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Mechanisms of Bioadhesion: Aquatic Bio-Inspired Strategies and Biomedical Applications

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Abstract. Bioadhesives, particularly those inspired by aquatic organisms like octopuses and mussels, have become key innovations in biomedical engineering, addressing the core challenge of achieving strong adhesion in wet physiological environments. These materials achieve effective adhesion to biological tissues through a complex interplay of intermolecular forces, chemical reactions, and structural adaptability. Studies have shown that aquatic-inspired designs draw on natural mechanisms: octopuses utilize microstructured suction cups to generate negative pressure for mechanical anchoring, while mussels rely on catechol-containing proteins to form covalent and coordination bonds via L-3,4-dihydroxyphenylalanine (DOPA) residues. These mechanisms have driven the development of synthetic formulations, including polydopamine composites and microstructured hydrogels, that enhance wet adhesion through a synergistic combination of chemical and physical interactions. Biomedical applications encompass wound closure, hemostasis, tissue regeneration, and drug delivery, offering minimally invasive alternatives to traditional sutures. Employing a combination of literature review and case analysis, this paper systematically elaborates on the basic mechanisms of bioadhesion, aquatic bio-inspired innovations, and their biomedical applications.Current research focuses on overcoming limitations such as catechol oxidation and mechanical mismatch with dynamic tissues, while also exploring stimuli-responsive and multifunctional designs to expand clinical applications. The fusion of natural inspiration and materials engineering highlights the growing importance of bioadhesives in modern medicine.

Keywords: Bioadhesives, Adhesion ,Mechanisms, Aquatic Bio-inspiration, Catechol Chemistry, Biomedical Applications

1. Introduction

The development of highly effective bioadhesives has had a transformative impact on biomedical practice, providing minimally invasive solutions for wound closure, tissue repair, and drug delivery, and can replace traditional sutures and staples [1]. Unlike traditional adhesives that fail in wet environments, bioadhesives must maintain their functionality in blood, tissue fluids, and dynamic physiological conditions [2]. Their efficacy stems from the exploitation of intermolecular forces, chemical reactions, and structural adaptability, many of which are inspired by natural systems. Aquatic organisms have evolved remarkable adhesion strategies: octopuses use suction cup

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microstructures for mechanical anchoring, while mussels rely on catechol-containing proteins to form chemical bonds underwater [3]. These natural mechanisms guide for the design of synthetic bioadhesives and facilitate the development of materials with enhanced wet adhesion properties. Despite significant progress in recent years, existing research still faces key challenges and gaps: insufficient adhesion stability under strong shear forces and long-term hydration conditions, making it difficult to meet the needs of dynamic tissue repair such as the myocardium and joints; most materials focus on a single adhesion mechanism and lack the systematically research of their cooperation, Issues such as the matching of biocompatibility and degradation rate, and cost control of large-scale production have not yet been fully resolved. The study employs literature review and case analysis to find the basic mechanisms of bioadhesion. It also explores innovative results inspired by aquatic organisms, and evaluates the applications in the biomedical field, focusing on relevant progress and existing challenges. This study provides systematic theoretical guidance for the design of high-performance bioadhesives.

2. Literature review

Bioadhesion relies on the synergistic effects of chemical interactions, physical forces, and structural design to achieve stable adhesion to biological tissues. These mechanisms are highly adaptable to wet environments and address the core challenge of displacing interfacial water to form intimate contacts.

2.1. Chemical bonding

Covalent bonds play a key role in irreversible adhesion, especially in catechol-based systems inspired by mussel foot protein. MFP contains L-3,4-dihydroxyphenylalanine (DOPA), whose catechol groups, upon oxidation, can form covalent crosslinks with amino or thiol groups on tissue surfaces [4]. For example, polydopamine (PDA) coatings that mimic the chemical properties of MFP can form strong covalent bonds with proteins in the skin and internal tissues even in aqueous environments. Coordination bonds can further enhance cohesion. DOPA residues react with metal ions (e.g., Fe^{3+}, Cu^{2+}) to form stable complexes, thereby strengthening the adhesive matrix. Synthetic adhesives such as chitosan-DOPA-Fe^{3+} composites utilize this mechanism, and their shear strength under wet conditions is significantly improved compared to unchelated adhesives [5].

2.2. Non-covalent interactions

Electrostatic forces drive the adhesion of charged polymers to tissue surfaces. Cationic polymers (e.g., chitosan) interact with anionic glycosaminoglycans in tissues through ionic bonds, promoting initial contact [6]. Hydrogen bonds play a complementary role: hydroxyl and amine groups in adhesives form hydrogen bonds with water molecules and tissue proteins, helping to achieve wet adhesion. Hydrophobic interactions and van der Waals forces promote interfacial contact by repelling water molecules. Hydrophobic domains in adhesives (e.g., those in polyurethane-acrylate copolymers) aggregate at the tissue interface, reducing water interference and enhancing van der Waals interactions. Such forces are particularly critical for adhesion to lipid-rich surfaces such as cell membranes.

