
Review

Polydopamine platforms in periodontal therapy: current evidence and future perspectives - a narrative review

Aditya Pawar*, Prasad Dhadse, Shreya Warkad, Aniket Meghawat, Aniket Bhatkar and Deepa Pazare

Department of Periodontology and Implantology, Sharad Pawar Dental College and Hospital, Datta Meghe Institute of Higher Education and Research, Sawangi(M), Wardha 442001, India

* **Correspondence:** Email: dradityaperio@gmail.com.

Abstract: Periodontal regeneration remains a major challenge in the management of periodontal disease because the periodontium consists of a highly organized complex of soft and hard tissues. Conventional periodontal therapies can reduce inflammation and control infection, but healing often results in repair rather than true regeneration of cementum, periodontal ligament, and alveolar bone. In this context, biomaterials that can enhance cell attachment, modulate inflammation, and support tissue regeneration have gained increasing interest. Polydopamine (PDA), a mussel-inspired polymer formed through the oxidative self-polymerization of dopamine hydrochloride, has emerged as a versatile platform in periodontal tissue engineering. It exhibits strong adhesion under wet oral conditions and can form stable coatings on a wide range of dental and biomaterial surfaces. Its catechol- and amine-rich chemistry allows functionalization with growth factors, antimicrobial agents, and therapeutic molecules. Importantly, PDA also demonstrates intrinsic antioxidant and immunomodulatory properties, including reactive oxygen species scavenging and the promotion of macrophage polarization toward pro-healing phenotypes, which are particularly relevant in the inflammatory microenvironment of periodontitis. Preclinical studies suggest that PDA-based scaffolds, membranes, nanoparticles, and implant coatings can enhance biomineralization, improve periodontal ligament cell responses, promote alveolar bone regeneration, and reduce microbial biofilm burden. However, challenges such as coating variability, incomplete understanding of degradation behavior, and limited clinical trial evidence remain. This narrative review summarizes current evidence and future perspectives on PDA-enabled systems in periodontal therapy.

Keywords: polydopamine; periodontal regeneration; periodontitis; biomaterials; guided tissue regeneration; tissue engineering; drug delivery systems; dental implants

1. Introduction

The periodontium is a complex structure composed of the periodontal ligament, alveolar bone, gingiva, and cementum. Pathologic and traumatic events often lead to the loss or damage of the periodontal ligament, alveolar bone, and gingival structures, while the cementum typically becomes contaminated due to exposure to the oral environment or due to incorporation of calculus into the cementum. Repair and regeneration of periodontal tissues remain a major goal in the management of periodontal disease, with periodontal therapy aiming to restore lost or damaged attachment tissues and supporting alveolar bone to their original form and function through non-surgical or surgical procedures [1]. In general, the most common pattern of healing following periodontal therapy is repair, characterized by the formation of a long junctional epithelium extending apically along the root surface, or connective tissue repair, where collagen fibers are positioned parallel to the previously exposed root surface [2].

Periodontitis is characterized by a dysbiotic subgingival biofilm and a dysregulated host immune response. Keystone pathogens such as *Porphyromonas gingivalis* disrupt microbial homeostasis and drive chronic inflammation through immune subversion mechanisms [3]. Elevated levels of pro-inflammatory cytokines, including interleukin (IL)-1 β , IL-6, and tumor necrosis factor- α (TNF- α), are consistently detected in periodontal lesions and contribute to connective tissue degradation and bone resorption [4]. Furthermore, increased expression of receptor activator of nuclear factor kappa-B ligand (RANKL) promotes osteoclast differentiation and alveolar bone loss [5]. Excessive production of reactive oxygen species (ROS) by activated neutrophils and macrophages amplifies oxidative stress, leading to extracellular matrix breakdown and impaired periodontal ligament cell function [6]. This inflammatory and oxidative microenvironment disrupts the balance between bone formation and resorption and compromises regenerative healing. Therefore, therapeutic strategies capable of modulating inflammation, reducing oxidative stress, and restoring immune balance are particularly relevant in periodontal tissue engineering.

Biomaterials play a pivotal role in periodontal regeneration by providing a conducive environment for the restoration of lost periodontal structures. The primary role of biomaterials in periodontal regeneration is to create a conducive microenvironment for tissue repair by acting as a physical barrier to prevent the invasion of fast-growing epithelial and gingival fibroblast cells into the defect site, thereby allowing periodontal ligament (PDL) stem cells and progenitor bone cells to migrate, proliferate, and differentiate [7]. These molecules stimulate cellular activity and enhance osteogenic and cementogenic responses, while modulating bone microenvironment, promoting angiogenesis, and exerting antimicrobial effects that reduce infection risk during healing. Through these combined functions—barrier action, scaffold support, molecular delivery, and antimicrobial effects—biomaterials effectively guide the organized reconstruction of the complex periodontium. Their use facilitates the formation of new cementum, connective tissue, and alveolar bone, thereby restoring both the structure and function of the periodontium.

