JOURNAL OF PHARMA INSIGHTS AND RESEARCH ISSN NO. 3048-5428

REVIEW ARTICLE

Applications of Oyster-Inspired Biomimetic Bone Adhesive in Orthopedic Surgery

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Publication history: Received on 6th October 2025; Revised on 21st October 2025; Accepted on 24th October 2025

Article DOI: 10.69613/3jhgx960

Abstract: Fracture management has traditionally relied on rigid metallic fixation systems, such as plates and screws, which often necessitate invasive surgical procedures and subsequent operations for hardware removal. Recent advancements in Chinese biomedical engineering have introduced a novel bio-adhesive, designated as Bone-02, which addresses these limitations through biomimetic principles. Developed by researchers at Zhejiang University and Sir Run Run Shaw Hospital, this material mimics the adhesive proteins found in oysters, demonstrating the unique capability to bond bone fragments rapidly within physiological, fluid-rich environments. The synthesis involves complex polymer cross-linking that achieves significant bonding strength and mechanical stability comparable to conventional hardware, with setting times ranging between two to three minutes. Clinical applications involving over 150 patients indicate that this adhesive facilitates minimally invasive repair of comminuted fractures with reduced operative time and the elimination of hardware removal requirements. The material is engineered to be bioabsorbable, degrading synchronously with natural bone regeneration, thereby mitigating long-term foreign body reactions and infection risks. While early clinical translation is promising, the transition from controlled trials to widespread adoption requires extensive longitudinal studies regarding load-bearing efficacy in major skeletal structures. This article presents an analysis of the chemical engineering, mechanical properties, and clinical translation of this specific bone glue, situating it within the broader context of orthopedic innovation and the shift toward bio-integrative surgical solutions.

Keywords: Bone-02; Biomimetic Adhesives; Orthopedic Fixation; Bioabsorbable Polymers; Minimally Invasive Surgery.

1. Introduction

Orthopedic surgery has long been defined by the pursuit of mechanical stability in fracture management. For decades, the gold standard for stabilizing disrupted skeletal structures has been internal fixation using metallic implants, primarily titanium or stainless steel plates, screws, and intramedullary nails. While these devices provide the necessary load-bearing capacity to facilitate union, they are associated with significant biological drawbacks. The rigidity of metal often exceeds that of natural bone, leading to stress shielding—a phenomenon where the bone, relieved of normal physiological stress, becomes osteopenic and prone to refracture [1]. Moreover, the invasive nature of implanting these hardware systems requires extensive soft tissue dissection, which can compromise the vascular supply essential for healing. Perhaps most critically, a significant proportion of patients require a second surgical procedure to remove the hardware due to pain, infection, or implant prominence, thereby doubling the surgical risk and economic burden [2].

In order to overcome these limitations, the field has gradually shifted focus toward bio-integrative solutions. The concept of "bone glue" has existed for decades, yet the practical realization has been hindered by the specific chemical challenges of the physiological environment. Unlike industrial adhesives that function on dry surfaces, orthopedic adhesives must adhere to substrates submerged in blood, interstitial fluid, and lipids. Conventional cyanoacrylates or fibrin glues, while useful for soft tissue, lack the requisite mechanical strength for bone fixation and often exhibit cytotoxicity or poor adhesion in wet environments [3]. The clinical need for a high-strength, biocompatible, and biodegradable adhesive has driven researchers to look beyond synthetic chemistry toward biological systems that have evolved to solve similar engineering problems. Within this context, the development of Bone-02 represents a substantial advancement in the application of biomimetics to trauma surgery. Originating from a collaborative effort between the Zhejiang University School of Medicine and Sir Run Run Shaw Hospital in China, this project exemplifies the integration of advanced material science with clinical necessity [4]. The development team identified that the failure of previous

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bone adhesives was largely due to an inability to displace surface water molecules effectively. By investigating the natural adhesion mechanisms of marine organisms, specifically oysters, they engineered a synthetic polymer capable of robust wet adhesion. This innovation reflects a broader trend in Chinese medical research, which is increasingly characterizing the intersection of traditional natural observation and high-tech polymer engineering to create sustainable, bio-absorbable alternatives to permanent metallic implants [5].