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2.3. Physical and structural adaptation

Mechanical interlocking driven by micro- and nanostructure design replicates the physical adhesion strategies of aquatic organisms to overcome the limitations of wet environments. For example, the layered structure of the octopus sucker has a layered structure: the glycoprotein coating of the epithelial cell that can reduce the surface tension of water and reduce the interference of interfacial water on the seal [7]. The graded contraction of the muscle cavity (first weak squeezing to drain the liquid, then strong contraction to form negative pressure) can avoid the instantaneous negative pressure causing water to re-infiltrate [8]. This dual mechanism of sealing to displace interfacial water to exploit pressure difference allows it to adhere to smooth substrates (such as rocks) and rough tissues (such as internal organs). Synthetic adhesives mimic this design through microtip arrays and porous structures.

Stimuli-responsive structural changes can further optimize adhesion dynamics. Thermosensitive pNIPAM-based adhesives take advantage of their low critical solution temperature (LCST≈32°C): below the LCST, the polymer becomes hydrophilic and swells, facilitating spreading. Above the LCST (e.g., body temperature), hydrophobic interactions trigger molecular chain aggregation, causing the material to shrink by 40% to 50% [9]. This shrinkage generates local negative pressure, enhancing contact with tissue and increasing adhesion by 2 to 3 times. pH-responsive adhesives (typically carboxyl-functionalized) swell in an acidic wound environment (pH 5.0 to 6.5). This process is driven by protonation of the carboxyl group and increased water absorption, enabling the adhesive to fill irregular wound cavities and improve adhesion by 50% compared to neutral conditions [10]. This adaptability is crucial during the dynamic healing phase, as pH fluctuates during healing due to inflammation and tissue regeneration. These physical and responsive designs work together to enable strong adhesion in diverse biological environments and complement chemical bonding mechanisms.

3. Case study: biomimetic material systems and their adhesion principles

The natural adhesion strategies of aquatic organisms provide a design blueprint for high-performance bioadhesives. Octopuses and mussels in particular offer inspiration for the development of materials that address the unique challenges of wet adhesion.

3.1. Octopus-inspired mechanical adhesives

Octopuses achieve reversible adhesion via suckers featuring hierarchical microstructures: flexible edges form a tight seal, and muscle contraction reduces internal pressure to generate negative pressure. This mechanism has inspired the development of polydimethylsiloxane (PDMS) nano-sucker arrays, which adhere to both and dry surfaces by displacing interfacial water and forming mechanical anchors. A key innovation is the PDMS/pNIPAM smart adhesive, which can regulate adhesion strength by temperature: heating shrinks the pNIPAM, increasing negative pressure and adhesion; cooling reverses the process, facilitating removal [11]. This reversibility functionality is valuable for temporary applications such as wound dressings and sensor fixation. Another octopus-inspired design is based on a polyurethane acrylate (s-PUA) adhesive containing microcavities that trap liquids and generate suction upon compression. This material adhesive exhibits a wet bond strength 3.5 times greater than traditional surgical glue with minimal tissue damage.

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3.2. Mussel-inspired chemical adhesives

Mussel-secreted microglobulin (MFP) contains dopamine (DOPA), which can form a strong bond with the substrate through catechol oxidation and metal chelation. Synthetic analogs (such as dopamine-coupled chitosan) can replicate this chemical reaction [5]. For example, catechol-modified chitosan (CatCS) hydrogels have enhanced mucosal adhesion after cross-linking with genipin, making them suitable for buccal drug delivery.

Nanocomposite adhesives further leverage mussel-inspired chemstry: for exapmle, PLGA-NHS-ALG-DOPA adhesives combine dopamine-mediated tissue adhesion with NHS ester cross-linking, and have a shear strength of 8.2±0.5 kPa on wet porcine skin, which is superior to commercial fibrin glue [12]. Chitin nanocrystal (ChiNC)-enhanced POEC-d adhesives improve wet adhesion and mechanical stability through the synergistic effect of catechol groups and nanofillers [13]. Polydopamine (PDA) nanosheets prepared by layer-by-layer polymerization have multiple adhesive properties and can adhere to a variety of surfaces, promote cell proliferation and resist degradation in harsh environments, making them an ideal choice for tissue engineering scaffolds.

4. Clinical transformation and functional performance

Biomimetic aquatic bioadhesives are widely used in the medical field and can meet the unmet needs in wound care, hemostasis and regenerative medicine.

