of control over the internal pore space.

3.3. Hydrogels and hydrated coatings

Bulk hydrogels store water and conform to irregular tissue. Hydrated coatings confine the active layer to a device surface. Physical gels are easy to process but often erode in ionic media. Covalent networks improve retention but introduce initiator, crosslinker and degradation concerns. Dynamic covalent bonds permit injection and self-healing but can increase creep under load. Multiple networks can separate water retention from mechanical energy dissipation [38,39].

Coating attachment must be tested under use conditions. Surface-initiated polymerization, substrate interpenetration and catechol anchoring can improve retention. The self-defensive zwitterionic coating illustrates a hydrated surface layer integrated with an internal responsive phase [40]. Its structural validation requires repeated measurements of hydration, release threshold, cohesion and cycle performance.

An alginate, chitosan oligosaccharide and ZnO hydrogel assigns distinct functions to each component. Alginate forms the hydrated matrix, while cationic chitosan and ZnO are incorporated as additional functional components [41]. Higher crosslink density can improve wet adhesion but reduce spreading and drug diffusion [42].

Hyaluronic acid usually provides hydration, lubrication or enzyme responsiveness. In multicomponent coatings and gels, hyaluronic acid can form the hydrated matrix around drug-bearing or photoactive phases [40,43,44].

Oxidized dextran forms Schiff base networks with amino polymers or proteins. These networks can be injectable, self-healing and pH responsive. Zwitterionic dextran instead provides a low-fouling hydrated surface. Dextran-based architectures can therefore present dynamic covalent networks, hydrated zwitterionic domains or embedded functional phases within the same polysaccharide platform [45–48].

3.4. Hybrid interfaces and manufacturing constraints

Inorganic phases add defined functional domains. Silver, ZnO, TiO_2, CuS, Prussian blue, polydopamine, MXene and metal-organic frameworks can be incorporated as dispersed, surface-exposed or reservoir phases. The polysaccharide matrix can control water transport and active phase exposure. In bacterial cellulose composites, silver or TiO_2 and ZnO are integrated into the fibrous polysaccharide framework [33,34].

These composites introduce leaching and batch variation. Particle aggregation or loss can also change surface composition, roughness and the continuity of the hydrated interface.

Failure depends on architecture. Grafted layers lose coverage through bond cleavage or abrasion. Bulk hydrogels soften, fracture or dehydrate. Fibrous mats fuse, delaminate or block. Particle composites aggregate or leach. Scratch and rewet tests assess coating recovery. Cyclic compression and rehydration assess capillary transport in absorbent structures. Repeat wetting after these tests and after protein conditioning.

Manufacturing changes the final interface. Surface initiated grafting controls thickness but is difficult on complex devices. Dip and spray coating are scalable but sensitive to drainage, edge buildup and curing. Photopolymerization requires control of light penetration and residual initiator. Freeze drying changes pore orientation and hydration history. Electrospinning requires solvent removal and tests for fiber fusion or particle shedding after sterilization. Batch specifications must include dry and hydrated thickness, coverage, attachment strength, water uptake, spreading, active dose and variability.

Table 1 applies the same evidence fields to each representative system: material architecture, quantitative wetting evidence, conditioning or durability evidence, bacterial endpoint and overall evidence status. Reported numerical values are retained, whereas missing information is marked as not reported or not confirmed (NR) rather than inferred from qualitative descriptions.

Four additional recent studies reporting both wetting and bacterial measurements were identified [49–52]. None repeated both measurements using matched specimens from the same preparation batch subjected to the same conditioning protocol.

Table 1 records missing measurements as well as positive results. No listed biomedical candidate reports quantitative wetting, retained wetting after conditioning and a matched bacterial endpoint in one testing sequence.

Table 1. Evidence available for candidate polysaccharide wetting and antibacterial interfaces and selected wetting benchmarks.

Material and architecture	Quantitative wetting evidence	Conditioning or durability evidence	Antibacterial or antibiofilm endpoint	Evidence status	Reference
Zwitterionic carboxymethyl chitosan (CMCS) hydrogel coating on thermoplastic polyurethane (TPU)	Captive bubble WCA: 46.0°; TPU: 90.45°; carboxymethyl cellulose (CMC): 59.23°. Complete swelling occurred within 1 min. Near-zero sessile-droplet WCA: NR.	Wet friction against bovine aorta for at least 1000 cycles. Wetting and bacterial outcome after the same cycling sequence: NR.	After 2 h, antimicrobial efficiency was 94.6% for *E. coli*, above 70% for *S. epidermidis*, 71.5% for methicillin-sensitive *S. aureus* and 79.8% for methicillin-resistant Staphylococcus aureus (MRSA). Quantitative biofilm reduction: NR.	Wetting and bacterial data reported. Paired testing after friction: NR.	[24]
Bacterial-cellulose/SiO_2-polydopamine membrane	Reported superhydrophilic and underwater oil repellent behavior during oil and water separation. Quantitative WCA or underwater oil contact angle (UWOCA), droplet identity, volume and acquisition time: NR. Quantitative superwetting classification: not confirmed.	Retained wetting after harsh treatment or recycling: NR.	Oil and water separation above 99.9%. Biomedical bacterial endpoints were not investigated.	Wetting comparator only; not assessed as a biomedical antibacterial claim.	[28]
Ag-nanoparticle-coated tunicate-cellulose-nanocrystal membrane	Reported superhydrophilic and underwater oil repellent behavior. Quantitative WCA or UWOCA, test medium and acquisition time: NR. Quantitative superwetting classification: not confirmed.	Retained wetting after cycling: NR.	Activity reported against *E. coli* and *S. aureus*. Contact time, CFU, log reduction and antibacterial efficiency: NR. Oil rejection was above 99%. Biomedical validation: not evaluated.	Wetting/materials benchmark; antibacterial activity reported in the original application context.	[29]
Hyaluronic-acid-cross-linked poly(sulfobetaine methacrylate) coating with gentamicin	Hydrated antifouling surface reported. Quantitative WCA or spreading, geometry, medium and acquisition time: NR.	Enzyme-driven surface renewal reported. Retained wetting after conditioning: NR.	Reduced attachment and triggered killing of *E. coli* and *S. aureus in vitro* and *in vivo*. CFU, log reduction and biofilm metric: NR.	Hydration and bacterial results reported. Quantitative wetting and paired post-conditioning testing: NR.	[36]
Star-like ZnO-functionalized cellulose fibers	Sessile droplet WCA: cellulose about 12°; 3 wt% ZnO cellulose about 23°. Droplets reached 0° within 1 s because of absorption. Droplet volume: NR. Initial WCA indicates hydrophilicity; rapid droplet loss reflects absorption rather than confirmed superhydrophilic spreading.	Paired wetting and antibacterial testing after conditioning: NR.	*E. coli* reduction at 3 and 24 h: 50.73% and 92.15%. *S. epidermidis* was not detected after 3 h for the 3 wt% ZnO sample. Detection limit: NR.	Absorption kinetics and antibacterial data reported. Superhydrophilic spreading not demonstrated. Paired post-conditioning testing: NR.	[45]