2. Biomimetic Design and Composition

The engineering of Bone-02 is predicated on understanding the molecular strategies employed by marine sessile organisms. Oysters and mussels are capable of adhering firmly to rocks, ship hulls, and other substrates despite the constant presence of saline water, turbulence, and biofilm contaminants. The translation of this biological capability into a clinical product involves a complex synthesis of polymer chemistry and structural engineering.

2.1. Wet Adhesion Mechanisms Inspired from Oyster

The primary barrier to adhesion in a surgical field is the hydration layer—a film of water molecules that coats the surface of the bone, preventing direct contact between the adhesive and the substrate. Synthetic glues typically float on top of this layer, resulting in weak bonds that fail under shear stress. The researchers behind Bone-02 focused on the protein chemistries found in the foot of the oyster, which secretes a specialized adhesive substance [6].

Table 1. Biomimetic Mechanisms

Biological Inspiration (Oyster)	Engineering Challenge	Bone-02 Technological Solution
DOPA Proteins	Adhering to wet, saline surfaces.	Catechol-functionalized polymers displace surface water molecules.
Mineralization	Creating a rock-hard interface.	Incorporation of Metal-Organic Frameworks (ZIF-8) and calcium motifs.
Cross-linking	Rapid hardening in turbulence.	Rapid polymerization kinetics triggered upon mixing components.
Amphiphilicity	Balancing water affinity and repulsion.	Hydrophobic/Hydrophilic domains to wet the surface but repel bulk blood.

2.1.1. The Role of DOPA and Catechol

Central to this adhesive mechanism is the presence of 3,4-dihydroxyphenylalanine (DOPA), an amino acid abundant in marine adhesive proteins. DOPA contains catechol groups that are uniquely capable of displacing water molecules from the surface of inorganic materials. When applied to bone, these catechol functionalities penetrate the hydration layer and form strong hydrogen bonds and coordination bonds with the calcium and phosphate ions in the hydroxyapatite mineral matrix of the bone [7]. This molecular bridging allows the adhesive to establish a "dry" contact patch on a "wet" surface, which is the critical first step in achieving surgical-grade fixation.

2.1.2. Hydrophobic and Hydrophilic Balance

To further enhance this effect, the Bone-02 formulation mimics the oyster's ability to regulate hydrophobicity. The material is designed to be amphiphilic; it possesses hydrophilic components that allow it to flow and wet the surface of the bone, coupled with hydrophobic domains that repel bulk water and facilitate the curing process. This dual nature ensures that the adhesive spreads adequately into the irregularities of the fracture site without being diluted or washed away by the surrounding blood and tissue fluids [8].

2.2. Chemical Synthesis

While the precise commercial formulation of Bone-02 involves proprietary trade secrets, patent literature and related research suggest a sophisticated composite structure. The adhesive is not a simple glue but a reactive system that polymerizes in situ.

2.2.1. Metal-Organic Frameworks and Cross-linking

The structural integrity of Bone-02 is achieved through the incorporation of metal-organic frameworks (MOFs), such as Zeolitic Imidazolate Framework-8 (ZIF-8), combined with L-DOPA grafted polymers, such as polyvinyl alcohol (PVA) or similar biocompatible backbones [9]. The inclusion of ZIF-8 nanoparticles serves multiple functions: it acts as a reinforcing filler to increase the mechanical modulus of the cured glue, and it provides coordination sites for the catechol groups, enhancing the cross-linking density. When the components are mixed, a rapid cross-linking reaction occurs, creating a dense, three-dimensional network that locks the polymer chains together [10].