4.1. Wound closure and hemostasis

In acute trauma, rapid hemostasis and wound closure are crucial for patient survival. The octopus-inspired s-PUA adhesive achieves this need with its microcavity structure: when applied to bleeding tissue, its micron-sized pores capture plasma to form a physical barrier, slowing blood flow and initiating blood clot formation. In a pig liver injury model, this mechanism reduced bleeding time from 12±2 minutes (suture group) to 4.8±0.5 minutes and decreased blood loss by 60%. Its elasticity can adapt to the dynamic movement of internal organs, reducing the risk of rebleeding, which has significant advantages over rigid sutures that may destroy blood clots. The chitosan-dopamine adhesive, inspired by mussels, is particularly valuable in treating platelet deficiency and remain effective even when traditional hemostatic agents due to impaired coagulation cascade. After its catechol groups come into contact with blood, they interact with fibrinogen and platelets, accelerating the formation of a porous fibrin-chitosan membrane. For superficial wounds, catechol-modified 2-octyl cyanoacrylate can enhance wet adhesion while avoid tissue damage caused by sutures. Clinical trials have shown that it can quickly close wounds and reduce scar formation and infection risks.

4.2. Tissue repair and regeneration

Mussel-inspired hydrogels, due to their catechol chemical properties, serve as tissue scaffolds for tissue regeneration by supporting cell infiltration and matrix deposition. For example, catechol-functionalized hyaluronic acid hydrogels promote cranial defect repair through multiple mechanisms: catechol groups form coordination bonds with bone mineral (hydroxyapatite) to anchor the hydrogel, while simultaneously upregulating the expression of vascular endothelial growth factor (VEGF) in local fibroblasts to stimulate angiogenesis..

Elastin adhesives that mimic MFP have shown great promise in cartilage repair by combining mechanical flexibility with biocompatibility. These adhesives can replicate the elasticity of natural

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cartilage (Young's modulus of approximately 0.5-1 MPa) and contain dopamine residues that can bind to chondrocyte surface proteins, promoting cell attachment [5]. In vitro, chondrocytes seeded on these adhesive reached 85% within 21 days, and showed increased glycosaminoglycans (GAGs) production. GAGs are key components of the extracellular matrix of cartilage cells. After 12 weeks of implantation into rabbit knee defects, the GAG content of the adhesive was 2.3 times higher than that of the control group, indicating functional tissue regeneration. Beyond therapeutic applications, the principles of bioadhesion also advance medical device technology.The octopus-inspired microstructured adhesive performs well in non-invasive device fixation, meeting the core requirements of wearable health monitors.

4.3. Drug and cell delivery

Bioadhesive materials can adhere to tissues for a long time, providing an ideal carrier for local drug delivery, thereby reducing systemic side effects. For example, alginate-dopamine hydrogels act on mucosal surfaces through catechol-mediated adhesion and regulate drug release through a porous structure. Such hydrogels loaded with vancomycin release the antibiotic through diffusion and degradation: an initial burst release (20% of the load) kills planktonic bacteria, followed by a sustained release (80% within 7 days) to clear biofilms. In a mouse model of methicillin-resistant Staphylococcus aureus (MRSA) wounds, this release kinetics reduced the bacterial load by 90% within 7 days, with no detectable systemic vancomycin—a stark contrast to intravenous administration, which often causes nephrotoxicity.

pH-responsive mussel adhesives can target the acidic tumor microenvironment (pH 6.0-6.5), which is characteristic of solid cancers. This type of adhesive contains catechol groups and pH-labile bonds: it remains stable and non-adhesive under neutral conditions in healthy tissue; in the acidic tumor environment, the bond hydrolyzes, triggering catechol oxidation and adhesion, while releasing doxorubicin [12].

5. Challenges and future directions

Despite significant progress, biomimetic aquatic bioadhesive materials still face inherent limitations, hindering their transition from laboratory innovation to widespread clinical application. These challenges stem from the complex balance between chemical stability, mechanical functionality, and biocompatibility, requiring targeted engineering solutions.

5.1. Limitations

5.1.1. Chemical stability

Mussel-based adhesives suffer from the instability of catechol groups, particularly L-3,4-dihydroxyphenylalanine (dopamine). In physiological environments, dopamine undergoes spontaneous oxidation to quinone, accelerated by neutral/alkaline pH, metal ions (such as Cu^{2+} and Fe^{3+}), and inflammatory reactive oxygen species (ROS). This oxidation disrupts covalent and metal coordination bonds between tissues, leading to a gradual weakening of adhesion. For example, in a mouse model, the shear strength of a catechol-modified chitosan adhesive decreased by 50% within 72 hours, limiting its long-term application in applications such as bone repair, which require stable adhesion for weeks to months.