Table 1. *Cont.*

Material and architecture	Quantitative wetting evidence	Conditioning or durability evidence	Antibacterial or antibiofilm endpoint	Evidence status	Reference
Ultrasonically deposited aldehyde-chitosan layer-by-layer (LbL) coating on poly(lactic acid) (PLA)	Water contact angle in air: chitosan (CTS), 83.0°; aldehyde-modified chitosan (CTS-CHO), 28.1°. Droplet volume and acquisition time: NR. The coating is hydrophilic but not superhydrophilic.	Paired wetting and antibacterial testing after conditioning: NR.	Modified ISO 22196 with *E. coli*. Exposure: 24 h; plate incubation: 48 h. Antibacterial activity R was about 4 for coatings prepared with 10 and 20 spray cycles.	Hydrophilic antibacterial coating. Superwetting not demonstrated.	[46]
Porous microfibrillated-cellulose thin film on glass	Goniometer at about 21 °C and 48 to 50% relative humidity (RH). WCA reduction relative to glass was about one third for MFC-I and one half for MFC-II. Absolute WCA: NR. Droplet loss reflected absorption and evaporation rather than confirmed surface spreading.	Nearly complete resistance to repeated dry scraping, but removal after one wet abrasion. Wetting and bacterial results after scraping: NR.	*E. coli* viability fell 43% at 1 h and 54% at 24 h. No viable *S. epidermidis* was recovered at 1 h.	Relative wetting and antibacterial results reported. Absolute WCA and paired conditioning: NR.	[47]
Chitosan/CuO-graphene oxide (GO) LbL nanocomposite coating on leather	Sessile droplet WCA: pristine leather, 91.2 ± 1.9°; chitosan coating, 110 ± 2.5°; CS/CuO-GO-1, 71 ± 1.5°; CS/CuO-GO-5, 78 ± 2.3°. The composites are hydrophilic, not superhydrophilic.	Three bacterial exposure and washing cycles plus dry and wet rub tests. WCA after cycling: NR.	Killing above 99.5% after three cycles against *E. coli* and *B. subtilis*. Chitosan, CuO and GO provide the active effect.	Hydrophilic antibacterial coating. Superwetting not demonstrated.	[48]

Abbreviations: CMCS, carboxymethyl chitosan; TPU, thermoplastic polyurethane; CMC, carboxymethyl cellulose; WCA, water contact angle; UWOCA, underwater oil contact angle; CFU, colony-forming unit; MRSA, methicillin-resistant *Staphylococcus aureus*; CTS, chitosan; CTS-CHO, aldehyde-modified chitosan; LbL, layer-by-layer; PLA, poly(lactic acid); MFC, microfibrillated cellulose; GO, graphene oxide; NR, not reported or not confirmed in the accessible article. Captive bubble and sessile droplet angles are not directly comparable. On porous materials, rapid droplet loss may reflect absorption rather than surface spreading. Conditioning or durability evidence denotes a defined chemical, biological or mechanical exposure. Paired testing requires wetting or hydration and the bacterial endpoint to be evaluated after the same conditioning protocol using batch-matched specimens. A quantitative bacterial endpoint requires a defined organism and exposure period together with a numerical adhesion, viability or biofilm outcome. References [32] and [33] are retained as non-biomedical wetting/materials benchmarks; the absence of biomedical bacterial endpoints is not considered a limitation of their original studies, but these data are not used as evidence of biomedical antibacterial performance. A complete test sequence requires quantitative wetting, conditioning or durability, and a bacterial endpoint using matched specimens from the same preparation batch subjected to the same conditioning protocol.

Table 1 shows that architecture predicts the evidence gap better than polymer identity. Bulk swelling did not establish a stable surface hydration state. The polysaccharide must control water at the exposed interface, and added components must address a measured failure such as wear, protein masking or insufficient killing.

4. Hydrated interfaces and active antibacterial mechanisms

Within the systems reviewed here, hydration was associated with reduced adsorption and attachment, but bactericidal activity was not established for hydration alone [28,45]. Cationic groups, released agents, metals and light-activated phases provide active treatment. These functions require separate evidence because their expected bacterial endpoints and mechanism-specific controls are different.

4.1. Hydration-mediated resistance to adhesion

A hydrated surface limits the close contact needed for protein adsorption and bacterial attachment. Hydrophilic or zwitterionic chains increase the energy required to remove interfacial water and also create steric resistance. The expected result is lower adsorption and attachment; any accompanying loss of bacterial viability requires separate attribution [7,11].

Evidence for this mechanism requires a retained hydration or adsorption measurement after conditioning rather than rapid droplet loss alone.

Reported polysaccharide examples include zwitterionic carboxymethyl chitosan and dextran. The carboxymethyl chitosan coating reduced protein and platelet interactions and limited biofilm development against S. aureus and E. coli [28]. However, wetting and bacterial outcomes were not paired after the reported friction test. A zwitterionic dextran dressing reduced protein adsorption and bacterial attachment while supporting fibroblasts [45]. Neither study used swelling as a substitute for surface hydration.

Protein adsorption precedes bacterial attachment but is not a quantitative surrogate for it. The adsorbed layer changes the interfacial chemistry and receptor environment presented to bacteria, whereas attachment also depends on bacterial surface properties and hydrodynamic conditions [1,8–10,53]. Total protein adsorption can therefore describe conditioning of the interface, but anti-adhesion must be demonstrated by direct bacterial attachment measurements after the same conditioning exposure.

Catheter, poly(ethylene glycol) (PEG)-textured and zwitterionic model surfaces further show that antifouling behavior can change after exposure to urine, proteins or host cells, making the conditioned rather than pristine interface the relevant comparison [53–55]. These systems are included only to define relevant conditioning tests.

Hydration-mediated protection is most relevant before stable bacterial attachment. Once an extracellular-matrix-rich biofilm is established, retained hydration does not demonstrate removal or killing of the existing community; claims of mature-biofilm control require testing against a preformed biofilm, with an independently validated active treatment when killing or disruption is intended [3,4,26].

To test a hydration contribution, compare interfaces with closely matched charge, topography, coating coverage and active-component exposure but different retained hydration. Report residual differences because changing hydration may also change polymer conformation or surface chemistry. Apply the same conditioning and evaluate attachment separately from viability. Such comparisons support causal attribution only to the extent that competing explanations are controlled.

4.2. Contact-active antibacterial interfaces

Contact-active polysaccharides use protonated or permanent cationic groups to damage bacterial envelopes. Activity persists only while those groups remain exposed. Proteins and dead cells can mask them. Excess charge can also increase fouling and mammalian cell injury. A hydrated outer layer can reduce masking, but it must not block contact with the active region.

A neutral or zwitterionic outer domain can cover an immobilized cationic region. To verify this arrangement, surface composition, hydrated thickness and active group accessibility must be measured before and after protein exposure. These data distinguish loss of hydration from loss of contact activity.

Quaternary ammonium pullulan disrupted bacterial membranes and depolarized S. aureus. Infected wound experiments also showed disinfection [56]. A photocrosslinked cationic dextran hydrogel killed multidrug resistant bacteria and reduced burden in a murine burn model [57]. These results establish active killing. Chitosan and chitosan with dextran gels have similar short-term uses, but their active dose depends on molecular mass and degree of substitution [30,31].

Hydrated contact-active model coatings show that wetting and killing can coexist [58,59]. For polysaccharides, wear may expose a cationic region beneath a neutral surface. Surface spectroscopy and antibacterial tests before and after wear are needed to verify this depth-dependent design.

A causal comparison must keep active group density and exposure constant while changing retained wetting. Attachment, membrane damage and viability must be reported separately.

4.3. Controlled antimicrobial release

Release systems can combine a hydrated surface with an internal drug reservoir. Hydration may reduce initial attachment, while the released agent treats bacteria that reach the material. Burst release, reservoir depletion, protein binding and subinhibitory late exposure are drug delivery failures.