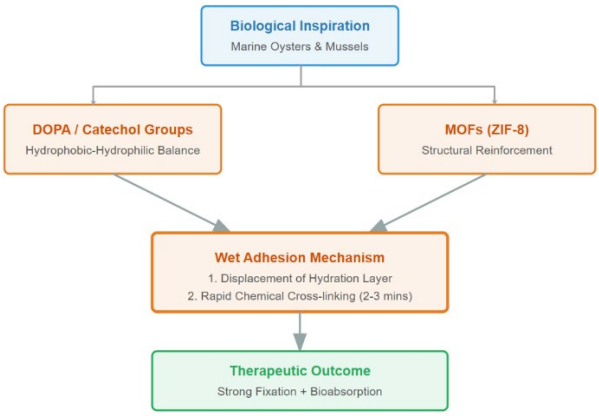

Figure 1. Biomimetic design process for Bone-02

2.2.2. Phase Transition and Setting Kinetics

A critical operational requirement for any surgical adhesive is the control of setting time. If the glue sets too quickly, the surgeon cannot manipulate the bone fragments into alignment; if it sets too slowly, the operation is prolonged, and the reduction may differ. Bone-02 is engineered to undergo a phase transition from a viscous, injectable liquid to a load-bearing solid within approximately two to three minutes [11]. This timeframe is optimized for the surgical workflow, allowing sufficient time for the injection of the material into the fracture gap and the final positioning of bone fragments before the material hardens. The polymerization process is exothermic but controlled to ensure that the heat generated does not cause thermal necrosis to the surrounding bone tissue or periosteum [12].

3. Mechanical Performance

The transition of a biomaterial from the laboratory to the operating theater is contingent upon two critical performance metrics: mechanical reliability under physiological loads and biological compatibility with the host tissue. Bone-02 has been subjected to rigorous physicochemical characterization to ensure that its material properties align with the dynamic requirements of skeletal repair.

3.1. Mechanical Characterization

The primary failure mode of early bone adhesives was an inability to withstand the mechanical forces exerted during early mobilization. Skeletal structures are subjected to complex loading patterns involving compression, tension, torsion, and shear.

3.1.1. Bonding Strength vs. Physiological Loads

Laboratory evaluations of Bone-02 have quantified its adhesive capabilities, revealing a bonding strength exceeding 400 pounds (approximately 1780 Newtons). This magnitude of adhesion is critical for maintaining the reduction of fracture fragments against the pull of muscle contraction and gravity [13]. In terms of specific mechanical moduli, the material exhibits a compressive strength nearing 10 MPa. While this is lower than that of cortical bone (which ranges from 100-200 MPa), it is sufficient to maintain structural integrity in cancellous bone regions and for the fixation of non-weight-bearing fragments where high compressive loads are distributed across a wider surface area [14]. The shear strength is reported at approximately 0.5 MPa. Although this value is modest compared to the shear resistance of a locking plate construct, it is effective for preventing the micromotion of small, comminuted fragments, which is the primary indication for this adhesive [15].

Table 2. Mechanical and Physical Properties

Property	Value / Description	Clinical Significance
Bonding Strength	> 400 lbs (> 1780 N)	Sufficient to resist muscle contraction forces in non-weight bearing extremities.
Compressive Strength	~10 MPa	Adequate for cancellous bone void filling; lower than cortical bone (100-200 MPa).
Shear Strength	~0.5 MPa	Effective for preventing micromotion of small fragments; currently insufficient for major load-bearing shafts.
Setting Time	120 – 180 Seconds	Allows short window for fracture reduction; reduces anesthesia time.
Degradation Profile	~6 Months	Matches the physiological timeline of the bone remodeling phase.

3.1.2. Prevention of Stress Shielding

A distinct biomechanical advantage of Bone-02 over metallic implants is its modulus of elasticity. Traditional titanium or stainless steel implants possess an elastic modulus significantly higher than that of human bone (110 GPa for Ti-6Al-4V vs. 10-30 GPa for cortical bone). This mismatch results in "stress shielding," where the stiff implant absorbs the mechanical load, depriving the bone of the physical stimuli required for remodeling, often leading to localized osteopenia [16]. Bone-02, being a polymeric composite, possesses viscoelastic properties that more closely mimic the natural bone matrix. This allows for physiological load transfer across the fracture site, stimulating osteoblastic activity and promoting stronger callus formation in accordance with Wolff's Law [17].