Polydopamine (PDA) is a versatile, mussel-inspired polymer platform whose catechol- and amine-rich surface chemistry supports strong wet adhesion, facile conjugation of bioactive molecules,

and intrinsic redox and anti-inflammatory functions that are highly relevant to periodontal regeneration and soft-tissue healing in inflamed oral environments. Polydopamine used in biomaterials is typically synthesized in situ by oxidatively polymerizing dopamine (commonly supplied as dopamine hydrochloride) under mildly alkaline, oxygenated conditions to form coatings or nanoparticles on demand. PDA nanoparticles can localize therapeutics, scavenge reactive oxygen species (ROS), and modulate macrophage phenotypes, thereby addressing core biological barriers to periodontal repair such as persistent inflammation, oxidative stress, and poor retention of regenerative cues in saliva-exposed defects [8,9]. Figure 1 depicts the periodontal microenvironment and the scope for PDA-based therapeutic modulation.

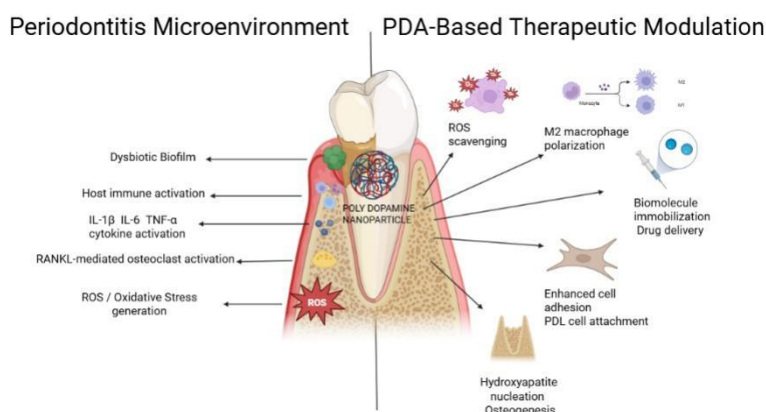


Figure 1. Pathological microenvironment of periodontitis and mechanistic targets of polydopamine (PDA). (Created with BioRender.com)

While polydopamine has been widely reviewed in the broader context of regenerative medicine and multifunctional biomaterials, most existing reviews discuss its applications across diverse tissues without focused evaluation of periodontal-specific outcomes. The present narrative review specifically consolidates evidence related to periodontal regeneration, organizes PDA-enabled systems into defined translational platforms (scaffolds, membranes, nanoparticles, implant coatings, and antibiofilm systems), critically distinguishes repair from true periodontal regeneration, and benchmarks PDA against established periodontal biomaterials. By integrating mechanistic insights with translational benchmarks and clinically relevant endpoints, this review provides a structured, periodontal-focused perspective that has not been comprehensively synthesized in previous reports.

2. History of polydopamine

Mussels are fouling organisms capable of adhering to a diverse variety of surfaces, even those traditionally considered adhesion-resistant, such as polytetrafluoroethylene (PTFE) (Waite and Tanzer, 1981; Lee et al., 2007). This remarkable adhesive ability is attributed to specialized proteins secreted by mussels that enable firm attachment under diverse environmental conditions. Waite and Qin (2001) discovered that proteins localized near the interface of the mussel plaque and substrate were particularly rich in 3,4-dihydroxy-L-phenylalanine (dopamine, DA), suggesting that their unique amino acid composition contributes directly to mussel adhesion. Inspired by natural melanin formation mechanisms, recent studies have also demonstrated alternative polymerization strategies for dopamine,

including light-induced oxidative polymerization approaches that enable controlled formation of melanin-like PDA structures [10].

3. Physicochemical properties of polydopamine hydrochloride

Dopamine hydrochloride is a white, crystalline powder known for its distinctive physicochemical properties that make it valuable in biomedical and pharmaceutical applications. It has the molecular formula $C_8H_{11}NO_2 \cdot HCl$ and a molecular weight of approximately 189.64 g/mol (Figure 2). This compound is highly soluble in water and methanol but insoluble in organic solvents such as ether and chloroform, which facilitates its use in aqueous biological systems. It has a melting point range of 240–250 °C, decomposing upon melting. Structurally, dopamine hydrochloride is zwitterionic, containing both basic amino groups and acidic catechol groups, enabling it to undergo oxidative polymerization to form polydopamine. The polar surface area and pKa values contribute to its reactivity and interaction with other molecules. Due to its sensitivity to light and oxidizing agents, it requires careful handling and storage conditions.

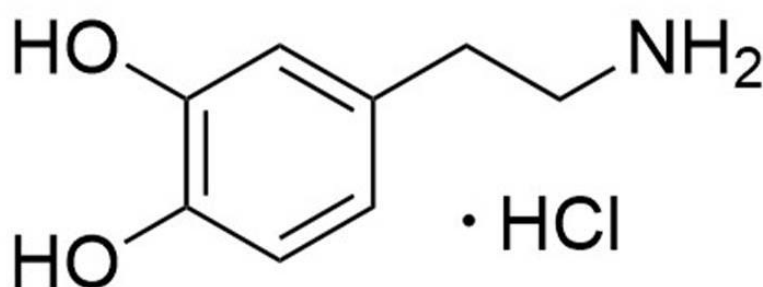


Figure 2. Molecular formula of dopamine hydrochloride.