Release and antibacterial tests must use the same fluid and conditioning state. Swelling, adsorption and degradation can change effective dose. A wetting comparison is interpretable only when agent loading and exposure are equivalent between the matched materials.

A bacteria-responsive hydrogel released tobramycin after exposure to P. aeruginosa and treated infected burns [60]. A hyaluronic acid and zwitterionic coating combined reduced attachment, bacteria-triggered gentamicin release and enzyme-driven surface renewal [40]. An oxidized dextran system combined pH-responsive amikacin release with a photosensitizer [46]. In each case, a matched adhesion test is needed before lower colony recovery can be attributed partly to wetting.

Curcumin, rosmarinic acid, food gum and metformin systems show that polysaccharide matrices can carry therapeutic agents [48,61–63]. They are not evidence of superwetting antibacterial action. A complete release dataset includes unloaded matrix and free agent controls, loading, residual mass, concentration over time in protein-containing medium, detection limits, biofilm penetration and host cell response.

A wetting contribution can be tested with chemistry-matched interfaces that have the same drug loading and release profile but different retained wetting. Wetting, surface adhesion and viability must be measured using batch-matched specimens subjected to the same conditioning protocol.

4.4. Metal, photothermal and photodynamic systems

Metal and light-activated phases create a strong attribution problem because they alter both bacteria and the interface. Silver releases ions. ZnO and TiO_2 release ions or generate reactive oxygen species. CuS, Prussian blue, polydopamine and MXene convert light to heat. Metal-organic frameworks (MOFs) can capture bacteria or carry drugs. In a silver-coated nanocellulose membrane, cellulose supported underwater wetting while silver caused killing [33]. ZnO, TiO_2, selenium and related composites require measurements of ion release, leachate toxicity and wetting after conditioning [34,35,41,64].

Leaching, irradiation and washing can change roughness, chemistry and apparent contact angle. Wetting must be measured after treatment. Factorial controls must separate the substrate, polysaccharide layer, active exposure and conditioned wetting state.

A bacteria capturing photothermal hydrogel permits separate control of capture, light dose and temperature [65]. Other composites confirm the need to report the contribution of MOFs, MXene, metals and pigments instead of assigning the full effect to the polysaccharide matrix [43,66,67].

An oxidized dextran system with amikacin and a photosensitizer represents photodynamic treatment in a polysaccharide matrix [46]. A dextran aerogel provides a second wound example [68]. Photodynamic tests need oxygen and reactive oxygen measurements. Photothermal tests need spatial temperature maps and tissue injury thresholds.

Antioxidant activity in dextran-based systems is a separate chemical effect. When dextran is combined with chitosan, photosensitizers, amikacin, copper peroxide or plant antioxidants, killing must be assigned to contact activity, light treatment or released agents [45–48].

Metal and light studies need active agent only, sham light, dark and temperature-matched controls where applicable. Ion dose, irradiance, temperature and reactive oxygen exposure must remain constant when wetting is varied.

4.5. Criteria for combining passive and active functions

A combined system must outperform its individual components. The passive surface must retain hydration after the active phase is added. The combined material must reduce attachment or reach the required bacterial endpoint at a lower active dose than the active-only control. This advantage must persist after biological conditioning, repeated challenge and the main mechanical stress expected during use.

The zwitterionic self renewing coating and the carboxymethyl chitosan coating separate passive and active outcomes, although neither completes the full post-conditioning test sequence [28,40].

Use four factorial groups: hydrated matrix alone, active component alone, combined material and trigger alone. After conditioning, test matched specimens from the same preparation batch and conditioning protocol for wetting, attachment, viability, biofilm, active dose and cytocompatibility. Lower drug dose without retained hydration does not show coupling. Retained hydration without a better bacterial result does not show synergy.

Figure 2 distinguishes antibacterial mechanisms from biofilm outcomes, and Table 2 lists the bacterial endpoints required to validate each strategy alongside its main limitations.

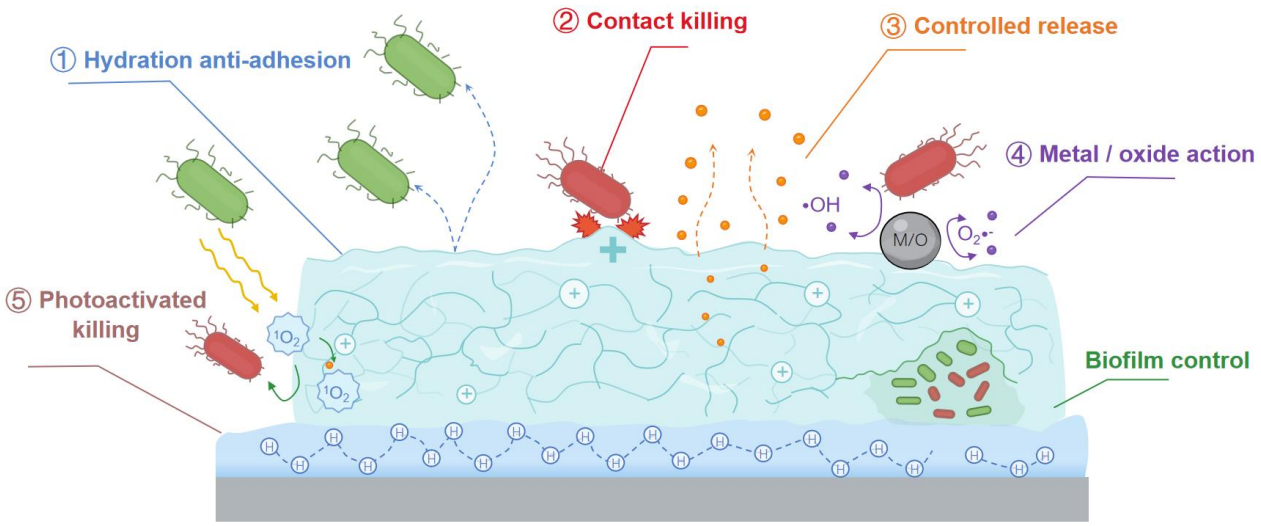


Figure 2. Antibacterial mechanisms and biofilm outcomes of polysaccharide-based superwetting and hydrated interfaces. Five representative mechanisms are illustrated: hydration-layer-mediated resistance to bacterial adhesion, contact-active membrane disruption, controlled release of antibacterial agents, metal- or metal-oxide-mediated antibacterial action, photoactivated production of reactive oxygen species. Biofilm control is evaluated as an outcome, with prevention of biofilm formation distinguished from treatment of an established biofilm [26]. The positively charged groups within the polymer network represent contact-active cationic sites, orange spheres represent released antibacterial agents, and M/O represents antibacterial metals or metal oxides. Photoactivated and metal-mediated processes may generate reactive oxygen species, including singlet oxygen ($^1O_2$), hydroxyl radicals (•OH), and superoxide radicals (O_2•$^-$). The green matrix surrounding clustered bacteria represents the extracellular polymeric substance of a biofilm. Green bacteria represent viable cells, whereas red bacteria represent killed or membrane-damaged cells. These colors are schematic conventions rather than experimental viability measurements. These mechanisms are not mutually exclusive and may operate together within a single interface. This Figure was created by our team using BioGDP software.

Table 2. Antibacterial mechanisms and representative strategies.