Table 3. Comparison of Orthopedic Fixation Strategies

Feature	Bone-02 Bio-Adhesive	Metal Implants (Ti/SS)	Traditional Bioadhesives (Fibrin/Cyanoacrylate)
Primary Mechanism	Chemical cross-linking & mineral bonding	Mechanical friction & compression	Surface adhesion (weak)
Invasiveness	Minimally Invasive (Injectable)	Open Surgery (Extensive dissection)	Minimally Invasive
Wet Adhesion	High (Displaces hydration layer)	N/A (Mechanical)	Poor (Fails in blood)
Bioabsorbability	Yes (~6 months)	No (Permanent or requires removal)	Yes (Variable rates)
Stress Shielding	Low (Modulus similar to bone)	High (Stiffer than bone)	N/A (Not load-bearing)
Secondary Surgery	Not Required	Frequently Required (~30-50%)	Not Required
Setting Time	2–3 Minutes	N/A (Immediate fixation upon screw insertion)	Varies (Secs to Mins)

3.2. Biodegradation and Resorption

Unlike permanent metallic hardware, Bone-02 is engineered as a temporary scaffold that is gradually replaced by host tissue. The biodegradation profile is a critical design parameter; if the material degrades too quickly, fixation fails before union; if too slowly, it may impede bone ingrowth.

3.2.1. Metabolic Pathways of Degradation

The polymer matrix of Bone-02 is designed to undergo hydrolytic and enzymatic degradation over a period of approximately six months. This timeline correlates with the remodeling phase of secondary bone healing [18]. As the fracture callus mineralizes and regains structural competence, the adhesive gradually depolymerizes into low-molecular-weight byproducts. These metabolites are non-toxic and are processed via standard metabolic pathways, eventually being excreted or resorbed without accumulating in vital organs [19]. This synchronized degradation ensures that the mechanical load is gradually transferred back to the healing bone, further preventing refracture upon the eventual disappearance of the adhesive.

3.2.2. Biocompatibility and Tissue Response

Biocompatibility assessments have shown that the adhesive supports cell adhesion and proliferation. The inclusion of components such as calcium or phosphate motifs within the polymer network renders the surface osteoconductive, encouraging the migration

of mesenchymal stem cells and osteoblasts into the fracture gap [20]. Histological studies in animal models have shown minimal inflammatory response, with the absence of the fibrous encapsulation typically seen around inert foreign bodies. Instead, the interface between the adhesive and the bone shows signs of direct osseointegration, a vital factor for the long-term stability of the repair [21].

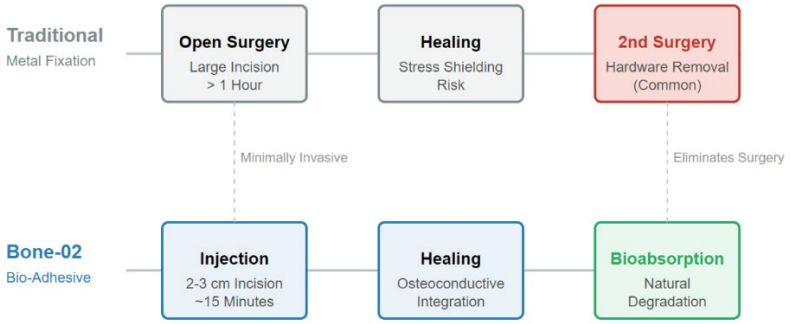

Figure 2. Comparison of Traditional and Bone-O2 Based Treatment

4. Clinical and Surgical Applications

The clinical utility of Bone-02 has been validated through its application in over 150 patients across multiple medical centers in China. These clinical trials have highlighted the transformative potential of the adhesive in simplifying complex orthopedic procedures and improving patient recovery.