PDA forms via the alkaline oxidative polymerization of dopamine (often from dopamine hydrochloride stocks), yielding a melanin-like, π -conjugated network rich in catechol/quinone groups that participate in covalent and noncovalent interactions with diverse substrates and biomolecules. Recent studies further demonstrate that melanin-like polymers can exhibit highly ordered supramolecular structures through π - π stacking interactions, which contribute to their unique electronic and photothermal properties [11]. Polydopamine adheres to the root surface primarily through catechol- and amine-mediated interactions that create a thin, conformal coating on dentin and cementum, enabling strong attachment even in wet conditions. The adhesion involves a mix of covalent bonding with surface nucleophiles and multiple noncovalent forces like hydrogen bonding, π - π stacking, and metal coordination with hydroxyapatite components of the root surface. In mildly alkaline aqueous conditions, dopamine oxidizes to o-quinone and undergoes self-polymerization to form polydopamine, depositing as a nanoscale film on virtually any substrate, including moist dentin and cementum [12]. The catechol/quinone groups enable surface coupling and crosslinking during this deposition. On root dentin, catechols can chelate surface calcium in hydroxyapatite and form hydrogen bonding with collagen, while quinones can react covalently with nucleophiles (amines, thiols) via Schiff base or Michael-type additions, anchoring the coating to the hybrid inorganic–organic surface.

On a root surface, hydroxyapatite-rich regions allow catechol–metal (Ca^{2+}) coordination and ionic interactions, while organic collagen-rich regions provide amine and thiol groups for covalent coupling with oxidized catechol (quinone) moieties. The coating grows conformally, increasing surface energy and wettability, which enhances interfacial contact and mechanical interlocking at the micro/nanoscale of etched or smear-layer-modified dentin [13].

4. Biodegradability and biocompatibility

PDA exhibits excellent biocompatibility and biodegradability, making it a promising biomaterial for applications in the oral environment. Its chemical structure, rich in catechol and amine groups, enables strong adhesion to a variety of surfaces, including oral tissues, without eliciting significant cytotoxic effects. Its structural similarity to natural melanin contributes to low cytotoxicity, minimal immune response, and good cell viability across multiple cell lines—including human keratinocytes (HaCaT), glioma cells (U87MG, C6), osteoblasts (MG-63), and endothelial cells [14].

In terms of biodegradability, PDA exhibits gradual oxidative degradation in inflammatory microenvironments, but its long-term biotransformation products and clearance kinetics in periodontal tissues remain insufficiently characterized. The degradation rate depends on the local microenvironment, including pH and oxidative stress levels, which are variable in oral disease conditions. Overall, PDA's compatibility with human cells and its ability to biodegrade safely make it an attractive candidate for clinical use in periodontal therapies and oral regeneration.

5. Mechanisms relevant to periodontal regeneration

Periodontitis features a chronically inflamed, ROS-rich microenvironment that disrupts osteogenesis, angiogenesis, and soft-tissue attachment, making redox control and immune rebalancing central to any regenerative strategy. Polydopamine (PDA) supports periodontal regeneration through catechol/amine-driven surface adhesion, immunomodulation, antioxidant ROS scavenging, osteogenic microenvironment engineering, and broad-spectrum antibiofilm/photothermal antibacterial actions that collectively favor periodontal ligament and alveolar bone repair in inflamed sites. Mechanistically, PDA's mussel-inspired catechols prime biomaterial and tissue interfaces for mineral-ion chelation, protein/cell attachment, and pro-healing signaling while mitigating oxidative stress and polarizing macrophages toward pro-regenerative M2 phenotypes in periodontal defects, including diabetic periodontitis models.

The mechanistic basis of PDA in periodontal regeneration is multifactorial and extends beyond simple surface adhesion. As summarized in Table 1, PDA's catechol–quinone chemistry enables dynamic interactions at the biointerface, including covalent bonding with nucleophilic groups, metal-ion coordination, and redox-mediated signaling modulation. These chemical features translate into biologically relevant effects such as enhanced cell adhesion, mineral nucleation, and immune regulation. The photothermal behavior of PDA arises from its melanin-like π -conjugated structure, which enables broadband light absorption and efficient photothermal conversion. Importantly, the antioxidant capacity of catechol groups directly mitigates oxidative stress, while modulation of macrophage polarization influences the inflammatory milieu that governs osteogenesis. Thus, PDA does not act through a single pathway but rather functions as a multifunctional interfacial regulator integrating physicochemical adhesion with biochemical signaling.

Table 1. Mechanistic pathways of polydopamine for possible biologic outcomes relevant to periodontal regeneration.