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5.1.2. Mechanical mismatch

Mechanical mismatch with the target tissue remains a key obstacle. Dynamic tissues such as the myocardium and lung parenchyma undergo cyclic strain (10%-20% deformation) during physiological activities and require adhesives with high elasticity (Young's modulus <1 MPa) and fatigue resistance. However, many synthetic adhesives designed for strength are rigid (Young's modulus > 5 MPa), which can easily lead to interfacial failure and leakage [2]. Conversely, overly flexible natural adhesives (such as alginate hydrogels) lack the compressive strength (>50 MPa) required for load-bearing applications such as vertebral fusion, which can cause implant loosening [13]. This contradiction highlights the need for adjustable mechanical properties to adapt to specific tissue microenvironments.

5.1.3. Biocompatibility risk

Biocompatibility issues between synthetic and natural preparations remain. Synthetic adhesives represented by cyanoacrylates produce small molecular products such as formaldehyde and cyanoacetate during degradation. They can activate the NLRP3 inflammasome in macrophages and induce chronic inflammation reactions. The incident of such inflammation is as high as 30% of clinical cases using 2-octylcyanoacrylate [14]. The other is the biosafety risk of the material itself. Fibrin glue derived from human plasma can trigger alloimmune reactions in 2%-5% of patients with fibrinogen antibodies. Furthermore, the long-term foreign body reaction of non-degradable components (such as the PDMS in octopus-inspired microstructures) can lead to fiber encapsulation and compromise tissue integration.

5.2. Future innovations

5.2.1. Multifunctional composite

Multifunctional design strategies have the potential to overcome these limitations by integrating complementary properties. For example, antimicrobial adhesives combine catechol chemistry with silver nanoparticles or nitric oxide-releasing systems maintaining wet adhesion while inhibiting infection and promoting angiogenesis. Conductive composites, such as polydopamine (PDA)-graphene hydrogels, further expand their functionality: their electrical conductivity (1-5 S/m) matches that of cardiac tissue, enabling synchronized contractions when applied as myocardial patches, while the catechol groups of PDA ensure strong adhesion to the cardiac surface.

5.2.2. Stimulus response

Stimuli-responsive systems enable spatiotemporal control of adhesion, improving application precision and mechanical regulation. Thermosensitive polyethylene glycol-polycaprolactone (PEG-PCL) copolymers utilize a low critical solution temperature (LCST) near 37°C: below the LCST, they are viscous liquids, making them easy to manipulate; at body temperature, they undergo a phase transition to form a cross-linked gel with adjustable strength (2-10 MPa), making them suitable for laparoscopic surgery requiring both compliance and stability. Photosensitive adhesives containing photoinitiators such as eosin Y cross-link within seconds upon irradiation with 450 nm light, allowing surgeons to precisely define bonding boundaries and reduce off-target adhesion in delicate areas such as the eye or vascular and neural bundles.

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5.2.3. Intelligent manufacturing

3D printing technology uses octopus-inspired microstructures to achieve customized repair of irregular wounds. Using stereolithography, arrays of octopus-like suckers (50-100 microns in diameter) can be printed onto a biodegradable PCL substrate, simulating the hierarchical structure of natural suckers. These patient-specific patches match wound morphology based on preoperative imaging, increasing coverage by 40% compared to standard dressings and reducing dead space and fluid accumulation – both key drivers of infection. Clinical trials have shown that 3D printed patches can speed up the healing of diabetic ulcers by 25%, thanks to improved fit and sustained adhesion during wound contraction [7]. These innovations, rooted in a deeper understanding of natural adhesion mechanisms, collectively address the core limitations of current bioadhesives and lay the foundation for their widespread clinical application.

6. Conclusion

Bioadhesives achieve their functions through the dynamic interaction of chemical bonds, intermolecular forces, and structural adaptability, with aquatic organisms providing important inspiration for wet adhesion. Octopus-inspired mechanical design and mussel-derived catechol chemistry have enabled the development of adhesives with excellent physiological performance for applications in wound care, hemostasis, and regeneration. These advancements highlight the transformative potential of aquatic bio-inspiration in addressing the longstanding challenge to achieving robust adhesion in wet physiological environments, thus bridging the gap between natural mechanisms and biomedical innovation.

This study also has certain limitations. First, the research primarily relied on literature review and case studies, lacking original experimental validation of the synergistic effects of multiple mechanisms. The interplay between chemical bonding, physical anchoring, and stimuli-responsiveness was not quantitatively explored; and data on long-term clinical safety and large-scale manufacturing feasibility are scarce.

Future research should prioritize quantifying these mechanisms through in vivo models and in vivo models. Additionally, developing degradable and mechanically adaptable composite materials is needed to address oxidation and mechanical mismatch issues. Optimizing clinical translation strategies (e.g., biocompatibility testing and scalable manufacturing processes) to accelerate the transition from benchtop to bedside.

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