Strategy	Mechanism	Representative materials	Advantages	Limitations	Bacterial endpoint for validation	Reference
Hydration resistance	Interfacial water resists displacement	Zwitterionic CMCS or dextran	No released residue and low selection pressure	Fails after conditioning, wear or dehydration	Attached-cell density after defined washing, viability assessed separately	[28,45]
Contact-active polymer	Cationic and hydrophobic groups damage the membrane	Quaternized chitosan or pullulan	No finite drug reservoir	Protein masking and host cell injury	Viable-cell counts and log reduction after defined surface contact, with leachate and no-contact controls	[52]
Responsive release	Delivery triggered by pH, enzymes or bacterial growth	Dextran/amikacin; hydrogel/tobramycin	High local exposure with lower systemic dose	Burst release, reservoir depletion and late exposure below the minimum inhibitory concentration (MIC)	Viable-cell counts and log reduction at a measured released-agent exposure	[46,60]
Metal/oxide	Ion release, reactive oxygen and membrane damage	Ag-cellulose; alginate-chitosan-ZnO	Broad activity from a compact active phase	Leaching, chronic toxicity and discoloration	Viable-cell counts and log reduction at a defined metal/oxide exposure	[33,41]
Photothermal	Localized heating after light absorption	MXene or polydopamine (PDA) composites	Triggered treatment without antibiotics	Limited light penetration and thermal injury	Viable-cell counts and log reduction at a defined light dose and temperature	[39]
Photodynamic	Photosensitized reactive oxygen production	Oxidized dextran/photosensitizer	Oxidative damage at several bacterial targets	Dependence on oxygen and light; oxidation of host tissue	Viable-cell counts and log reduction at a defined light dose and oxygen condition	[42]
Combined hydration and active treatment	Hydration limits attachment; the active phase treats cells that reach the surface	Self-defensive zwitterionic coating	Lower active dose and slower surface passivation	More controls and tighter manufacturing specifications	Attached-cell density and viable-cell counts relative to matched single-function controls	[36]

Abbreviations: CMCS, carboxymethyl chitosan; Ag, silver; ZnO, zinc oxide; MXene, transition-metal carbide or nitride; PDA, polydopamine; MIC, minimum inhibitory concentration. The endpoint column specifies validation requirements rather than a uniform set of measurements reported in every cited study. Viability measurements distinguish surface-associated and suspended bacteria and account for recovery efficiency and detection limits. Biofilm control is an outcome, not an independent mechanism. Prevention and treatment of an established biofilm require separate assays with distinct structural and viable-cell endpoints [26].

A combined material meets the proposed criterion only when retained hydration and controlled active exposure outperform matched single-component controls after relevant conditioning.

5. Application-specific performance requirements

Design targets differ by application. Wounds require exudate handling and short-term conformal contact. Catheters and implants require thin coatings that retain hydration under flow and friction. Porous barriers require controlled transport without bacterial retention, while scaffolds must also support host cell entry.

5.1. Wound dressings

A wound dressing needs lateral exudate spreading, controlled absorption and retained hydration against tissue. Maceration, drying, cohesive failure and traumatic removal end performance. Measure bacterial adhesion after exudate conditioning, viable burden and mature biofilm over the intended wear period. Infected and diabetic wounds usually need an active antibacterial component in addition to passive hydration.

Published dressings combine adhesion, conductivity, self-healing, biofilm treatment and responsive release [42,69,70]. Their relevance depends on measured exudate handling and wet mechanical stability. Dynamic bond systems improve conformity but can creep, while strong tissue adhesion can complicate removal [38,39,71,72]. Immune, vascular and remodeling outcomes do not replace conditioned wetting and antibacterial tests [68,73–76].

Increasing crosslink density can improve wet integrity, but its effects on hemostasis, adhesion, spreading and drug diffusion depend on network chemistry and must be measured [42]. Drying-induced hornification can limit rehydration of bacterial cellulose [77]; compare matched never-dried and dried–rewetted specimens for liquid transport, hydrated thickness and bacterial outcomes. For swelling matrices, follow dimensional changes and active-agent release over the intended wear interval [78]. Wet retentive wound networks show service stability but do not show that hydration caused killing [42,73].

Dark photothermal phases can prevent visual inspection of a wound. A skin-adaptive dressing shows how mild heating can be limited for wound use [79]. Local thermal exposure should therefore be evaluated together with the antibacterial endpoint rather than inferred from the presence of a photothermal phase.

5.2. Catheters and implants

A superhydrophilic layer that detaches during catheter insertion has no protective value. Catheters and implants need a thin hydrated coating that survives insertion, flow and friction. For calcium-crosslinked alginate, ion exchange can weaken the network [78]; measure matrix retention, hydration and active-agent exposure together with attached viable cells and biofilm in serum, artificial urine or blood analogue, as appropriate. For enzyme-responsive hyaluronic-acid-containing coatings, degradation may renew the surface [40]; assess residual coverage, release and bacterial recolonization over repeated challenges. Protein masking, coating defects, abrasion, encrustation and delamination remain relevant failures. Add thrombosis, encrustation and host-cell competition when relevant.

A biodegradable superhydrophilic ureteral stent provides a nonpolysaccharide benchmark for wetting, antibacterial activity and degradation [80]. Polysaccharide-containing stent coatings use different chemistry and must be tested under their own service conditions [81]. Implant coatings must also permit host cell integration, so indefinite broad cell repellence is undesirable [82]. For tissue-integrating implants, bacterial colonization and host-cell attachment compete for the same interface—the "race for the surface" [1,82]. The relevant target is therefore selective surface occupation: suppress bacterial colonization without preventing the host-cell attachment required for integration, and evaluate both responses on the same conditioned interface.

Zn-doped or TiO_2 implant coatings can improve antibacterial activity and wear resistance [83,84]. Wear and biological aging can reduce activity on implant coatings [83–85]. A polysaccharide overlayer must not block the active phase or hinder osseointegration.

5.3. Porous membranes and fibrous barriers

Porous membranes and fibrous barriers must maintain capillary transport or underwater repellence without redistributing contaminated fluid. Pore blockage, fiber shedding, delamination and loss of wetting during flow are relevant failures. The same pores can also protect bacteria from shear. Attachment depends on pore or feature size, orientation, bacterial shape and conditioning medium [86,87]. Viable cells must be recovered from both the surface and pores under flow.

A layered pin site dressing separated bacterial blocking from exudate absorption and placed antimicrobial activity in a distinct layer [88]. This architecture gives each layer a measurable role. Translation still requires tests for delamination, edge leakage and shrinkage after sterilization.

5.4. Regenerative scaffolds

Regenerative scaffolds must retain water and permit nutrient transport, host cell adhesion and tissue integration. Excess cell repellence, unstable degradation, inaccessible pores and bacterial retention are major failures. Bacterial adhesion and viability must be measured together with inflammatory response and tissue integration.

Bacterial cellulose reinforcement and chemical crosslinking can improve wet integrity, while added active phases address infection [64,89,90]. Comparisons require the same bacterial strain, inoculum, wetting protocol and host cell endpoint.

5.5. Other application environments and cross-application constraints

Oral, ocular, wearable and hemostatic materials operate in different fluids and geometries. The salt composition of application fluids can also alter the phase state of specific polysaccharide derivatives. Methylcellulose provides a materials benchmark for salt-dependent gelation and phase separation [91]. For formulations containing this derivative, assess salting-out by phase-state and surface-coverage measurements at the intended fluid composition and temperature, paired with bacterial endpoints under medium-matched controls. Relevant wetting endpoints include tear film stability, mucosal residence, exudate transport and seal formation. Washout, edge leakage, reduced oxygen transport, optical loss and sensing drift must be tested on the intended geometry.