Sr. No	Mechanism	Surface actions	Biological outcomes	Possible applications
1.	Catechol/quinone and amine presentation from dopamine self-oxidative polymerization [15]	Conformal universal coatings on metals, ceramics, polymers enabling robust adhesion, and secondary immobilization of biomolecules	Stabilizes clot; supports fibroblast and PDL cell attachment and spreading	Coatings for scaffolds, membranes, implants to enable tethering of peptides, growth factors, and antimicrobials
2.	Catechol metal/ion coordination and chelation (Ca^{2+} , PO_4^{3-} , transition metals) [16]	Promotes hydroxyapatite nucleation and protein adsorption, and coordinates metal-phenolic networks at the interface	Enhances integrin-mediated adhesion, early osteogenic cues at defect margins	Surface modification to increase HA formation and cell anchorage on grafts and implants
3.	PDA-based composite interfaces (PDA + rGO/graphene oxide/HA) and conductive scaffolds [17]	Provides interfacial electrical conductivity and topochemical cues that modulate cell signaling	Upregulates ALP, RUNX2, COL1A1, BMP2, and OCN and increases mineralization for alveolar bone regeneration	Conductive scaffolds for periodontal bone fill, especially under inflammatory conditions
4.	Immunomodulatory actions via ROS reduction and signaling pathway modulation (e.g., RhoA/ROCK) [18,19]	Alters macrophage phenotype at the biointerface, suppressing M1 and favoring M2 polarization	M2-associated cytokine milieu supports osteogenesis and reduces chronic inflammation in periodontal microenvironments	Osteoimmunomodulatory -oriented scaffold design to promote bone regeneration in peri-implant and periodontal defects
5.	Direct antioxidant (catechol) ROS scavenging and nanozyme-like activity [20]	Lowers oxidative stress at implant/defect sites and on immune/stem cells	Protects periodontal cells, reduces oxidative damage that sustains chronic periodontitis, improves repair outcomes	Antioxidant-enabled scaffolds or nanoparticle adjuncts to improve healing in oxidative or diabetic conditions
6.	Polyvalent bacterial adhesion capacity plus combination with antimicrobials/metal ions [21,22]	Captures bacteria and supports immobilization/release of antimicrobial peptides or metals; strong NIR absorption enables photothermal action	Reduces biofilm burden; photothermal disruption of biofilms with potential synergistic antibacterial effects	Antibiofilm coatings, PDA-based photothermal/antimicrobial nanoformulations for periodontal pocket therapy
7.	Quinone/catechol reactivity for covalent and noncovalent loading [23]	Sustained, localized loading and release of antibiotics, anti-inflammatories, growth factors, peptides	Targeted adjunctive delivery inside periodontal pockets and on implant surfaces to support regeneration	Drug- and factor-delivery platform for adjunctive periodontal therapy and implant surface functionalization

6. Platform-specific evidence of PDA-based systems in periodontal therapy

To better consolidate available evidence, PDA-enabled platforms in periodontology can be categorized into five major translational groups: (1) scaffold-based systems, (2) guided tissue regeneration membranes, (3) nanoparticle and drug-delivery systems, (4) implant/abutment surface coatings, and (5) antibiofilm and photothermal therapeutic systems. Although these platforms share the universal adhesion and biofunctionalization capacity of PDA, they differ in synthesis strategy, surface modification approaches, biological targets, and translational objectives as summarized in Table 2 and Figure 3.

1. PDA-based scaffolds: PDA is commonly deposited via alkaline oxidative polymerization (Tris buffer, pH ~8.5, 1–2 mg/mL dopamine hydrochloride) onto polymeric or ceramic scaffolds. These coatings enhance surface hydrophilicity, support cell attachment, and enable immobilization of osteogenic growth factors. Preclinical models demonstrate improved osteogenic marker expression (RUNX2, ALP, OCN) and enhanced bone defect fill. However, variability in coating thickness and long-term durability remains a limitation [24].

2. PDA-modified guided tissue regeneration (GTR) membranes: PDA coatings improve membrane wettability and provide anchoring sites for biomolecule conjugation. In rat periodontal defect models, PDA-modified membranes show enhanced bone formation and better integration compared with unmodified barriers. Limitations include insufficient long-term barrier stability data under simulated oral conditions [25].

3. PDA nanoparticles and drug-delivery systems: PDA nanoparticles are synthesized through self-polymerization under alkaline conditions and allow loading of antibiotics, anti-inflammatory agents, and growth factors via catechol/quinone interactions. In ligature-induced periodontitis models, such systems demonstrate ROS scavenging, reduced inflammatory cytokines, and decreased bone resorption. However, pharmacokinetics and long-term clearance profiles remain incompletely characterized [26].

4. PDA-coated implant and abutment surfaces: PDA serves as a universal primer for titanium surfaces, enabling immobilization of antimicrobial peptides, silver ions, or osteogenic factors. Preclinical studies report improved antibacterial activity and enhanced osseointegration. Yet, standardized coating protocols and clinical trials in peri-implantitis prevention are still lacking [27].

5. PDA-based antibiofilm and photothermal systems: Beyond passive antibacterial strategies, PDA exhibits strong near-infrared (NIR) absorption and photothermal conversion capability. PDA-coated titanium surfaces and PDA nanoparticles have demonstrated effective biofilm disruption upon NIR irradiation, offering a non-antibiotic adjunctive strategy for managing periodontal and peri-implant infections. These systems combine antibacterial activity with biointerface compatibility. However, thermal safety margins, optimal irradiation parameters, and long-term tissue response remain insufficiently validated for clinical translation [28].