4.1. Minimally Invasive Surgical Protocols

The flowable nature of the unpolymerized adhesive allows for a paradigm shift in surgical approach, moving from "open" surgery to "interventional" orthopedics. Standard Open Reduction and Internal Fixation (ORIF) requires large incisions to expose the fracture site and accommodate plates and screws. This extensive dissection strips the periosteum—the vascular membrane covering the bone—thereby impairing blood supply and delaying healing. In contrast, the application of Bone-02 utilizes a minimally invasive approach. Surgeons can manipulate fracture fragments using external fixation or percutaneous reduction forceps, followed by the injection of the adhesive through a small incision, typically 2 to 3 centimeters in length [22]. The adhesive's viscosity is tuned to allow injection through a delivery cannula, filling the irregular voids between bone fragments. The rapid setting time of 2 to 3 minutes allows the surgical team to hold the reduction manually until the bond solidifies, significantly reducing operative time and anesthesia duration [23].

4.2. Clinical Efficacy in Comminuted Fractures

The adhesive has proven particularly efficacious in the management of comminuted fractures, where the bone is shattered into multiple small pieces. Reconstructing such fractures with screws is technically demanding, often described as "assembling a jigsaw puzzle," and inserting screws into tiny fragments can cause them to split further [24]. Bone-02 functions as a grouting agent, unifying these disparate fragments into a cohesive block. This "monoblock" effect provides immediate stability without the risk of iatrogenic fragmentation associated with drilling and screwing. Clinical reports indicate that this method preserves the biological envelope of the fracture, leading to high rates of union even in difficult cases [25].

4.3. Post-Operative Recovery and Long-Term Outcomes

The postoperative course for patients treated with Bone-02 differs significantly from those receiving metallic implants.

4.3.1. Elimination of Secondary Surgical Interventions

One of the most profound benefits reported in clinical data is the elimination of the need for hardware removal. In conventional practice, a significant percentage of patients require a second surgery to remove painful, infected, or prominent metalwork, incurring additional healthcare costs, surgical risks, and recovery time [26]. Because Bone-02 is fully bioabsorbable, this secondary procedure is rendered obsolete. Patients experience a streamlined recovery process where functional restoration is achieved within three months, with no residual foreign material left in the body [27]. This reduction in the burden of care is a key driver for the adoption

of this technology in the broader healthcare landscape, offering a compelling health-economic argument alongside its clinical benefits.

Table 4. Clinical Outcomes for Using the Bone Glue

Metric	Traditional ORIF (Standard)	Bone-02 Protocol	Impact
Incision Size	Large (> 10 cm for plates)	2 – 3 cm	Preserves periosteal blood supply; better cosmetic outcome.
Operative Duration	60 – 120 Minutes	< 20 Minutes (approx.)	Reduced anesthesia risk; increased OR throughput.
Hardware Removal	Required in symptomatic cases	None	Eliminates cost and risk of second surgery.
Functional Recovery	3 – 6 Months	~3 Months	Accelerated return to work/daily activities.
Target Indication	All fractures	Comminuted / Articular	Solves the "bag of bones" puzzle that is hard to plate.

5. Challenges

The emergence of Bone-02 signals a potential turning point in orthopedic trauma management, yet its transition from a promising clinical trial candidate to a global standard of care involves navigating complex commercial, regulatory, and scientific hurdles.

5.1. Commercialization

The path to widespread adoption for Bone-02 is being paved by Hangzhou Yuannang Biotechnology Co., Ltd., a spin-off enterprise tasked with the commercial translation of the academic research. The company has reportedly secured substantial Series A funding, estimated at 100 million RMB, to facilitate mass production and regulatory filings [28]. In the regulatory landscape, Bone-02 is classified as a Class III medical device by China's National Medical Products Administration (NMPA). This classification is reserved for high-risk implants that sustain life or pose potential hazards, requiring the most stringent level of safety and efficacy data. The approval process necessitates not only the completion of the current multicenter trials but also rigorous post-market surveillance to monitor long-term biocompatibility. For international expansion, the developers must align their data with the requirements of the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). These bodies will likely demand independent validation studies to ensure that the adhesive's performance is consistent across diverse genetic populations and surgical practices. The disparity in regulatory frameworks between China and Western nations could delay global availability, making the standardization of clinical trial protocols a critical near-term objective.