Select the application before material optimization. High fluid uptake benefits some dressings but can destabilize a catheter coating. Strong wet adhesion can secure a hemostatic seal but injure tissue during removal. Ureteral stent coatings, glucose-responsive cellulose nanoreactors and conductive or nanozyme gels address different problems [36,69,81,92]. Their endpoints cannot be combined. Specify contact duration, fluid, mechanical load, microbial burden, desired host cell interaction, active dose and acceptable residual risk in the target product profile.

Bacterial access routes also differ. Wounds contain bacteria from the environment and infected tissue. Catheter infection can ascend along the outside or develop inside the lumen. Implant contamination can occur during surgery or through later bloodstream spread. Challenge full devices at exposed faces, edges, lumens and connectors. Measure wicking direction because superwetting can spread contaminated fluid.

Match durability testing to the service interval. A daily dressing must remain intact and release cleanly for its wear period. A catheter or ureteral stent needs weeks of hydration, low friction and resistance to thrombus or encrustation. An implant coating may require years of attachment even when its active phase is temporary. Do not extrapolate a 24 h result beyond the tested period.

Begin material selection with four stated variables: service interval, bacterial access route, permitted active exposure and the most likely mechanical or conditioning failure. Retention of antibacterial activity after sterilization does not demonstrate retention of hydration [93]. Differences between material lots can complicate comparisons of interfacial and bacterial outcomes [78]. Residual endotoxin and source-derived proteins can confound attribution of host-response differences to polysaccharide chemistry; alginate purification can also change wettability [78,94]. The cross-application mapping in Section 7 links each polysaccharide-specific failure mode to the evidence link it can invalidate. The entries are proposed verification requirements, not findings demonstrated uniformly across the reviewed studies.

Representative experimental images are summarized in Figure 3 to illustrate the different levels of evidence commonly used in this field. Contact-angle measurements characterize interfacial wetting, whereas fluorescence microscopy addresses surface-associated biofilm formation. Wound photographs and histological staining provide macroscopic and tissue-level repair outcomes, respectively. These measurements are complementary rather than interchangeable.

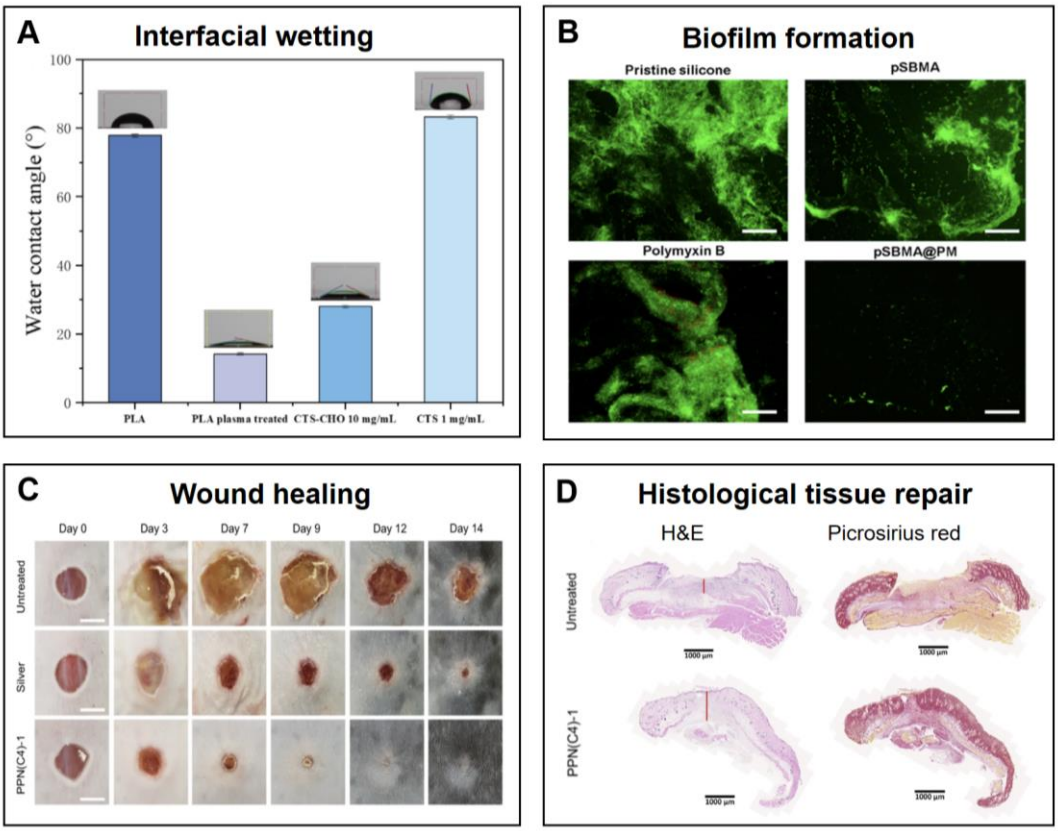


Figure 3. Representative experimental images illustrating distinct validation levels relevant to antibacterial interfaces and wound dressings. **(A)** Representative water contact-angle measurements showing differences in interfacial wetting of PLA-based surfaces; **(B)** Representative fluorescence microscopy images showing *Pseudomonas aeruginosa* biofilm formation on pristine and modified silicone surfaces; **(C)** Representative photographs showing the progression of infected diabetic wound healing under different dressing treatments; **(D)** Representative hematoxylin and eosin (H&E) and picrosirius red staining images showing histological tissue repair. These panels illustrate that interfacial wetting, biofilm formation, macroscopic wound closure, and histological regeneration represent different experimental endpoints and should not be interpreted interchangeably. Panel A was adapted from Wang *et al.* [50], panel B from Ivanova *et al.* [95], and panels C and D from Pranantyo *et al.* [70]. Panels were cropped and rearranged from Wang *et al.* [50] (© 2023 the authors), Ivanova *et al.* [95] (© 2021 the authors), and Pranantyo *et al.* [70] (© 2024 the authors), respectively. The source articles are licensed under the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/).

6. Measurement, comparability and failure analysis

Include a relevant single protein and serum or a mixed protein solution in adsorption tests. Albumin alone does not represent fibrinogen, fibronectin, immunoglobulins or lipoproteins. Fluorescence assays need controls for dye quenching and uptake by the hydrogel. Bicinchoninic acid (BCA) and enzyme-linked immunosorbent assays (ELISA) need complete protein recovery. QCM-D apparent mass includes coupled water. Normalize adsorbed mass with surface roughness and swelling in mind. Use protein

adsorption to characterize interfacial conditioning, and measure bacterial attachment separately after the same conditioning exposure.

Bacterial adhesion requires a defined contact, wash and recovery procedure. CFU counting measures recovered viable cells but depends on detachment efficiency and misses viable but nonculturable cells. Microscopy shows spatial distribution but must distinguish external, attached and embedded cells. LIVE/DEAD staining reports membrane permeability, not reproductive viability [96]. Report inoculum, strain, medium, sample area, contact time, wash or shear and attached cells per area. Measure planktonic and surface-associated survival as separate endpoints.

Biofilm tests need complementary endpoints. Crystal violet measures retained biomass. CFU measures recoverable viable cells. Confocal laser scanning microscopy (CLSM) measures thickness and spatial viability. Extracellular polymeric substance (EPS) stains assess matrix, and metabolic dyes assess activity. Include early and mature time points. Flow cells or microfluidic channels better represent catheters and membranes than static wells [86,87]. Flow studies must report shear rate or stress. Mature biofilm tests also need standardized growth conditions, viable cell recovery and recurrence after treatment [97–99].