Table 2. Platform-specific evidence of polydopamine-based systems in periodontal therapy.

Sr. No.	Platform	Synthesis/coating conditions	Functionalization strategy	Model system	Key outcomes	Reported limitations
1.	Scaffold coatings [24]	Dopamine HCl (1–2 mg/mL), Tris buffer pH 8.5, 12–24 h oxidative deposition	Growth factor immobilization, HA nucleation	Human mesenchymal stem cells	↑ RUNX2, ALP, mineralization, enhanced bone fill	Coating variability; long-term degradation unclear
2.	GTR membranes [25]	Surface deposition on collagen polymer membranes	PDA on or biomolecule conjugation	Human bone marrow stem cells (hBMSCs)	Enhanced osteogenesis, better integration	Limited oral-cycle durability data
3.	PDA nanoparticles [26]	Self-polymerized PDA NPs (alkaline conditions)	Antibiotic loading; ROS scavenging	Rat periodontal bone defect	Reduced ROS, enhanced antibacterial effect	Clearance kinetics unknown
4.	Implant coatings [27]	PDA primer layer on titanium	Immobilization of antimicrobials or osteogenic agents	Preclinical implant infection models	Improved antibacterial activity + osseointegration	Lack of human clinical trials
5.	Photothermal systems [28]	PDA-coated titanium nanoparticles	NIR-triggered photothermal effect	Biofilm models	Biofilm disruption	Thermal safety margins not clinically validated

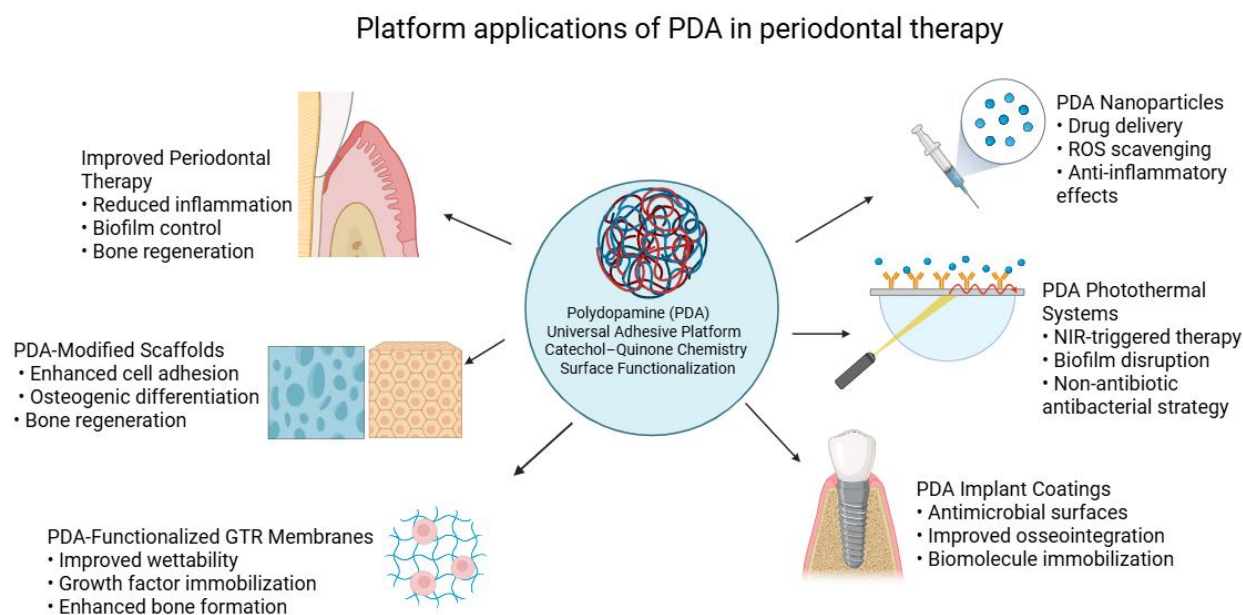


Figure 3. Platform-specific applications of polydopamine (PDA) in periodontal therapy. (Created with BioRender.com)

7. Evidence for true periodontal regeneration: histologic criteria and experimental findings

True periodontal regeneration is defined histologically by the formation of new cementum on the root surface with inserted periodontal ligament (PDL) fibers oriented perpendicularly or obliquely into both the cementum and newly formed alveolar bone, thereby restoring the native attachment apparatus. In contrast, periodontal repair typically refers to defect fill, long junctional epithelium formation, or fibrous connective tissue adaptation without functional fiber insertion [2].

Most PDA-based periodontal studies report enhanced bone formation, increased mineralization markers (e.g., ALP, RUNX2, OCN), and improved inflammatory modulation. However, these outcomes alone do not constitute true regeneration unless supported by histologic evidence demonstrating new cementum and inserting PDL fibers.