5.2. Expanding Clinical Indications

While current applications are largely restricted to comminuted fractures of the extremities (e.g., wrist and ankle), the scope of Bone-02 is poised for expansion.

5.2.1. Spinal Fixation

Researchers are investigating the adhesive's utility in spinal surgery, specifically for reinforcing vertebral compression fractures or augmenting screw fixation in osteoporotic bone. The ability to inject a reinforcing agent that integrates with the vertebral body could reduce the incidence of screw pull-out, a common failure mode in elderly patients [29].

5.2.2. Craniomaxillofacial Surgery

The aesthetic demands of facial reconstruction make Bone-02 an attractive alternative to titanium plates, which can be palpable under the thin skin of the face or require removal due to thermal sensitivity. The adhesive's ability to mold to irregular contours offers a distinct advantage in orbital and zygomatic arch fractures [30].

5.2.3. Dentistry

Potential uses in alveolar bone grafting and implant stabilization are also being explored, utilizing the adhesive's osteoconductive properties to accelerate osseointegration around dental implants.

Table 5. SWOT Analysis of Bone-02 Development

Strengths	Weaknesses
• True wet adhesion in blood. • Fully bioabsorbable. • Minimally invasive delivery. • Reduces total cost of care (no removal).	• Limited shear strength (0.5 MPa). • Not suitable for femoral/tibial shaft fractures alone. • Higher upfront material cost vs. steel. • Requires precise mixing/handling.
Opportunities	**Threats**
• Expansion to Spinal & Dental markets. • Use in battlefield/disaster medicine. • Pediatric orthopedics (no growth restriction). • Drug-eluting variations (antibiotics/growth factors).	• Stringent Class III regulatory hurdles (FDA/EMA). • Competition from other emerging bio-glues. • Long-term biocompatibility unknowns. • Surgeon resistance to changing standard protocols.

5.3. Challenges and Sustainability

Despite the optimism, significant challenges remain. The most pressing scientific concern is the material's performance in high-load environments. The current shear strength of 0.5 MPa, while adequate for non-weight-bearing fragments, is insufficient for major load-bearing bones like the mid-shaft femur or tibia, which experience massive torsional and compressive forces during ambulation. For these indications, Bone-02 is currently viewed as an adjunct to, rather than a replacement for, intramedullary nails or plates [31]. Moreover, the economic implications are complex. While the adhesive eliminates the cost of secondary removal surgeries, the upfront cost of the novel biomaterial is likely to be higher than mass-produced steel implants. Health economic models must demonstrate that the long-term savings (reduced hospital stay, no second surgery, lower infection rates) outweigh the initial procurement costs to justify reimbursement by insurance payers. Finally, manufacturing consistency is paramount; scaling the production of a complex bio-inspired polymer while maintaining strict sterility and preventing premature polymerization during storage is a substantial engineering challenge that manufacturers must overcome.

6. Conclusion

The development of Bone-02 is a significant breakthrough in Chinese biomedicine, moving from the imitation of Western hardware to the creation of novel, bio-inspired therapeutics. The research team at Zhejiang University and Sir Run Run Shaw Hospital has engineered a material that solves the century-old problem of wet adhesion in orthopedic surgery by successfully mimicking the underwater adhesion strategies of oysters. The ability to rapidly stabilize comminuted fractures without permanent hardware offers a glimpse into a future where orthopedic repair is transient, regenerative, and minimally invasive. However, the journey of Bone-02 is just beginning. Its ultimate success will depend on valid long-term data regarding its degradation behavior and mechanical reliability in diverse patient populations. If these challenges can be met, this oyster-inspired adhesive stands to revolutionize the management of skeletal trauma, offering a seamless bridge between mechanical fixation and biological healing.

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