Match the biocompatibility cell model to the application. Dressings require fibroblasts and keratinocytes. Vascular devices require endothelial and blood compatibility tests. Bone interfaces require osteoblast lineage or stromal cells. Extract and direct contact assays answer different questions. Blood-contacting materials need hemolysis, platelet, coagulation and complement measurements. Mechanical tests must use hydrated specimens. Coatings require abrasion, flow and friction tests; gels require creep and constrained swelling; fibrous mats require wet tear strength.

Comparison across studies is limited by different strains, media, inocula, geometries, wash methods, light doses and reporting units. A reported 99% reduction may refer to inoculum survival, recovered surface cells or fluorescence. Report absolute counts, normalized change, detection limits, independent replicate number and variance. Table 3 lists a minimum measurement set, criteria for determination and acceptable thresholds, distinguishing wetting classification from application-specific acceptance limits. Report assay maturity and end use relevance separately [100].

Geometry changes water storage, drug loading and bacterial recovery. A hydrogel disk stores more water and drug than a thin coating at the same projected area. A fibrous mat exposes internal pore area that is difficult to quantify. Report dry and hydrated mass, projected area, thickness and accessible volume. Separate external surface cells from cells recovered inside pores. Coating studies also require a substrate control and defect assessment.

Wetting and antibacterial performance change with time. Contact angle can change during droplet spreading, chain rearrangement and leaching. Release activity can peak during the initial burst, while contact active groups can later become masked. At minimum, test the same batch in fresh, conditioned and aged states. Each state requires wetting, protein adsorption, bacterial attachment and viability.

Biological outcomes must be paired with active component exposure. Metal systems need cumulative and time-resolved release in relevant media. Photothermal systems need spatial temperature maps. Photodynamic systems need reactive oxygen and oxygen consumption. Drug systems need mass balance and retained potency. Dextran fluorescent sensors for Ag nanoparticles show how a matrix can report active component distribution [101]. The signal still requires calibration against absolute concentration and biological effect.

Statistical analysis must follow the sampling hierarchy. A preparation batch is defined here as specimens produced in one continuous synthesis, coating or fabrication run using the same formulation and processing conditions. For comparative screening, use at least three independent preparation batches and, where feasible, at least three independently conditioned specimens per group within each batch. Several images from one specimen are not independent replicates. Several droplets on one coating do not establish batch reproducibility. Report synthesis batches, specimens per batch and fields or droplets per specimen. When subsamples are retained in the analysis, use a nested or mixed-effects model to account for batch and specimen levels. Report effect sizes, confidence intervals and assay detection limits when colony counts approach zero [102].

Figure 4 places the measurements in sequence. Wetting is tested after biological conditioning. Adhesion is then separated from killing and biofilm response. Sterilization, storage and mechanical use are applied before the final paired measurements.

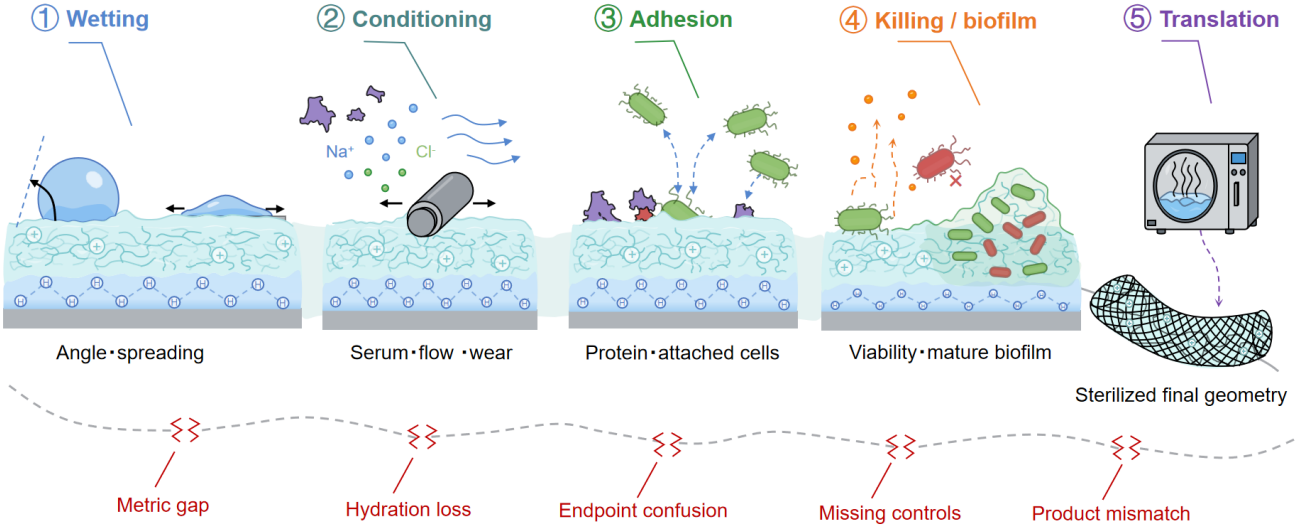


Figure 4. Linked evidence chain for evaluating polysaccharide-based superwetting and hydrated antibacterial interfaces. A rigorous evaluation should connect five sequential stages: wetting characterization, interfacial conditioning, microbial adhesion, antibacterial and antibiofilm efficacy, and translational validation. Wetting measurements should extend beyond contact angle to include spreading and liquid uptake. Interfacial stability should then be assessed in application-relevant biological fluids and under hydrodynamic exposure, mechanical wear, and sterilization. Subsequent tests should distinguish the adsorption of organic conditioning layers from bacterial attachment and should separately quantify cell viability, biofilm biomass, and mature biofilm formation. Translational evaluation should consider sterilization, storage, functional retention, and the geometry of the final device, implant, scaffold, or dressing. The broken grey pathway highlights common discontinuities in current studies, including metric gaps, hydration loss, endpoint confusion, inadequate controls, and mismatch between laboratory specimens and final products. Green bacteria represent viable cells, whereas red bacteria represent killed or damaged cells. Translation should proceed only when the complete evidence chain remains connected. This Figure was created by our team using BioGDP software.

Table 3. Evaluation methods and unresolved problems.