In scaffold-based periodontal defect models, Ding et al. (2021) reported enhanced alveolar bone regeneration and improved osteoimmunomodulatory responses; however, detailed histologic confirmation of new cementum with functionally oriented PDL insertion was limited [19]. Similarly, antioxidant PDA nanoparticle systems (Bao et al., 2018; Yan et al., 2023) demonstrated reduced inflammatory destruction and preservation of periodontal structures, yet primarily showed bone preservation or repair rather than complete regeneration of the attachment complex [20,21].

To date, most experimental evidence for PDA-enabled systems supports improved bone fill, modulation of oxidative stress, and enhanced cellular responses. Definitive histologic demonstration of coordinated new cementum formation with inserted Sharpey's fibers remains limited in periodontal-specific PDA models. This distinction is critical when interpreting regenerative claims and underscores the need for standardized histologic endpoints in future preclinical and clinical investigations. To date, no randomized controlled human clinical trial has demonstrated histologically confirmed true periodontal regeneration using PDA-modified systems.

8. Comparative perspective with established periodontal biomaterials

Several biomaterials are already established in periodontal tissue engineering, including collagen and gelatin membranes, chitosan-based systems, calcium phosphate and hydroxyapatite coatings, bioactive glass, extracellular matrix (ECM)-inspired coatings, and polyelectrolyte multilayers. Each offers specific advantages. Collagen membranes remain the clinical standard in guided tissue regeneration due to their biocompatibility and inherent cell-binding motifs, although they are susceptible to enzymatic degradation and limited in active biofunctionalization. Chitosan provides antimicrobial and hemostatic properties but requires modification to enhance mechanical stability and adhesion to inorganic substrates. Calcium phosphate and hydroxyapatite coatings promote osteoconductivity but do not intrinsically regulate inflammation or oxidative stress. Bioactive glass stimulates mineralization through ionic release but may alter local pH and lacks facile biomolecule conjugation capacity. Table 3 compares polydopamine among established periodontal biomaterial platforms.

In contrast, polydopamine functions primarily as a bioactive interfacial primer rather than a bulk structural scaffold. Its unique advantages include universal wet adhesion across organic and inorganic surfaces, facile secondary functionalization through catechol/quinone chemistry, intrinsic antioxidant activity, and compatibility with drug-loading and photothermal strategies. However, PDA alone does not provide mechanical support comparable to collagen matrices or mineralized scaffolds and is best positioned as a multifunctional surface-modification strategy that enhances, rather than replaces, established periodontal biomaterials.

Table 3. Comparison of polydopamine among established periodontal biomaterial platforms.

Sr. No.	Biomaterial platform	Strengths	Limitations	Distinct role of PDA
1.	Collagen/gelatin membranes	Clinical standard, biocompatible	Rapid degradation, passive bioactivity	Enables functionalization and antioxidant enhancement
2.	Chitosan systems	Antimicrobial, hemostatic	Limited adhesion, mechanical weakness	Improves surface adhesion and drug loading
3.	Calcium phosphate/HA	Osteoconductive	Limited immunomodulation	Adds redox control and surface coupling
4.	Bioactive glass	Ion-mediated mineralization	pH changes, brittle	Provides stable coating and biomolecule immobilization
5.	ECM-inspired coatings	Biomimetic	Complex fabrication	Single-step universal deposition
6.	Polyelectrolyte multilayers	Controlled layering	Technique-sensitive	Simpler universal coating alternative

9. Current challenges and translational benchmarks

Despite promising preclinical results, several barriers must be addressed before PDA-based systems can be translated clinically.

1. Coating reproducibility: PDA film formation is highly sensitive to pH, dopamine concentration, oxygen availability, and oxidation kinetics. The underlying amine–quinone competition during dopamine self-polymerization plays a central role in determining coating structure and stability. At higher dopamine concentrations, intermolecular amine–quinone reactions favor cross-linked adhesive networks, whereas lower concentrations promote intramolecular cyclization to 5,6-dihydroxyindole intermediates, resulting in less adhesive, heterogeneous aggregates [29]. Variations in this chemical balance can alter film thickness, catechol availability, and quinone reactivity, thereby directly affecting surface adhesion strength, biomolecule immobilization efficiency, antioxidant capacity, and long-term interfacial stability. Future studies should report standardized synthesis parameters, quantify coating thickness, and demonstrate batch-to-batch consistency.

2. Durability in oral conditions: Long-term stability under pH cycling, enzymatic exposure, salivary flow, and mechanical stress remains insufficiently evaluated. Accelerated aging models simulating oral environments should be incorporated.

3. True regenerative endpoints: Most studies report bone fill rather than histologically confirmed regeneration. Future investigations should demonstrate new cementum formation with inserted PDL fibers using standardized histomorphometric analysis.

4. Dose and safety considerations: Concentration-dependent effects, degradation products, and systemic clearance of PDA nanoparticles require rigorous toxicological assessment following established biocompatibility standards.

5. Reproducibility and clinical relevance: Validation in large-animal periodontal models and assessment of clinically relevant outcomes—such as clinical attachment level gain and probing depth reduction—are necessary to establish translational value.