Performance parameter	Common method	Reported indicator	Major limitation	Recommended improvement	Criteria for determination	Acceptable thresholds
Water contact angle	Sessile droplet plus advancing and receding angles	Angle and hysteresis over time	Absorption and roughness change the apparent angle	Report droplet volume, acquisition time and the conditioned state	Angle–time response at a defined material state, with uptake excluded as the dominant response	Hydrophilic: WCA < 90°; superhydrophilic: WCA ≤ 10° or independently verified complete surface spreading
Spreading time	Video of spreading and absorption	Time to defined area or disappearance	Droplet loss combines capillary uptake and surface wetting	Measure absorbed mass, area and sample thickness	Time-resolved surface-film area, residual external volume and uptake, classified as spreading, uptake, mixed or unresolved behavior	No universal time or volume-loss cutoff; classification within the measurement resolution
Underwater oil wetting	Oil droplet on a water-conditioned surface	Oil angle and adhesion force	Oil identity and prehydration differ between studies	Report oil, immersion time, droplet volume and temperature	Oil angle after defined prehydration, with separate force or sliding measurements for low-adhesion claims	UWOCA ≥ 150° for the specified oil and conditions; a separate force or sliding limit for low adhesion
Hydration stability	Differential scanning calorimetry (DSC), nuclear magnetic resonance (NMR) or QCM-D after aging	Bound water, retained mass and dissipation	No method captures every hydration component	Combine molecular water data with wetting after serum and flow	Method-specific hydration measurements before and after defined conditioning or aging	Minimum retained hydration after the intended exposure
Protein adsorption	Fluorescence, BCA, ELISA or QCM-D	Recovered mass or signal per area	Bovine serum albumin (BSA) alone misses competitive adsorption	Add serum or mixed proteins and recovery controls	Area-normalized adsorbed mass under matched fluid and exposure conditions, with background and recovery controls	Maximum adsorbed mass per area or minimum reduction relative to a specified control
Bacterial adhesion	CFU recovery, CLSM, scanning electron microscopy (SEM)	Recovered attached viable cells per area	Wash and detachment efficiency control the result	Report shear, wash, attached cells, dead cells and detached cells	Attached-cell density after matched contact, washing and recovery, evaluated separately from viability	Maximum attached-cell density or minimum attachment reduction under the intended conditions
Antibacterial activity	Colony count and growth kinetics	Absolute CFU and log viability reduction	Planktonic killing does not measure surface adhesion	Report surface and suspension CFU plus detection limits	Viable-cell reduction relative to a matched control, reported separately for the surface and suspension with stated detection limits	Minimum log reduction for the specified test compartment, exposure and intended use

Table 3. *Cont.*

Performance parameter	Common method	Reported indicator	Major limitation	Recommended improvement	Criteria for determination	Acceptable thresholds
LIVE/DEAD staining	Fluorescence microscopy	Positive area or cell ratio	Membrane permeability does not equal culturability	Calibrate with CFU and use blinded image sampling	Membrane-permeability staining assessed alongside an independent viable-cell endpoint	No standalone killing threshold from staining; confirmation by a viable-cell endpoint
Biofilm	Crystal violet, CFU, CLSM, EPS stains	Biomass, viable cells, thickness and matrix	These endpoints measure different biofilm properties	Include early and mature biofilm plus recurrence	Paired structural and viable-cell endpoints in prevention or established-biofilm treatment assays	Prevention- or treatment-specific limits, with regrowth assessment for eradication claims
Flow performance	Flow cell or microfluidic device	Cells retained or detached under known shear	Flat coupons omit device edges and connections	Use the intended fluid and geometry with repeated inoculation	Attachment or biofilm response under defined shear, fluid, exposure time and intended geometry	Attachment or biofilm limits after the application-relevant flow challenge
Biocompatibility	Direct contact, extract assays and blood tests	Cell viability, hemolysis and coagulation	Short extracts can miss late degradation products	Use relevant cells, repeated extracts and tests after activation	Application-relevant cell, extract and blood-test results, matched to tissue contact, exposure duration and activation state where applicable	Assay-specific biological safety limits for the intended contact and exposure duration
Durability	Wet wear, friction, fatigue and sterilization	Retained mass, wetting and biological activity	Fresh specimens overestimate service performance	Match the test interval to use and measure both retained functions	Structural, wetting or hydration, and bacterial performance after defined wear, sterilization and aging	Maximum material loss and minimum retained interfacial and bacterial performance over the intended service interval

Abbreviations: DSC, differential scanning calorimetry; NMR, nuclear magnetic resonance; QCM-D, quartz crystal microbalance with dissipation monitoring; BCA, bicinchoninic acid assay; ELISA, enzyme-linked immunosorbent assay; BSA, bovine serum albumin; CFU, colony-forming unit; CLSM, confocal laser scanning microscopy; EPS, extracellular polymeric substances; SEM, scanning electron microscopy. Where no universal cutoff is established, application-specific acceptance limits should be prespecified for the intended use and test conditions. Wetting boundaries classify an interfacial state; they are not antibacterial acceptance criteria. For each application-dependent limit, report the numerical value, reference control, exposure duration and justification. A value within measurement uncertainty of a wetting boundary should be treated as borderline.

Matched controls and specimens from the same preparation batch and conditioning protocol can link wetting to bacterial outcomes. Cross-study ranking requires matched protocols, recovery methods, dose and aging conditions. Report absolute results, detection limits and retained performance at each test stage.

7. Testable design and translation criteria

Use quantitative wetting terms only when their operational criteria are met. A droplet that disappears through absorption should be reported as liquid uptake rather than used alone to support a superhydrophilic claim. Hydration-based antifouling requires low adsorption after biological conditioning. Claims about bacterial adhesion, viability or biofilm control require the corresponding experimental results.

Use protein preadsorption as a routine stress test. Fibrinogen, lipoproteins and extracellular matrix proteins can mask a surface that is superhydrophilic in water. Compare pristine, serum conditioned and bacteria-conditioned specimens by dynamic wetting, spectroscopy and adhesion under flow. Model brush coatings already show that protein and bacterial resistance can coexist with macrophage and osteoblast responses [103].

Hydration must survive salt, protein exposure, deformation and aging. Crosslinking reduces erosion but can restrict chain mobility and bound water. Reinforcement improves wet strength but can close pores or expose hydrophobic particles. A useful stability specification includes retained bound water, polymer mass, contact angle hysteresis, protein resistance and wet mechanics after defined aging. Calibrate accelerated immersion against real-time flow and wear.

Drug release studies often report the initial curve but omit residual drug and late antibacterial exposure. Report loading efficiency, cumulative released mass, residual mass, local concentration relative to MIC or biofilm eradication concentration and potency after release. Responsive dextran and bacteria-triggered systems also need repeated trigger cycles and resistance selection tests [46,60].

Use static single-species assays for initial screening of catheter, implant and chronic wound materials. Add flow, host proteins, mixed species and repeated inoculation in later tests. Measure attachment, detachment, viable cells, biomass, matrix and recurrence. Full device tests must include edges, defects, lumens and connectors.

Animal and clinical evidence remains limited. Murine wound closure includes more contraction than human healing and can overstate reepithelialization effects [104]. Catheter and implant studies need indwelling models with motion, flow and host-cell competition. Practical endpoints include painless dressing removal, coating lubricity, transparency, shelf life and deployment.

Test manufacturing variables during development. Molecular mass, degree of substitution and biological source vary between polysaccharide batches. Sterilization can depolymerize chains, change crosslink density, oxidize catechols, aggregate particles and alter wetting [105]. Gamma irradiation can induce chain scission or network reorganization; in alginate/gelatin hydrogel macrospheres, 25 kGy irradiation reduced water absorption and accelerated degradation but retained vancomycin release and antibacterial activity [93]. Steam autoclaving can also alter swelling and rheology: a hyaluronic acid hydrogel required optimization of temperature and exposure time to retain its material properties after sterilization [106]. Ethylene oxide avoids high-temperature treatment but requires control of residual sterilant and verification that swelling and interfacial properties are retained [105]. Compare wetting, mechanics, release, adhesion and biological activity before and after sterilization.

Shelf-life aging introduces an additional source of functional drift after sterilization. Storage temperature and humidity, packaging conditions and the rehydration procedure should therefore be defined. During shelf-life aging, chain degradation or network relaxation can change water retention, mechanics and active-agent release, while dynamic networks may continue to evolve through bond exchange [106,107]. In steam-sterilized hyaluronic acid hydrogel, material stability over three months depended on storage temperature, indicating that properties measured immediately after sterilization did not necessarily persist during storage [106]. Critical wetting or hydration, mechanical, release and bacterial measurements should therefore be repeated at predefined shelf-life intervals.