10. Conclusion

Polydopamine (PDA) emerges from these discussions as a versatile interfacial molecule that reliably adheres under wet, protein-rich oral conditions while simultaneously activating biological processes central to periodontal regeneration, including cell adhesion, osteo/cementogenic differentiation, ROS scavenging, and in situ biomineralization. Its catechol/amine groups provide a universal primer on enamel, dentin, cementum, titanium, PEEK, and polymeric membranes, enabling stable coupling of proteins, growth factors, and antimicrobials without a harsh environment and promoting hydroxyapatite nucleation that stabilizes adhesive interfaces and favors hard-tissue integration adjacent to soft tissues. Preclinical studies with PDA-coated scaffolds, membranes, and nanoparticles demonstrate enhanced bone fill, improved periodontal ligament-related outcomes, and microenvironment modulation through antioxidant and immunoregulatory effects, including macrophage polarization toward pro-healing phenotypes in challenging diabetic or inflammatory settings. However, these advantages must be interpreted cautiously. Significant limitations remain, including variability in coating chemistry related to amine–quinone interactions, incomplete understanding of long-term degradation behavior in the dynamic oral environment, and limited standardization of synthesis protocols. Most available evidence derives from in vitro or small-animal

models, and histologically confirmed true periodontal regeneration remains insufficiently demonstrated. Furthermore, dose–response relationships, nanoparticle clearance profiles, and large-animal or human clinical validation studies are still lacking. These constraints highlight that PDA platforms remain at an advanced preclinical stage rather than an established clinical solution.

Translational outlook: Short-term, standardized PDA protocols (buffer, pH, time, concentration) and shelf-stable, QA-validated coated membranes/scaffolds should be advanced into pilot clinical studies powered for radiographic and clinical endpoints with adjunctive biomarker readouts of inflammation and oxidative stress. Mid-term, randomized trials should compare PDA-primed root surfaces and PDA-GTR constructs against state-of-the-art collagen or ePTFE membranes, with histologic substantiation where feasible to confirm true regeneration. Long term, GMP-grade PDA platforms integrating controlled drug release and immunomodulation may enable indication-specific solutions (e.g., diabetes-induced periodontitis), provided durability and degradation profiles are mapped under simulated oral cycling and post-market surveillance frameworks. If these gaps are addressed, PDA-enabled systems could shift periodontal regeneration from largely passive barriers to smart, bioactive interfaces that couple adhesion, antimicrobial protection, and guided mineralized tissue formation in a clinically scalable manner.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Conflict of interest

The authors declare no conflict of interest.

Author contributions:

Dr. Aditya Pawar was primarily responsible for the conception of the review, data collection, analysis, and drafting of the manuscript. Dr. Prasad Dhadse provided overall supervision, expert guidance, and critically reviewed the manuscript. Dr. Aniket Meghawar assisted with data interpretation, and provided valuable inputs during manuscript preparation. Dr. Shreya Warkad and Dr. Aniket Bhatkar contributed in diagrammatic representation of data and compilation of data. Dr. Deepa Pazare was involved in manuscript formatting. All authors have read and approved the final version of the manuscript.

References

1. Bădărașu-Șuster AM, Bechir ES, Bardocz-Veres Z, et al. (2025) Recent advances in regenerative therapies in periodontology. *Dent J* 13: 564. <https://doi.org/10.3390/dj13120564>
2. Wikesjö UME, Nilvéus RE, Selvig KA (1992) Significance of early healing events on periodontal repair: a review. *J Periodontol* 63: 158–165. <https://doi.org/10.1902/jop.1992.63.3.158>
3. Hajishengallis G (2014) Immunomicrobial pathogenesis of periodontitis: keystones, pathobionts, and host response. *Trends Immunol* 35: 3–11. <https://doi.org/10.1016/j.it.2013.09.001>