A four stage test sequence is proposed. Stage 1 measures composition, surface enrichment, bound water, spreading and buffer stability. Stage 2 adds mixed proteins, relevant biological fluid, bacterial adhesion, viability and early biofilm under defined shear. Stage 3 adds deformation, friction, repeated inoculation, active agent depletion, sterilization and storage aging. Stage 4 tests the intended device geometry with the relevant host response. Redesign after any failure of a predefined application-critical criterion before continuing.

Use the same synthesis batches at all four stages. Use a predefined sample matrix to assign specimens to wetting, conditioning and bacterial tests without mixing unrelated batches. Set acceptance limits before application testing. Non-negotiable limits should include biological safety, minimum retained interfacial function, mechanical integrity, permitted active exposure and the bacterial endpoint required for the intended use. Failure of any non-negotiable limit stops progression. The claim must also follow the failed evidence link: retained antibacterial activity after loss of wetting can support antibacterial activity but not hydration-mediated protection, whereas retained hydration without the required bacterial endpoint does not support antibacterial protection. This design identifies whether failure came from hydration loss, active dose, mechanical damage or an unsuitable model.

Under the U.S. Food and Drug Administration (FDA) framework, an antibiotic-releasing hydrogel may be a combination product; its lead review center is assigned according to the primary mode of action [108]. This rule concerns combination-product assignment and does not by itself establish the classification of a nonreleasing coating or a photoactivated nanoparticle system. Each added component creates specifications for identity, purity, loading, distribution, release and degradation. For other jurisdictions, product classification and submission requirements must be checked with the relevant regulator rather than inferred from the FDA pathway.

Raw material control is essential for polysaccharides. Chitosan deacetylation, alginate block composition, cellulose fibril size, hyaluronic acid molecular mass and dextran branching vary with source and processing. Endotoxin, protein and mineral impurities can change inflammation and apparent antibacterial activity. Incoming specifications must cover identity, molecular distribution, substitution, bioburden and endotoxin. A supplier or material-lot change should trigger a documented assessment of hydration, mechanics and bacterial performance, with requalification proportionate to its potential effect on critical functions. For pharmaceutical development within the scope of the International Council for Harmonisation (ICH) Q8(R2), assess source, molecular distribution and substitution as potentially critical material attributes, with criticality justified by their impact on drug-product quality [109]; this guideline is not a general requirement for device-only products.

Set performance limits before testing. Relevant limits include adsorbed protein, attached cells per area, log reduction, coating loss, hemolysis and cytotoxicity. The limits will differ by application and

contact duration. Trade-offs should be resolved hierarchically: biological safety and intended-use failure limits are non-negotiable; among materials that meet them, retention of the mechanism-defining function over the service interval takes priority over the largest initial response. A durable surface with moderate adhesion reduction may be more useful than a fragile surface with a high initial result. For medical-device biological safety, use ISO 10993-1:2025 to organize a biological risk evaluation based on material characterization, the nature and duration of contact, and existing evidence; identify additional testing from the remaining risks [110]. Confirm the edition and extent of recognition accepted by the target regulator, together with any applicable transition arrangements. Publication of an ISO edition does not establish identical regulatory recognition in all jurisdictions. Biological safety evaluation also does not validate an antibacterial efficacy claim. To further highlight the challenges associated with different polysaccharide-based systems, Table 4 summarizes the polysaccharide-specific failure modes and the corresponding evidence needed to address these limitations.

Table 4. Polysaccharide-specific failure modes and the evidence needed to resolve them.

Failure mode	Evidence gap	Required paired evidence	Interpretation limit
Salting-out [91]	Interfacial state in the intended fluid	For susceptible derivatives, measure phase state, surface coverage and retained hydration alongside bacterial attachment in medium-matched controls.	Salt-driven phase behavior is formulation-specific; do not generalize from methylcellulose to all polysaccharides.
Ion exchange [78]	Persistence of ionic networks	For calcium alginate, assess network retention and hydrated dimensions together with active-agent release and bacterial outcomes after relevant ionic exposure.	A changed bacterial result may reflect erosion or altered dose rather than hydration.
Enzymatic degradation [40]	Persistence *versus* surface renewal	Relate residual coating coverage and hydration to released-agent exposure and recolonization during degradation.	Surface renewal and loss of coverage require separate interpretation.
Dehydration [77]	Recovery of the hydrated interface	Compare never-dried and dried–rewetted cellulose for transport, hydrated thickness, attachment and viability under matched conditions.	Water uptake alone does not establish recovery of the original interfacial state.
Swelling [78]	Surface geometry and exposure during use	Follow hydrated dimensions, integrity and agent release together with attachment and viability over the intended service interval.	Bulk swelling cannot substitute for surface hydration or effective antibacterial exposure.
Sterilization [93,105,106]	Retention of both passive and active functions	Pair molecular or network changes with post-sterilization wetting/hydration, mechanics, release and bacterial outcomes.	Retained killing alone does not demonstrate retained hydration.
Material-lot variation [78]	Reproducibility of the structure–function relation	Characterize source-dependent molecular distribution and relevant composition or substitution, then compare retained hydration and bacterial outcomes across lots.	Several specimens from one material lot do not establish lot-to-lot reproducibility.
Endotoxin and protein impurities [78,94]	Attribution of interfacial and host responses	Quantify relevant impurities and assay interference; compare purification-related changes in wettability, adsorption, bacterial and host responses.	Separate polymer chemistry from contamination and from changes introduced by purification.

The cited examples establish material-specific concerns; the paired measurements are recommendations of this review. Select the challenge and acceptance limits for the formulation and intended application.

Define the wetting measurement. Repeat it after conditioning. Measure attachment, killing and biofilm separately. Quantify active exposure. Test the final geometry after sterilization. Advance a

material only when it meets the predefined application limits. Renewable origin and a long component list do not predict clinical performance.

8. Conclusions

Across the representative studies reviewed, the main evidence gap was the absence of paired wetting and bacterial tests after biological conditioning.

Causal testing requires closely matched interfaces that differ in retained wetting or hydration, with residual differences in chemistry, topography and active exposure explicitly assessed. Test matched specimens from the same preparation batches for wetting, hydration, attached bacteria, viability and biofilm. Both wetting and bacterial performance must be reassessed after protein exposure, mechanical aging, sterilization and under intended- use condition.

Future studies need five linked results: material architecture, quantitative wetting, retained wetting after conditioning, a mechanism-specific bacterial endpoint and performance on the intended geometry. Only this paired sequence can show whether the hydrated interface contributes to antibacterial protection during use.

Declaration of generative AI and AI-assisted technologies

During the preparation of this manuscript, the authors used ChatGPT (OpenAI) to assist with language editing. Figures 1, 2 and 4 were created by our team using BioGDP software. The authors reviewed and edited the content and take full responsibility for the content of the manuscript.

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Authors' contribution

Conceptualization, investigation, data curation, writing—original draft, and visualization, L.L. and F.X.; investigation, formal analysis, data curation, and visualization. H.S.; methodology, validation, formal analysis, and writing—review and editing, S.X.; conceptualization, methodology, supervision, and writing—review and editing, Y.D.; conceptualization, methodology, supervision, project administration, funding acquisition, and writing—review and editing, S.H. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

The authors declare no conflicts of interest.

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