4. Graves DT, Li J, Cochran DL (2011) Inflammation and uncoupling as mechanisms of periodontal bone loss. *J Dent Res* 90: 143–153. <https://doi.org/10.1177/0022034510385236>
5. Kawai T and Akira S (2007) Signaling to NF- κ B by Toll-like receptors. *Trends Mol Med* 13: 460–469. <https://doi.org/10.1016/j.molmed.2007.09.002>
6. Chapple ILC and Matthews JB (2007) The role of reactive oxygen and antioxidant species in periodontal tissue destruction. *Periodontol 2000* 43: 160–232. <https://doi.org/10.1111/j.1600-0757.2006.00178.x>
7. Santonocito S, Ferlito S, Polizzi A, et al. (2023) Impact exerted by scaffolds and biomaterials in periodontal bone and tissue regeneration engineering: new challenges and perspectives for disease treatment. *Explor Med* 4: 215–234. <https://doi.org/10.37349/emed.2023.00135>
8. Wu H, Zhao C, Lin K, et al. (2022) Mussel-inspired polydopamine-based multilayered coatings for enhanced bone formation. *Front Bioeng Biotech* 10: 952500. <https://doi.org/10.3389/fbioe.2022.952500>
9. Guo K, Wang Y, Feng ZX, et al. (2022) Recent development and applications of polydopamine in tissue repair and regeneration biomaterials. *Int J Nanomed* 31: 859–881. <https://doi.org/10.2147/IJN.S437854>
10. Zhang T, Liang B, Zhang JH, et al. (2025) Sunlight-induced permanent hair dyeing. *Chinese J Polym Sci* 43: 261–270. <https://doi.org/10.1007/s10118-025-3274-1>
11. Chen P, He S, Wang T, et al. (2025) Melanin-like nanofibers with highly ordered structures achieve ultrahigh specific electromagnetic interference shielding efficiency. *Nat Commun* 16: 7127. <https://doi.org/10.1038/s41467-025-62367-9>
12. Du J, Zhou Y, Bao X, et al. (2022) Surface polydopamine modification of bone defect repair materials: characteristics and applications. *Front Bioeng Biotech* 10: 974533. <https://doi.org/10.3389/fbioe.2022.974533>
13. Zhou Y, Yang Y, Liu R, et al. (2023) Research progress of polydopamine hydrogel in the prevention and treatment of oral diseases. *Int J Nanomed* 31: 2623–2645. <https://doi.org/10.2147/IJN.S407044>
14. Wu H, Wei M, Xu Y, et al. (2022) PDA-based drug delivery nanosystems: a potential approach for glioma treatment. *Int J Nanomed* 1: 3751–3775. <https://doi.org/10.2147/IJN.S378217>
15. Alfieri ML, Panzella L, Napolitano A (2024) Multifunctional coatings hinging on the catechol/amine interplay. *Eur J Org Chem* 27: e202301002. <https://doi.org/10.1002/ejoc.202301002>
16. Li H, Jia Y, Bai S, et al. (2024) Metal-chelated polydopamine nanomaterials: Nanoarchitectonics and applications in biomedicine, catalysis, and energy storage. *Adv Colloid Interface* 334: 103316. <https://doi.org/10.1016/j.cis.2024.103316>
17. Jiang X, Chen X, Li Q, et al. (2025) Synergistic effects of polydopamine-coated reduced graphene oxide on osteogenesis and anti-inflammation in periodontitis. *J Mater Sci Mater Med* 36: 51. <https://doi.org/10.1007/s10856-025-06905-3>
18. Lou X, Hu Y, Zhang H, et al. (2021) Polydopamine nanoparticles attenuate retina ganglion cell degeneration and restore visual function after optic nerve injury. *J Nanobiotechnol* 19: 436. <https://doi.org/10.1186/s12951-021-01199-3>
19. Ding T, Kang W, Li J, et al. (2021) An in situ tissue engineering scaffold with growth factors combining angiogenesis and osteoimmunomodulatory functions for advanced periodontal bone regeneration. *J Nanobiotechnol* 19: 247. <https://doi.org/10.1186/s12951-021-00992-4>

20. Bao X, Zhao J, Sun J, et al. (2018) Polydopamine nanoparticles as efficient scavengers for reactive oxygen species in periodontal disease. *ACS Nano* 12: 8882–8892. <https://doi.org/10.1021/acsnano.8b04022>
21. Yan M, Liang W, Du L, et al. (2023) Metronidazole-loaded polydopamine nanomedicine with antioxidant and antibacterial bioactivity for periodontitis. *Nanomedicine* 18: 2143–2157. <https://doi.org/10.2217/nnm-2023-0245>
22. Zou Y, Wang T, Lin X, et al. (2025) Regulation of the light absorption and photothermal performance of melanin-like polymers. *Acc Chem Res* 58: 2815–2829. <https://doi.org/10.1021/acs.accounts.5c00346>
23. Fraser D, Caton J, Benoit DS (2022) Periodontal wound healing and regeneration: insights for engineering new therapeutic approaches. *Front Dent Med* 3: 815810. <https://doi.org/10.3389/fdmed.2022.815810>
24. Godoy-Gallardo M, Portoles-Gil N, Lopez-Periago AM, et al. (2020) Multi-layered polydopamine coatings for the immobilization of growth factors onto highly-interconnected and bimodal PCL/HA-based scaffolds. *Mat Sci Eng C* 117: 111245. <https://doi.org/10.1016/j.msec.2020.111245>
25. Davaie S, Hooshmand T, Najafi F, et al. (2023) Synthesis, characterization, and induced osteogenic differentiation effect of collagen membranes functionalized by polydopamine/graphene oxide for bone tissue engineering. *ACS Appl Bio Mater* 6: 4629–4644. <https://doi.org/10.1021/acsabm.3c00400>
26. Guo J, Liu Y, Zhang Y, et al. (2025) Polydopamine dual-modal nanotherapy synergizes photothermal antibacterial and nanozyme anti-inflammatory effects for periodontitis treatment. *Int J Nanomed* 31: 11505–11524. <https://doi.org/10.2147/IJN.S533622>
27. Xu D, Wang X, Li M, et al. (2025) Enhancing titanium-osteointegration: antimicrobial, anti-inflammatory and osteogenic properties of multifunctional coatings through layer-by-layer self-assembly. *Appl Surf Sci* 686: 162149. <https://doi.org/10.1016/j.apsusc.2024.162149>
28. Wu M, Liu M, Feng G, et al. (2025) NIR-triggered temperature-sensitive polydopamine nanosystem with rapid phase transition for on-demand release to enhance antibacterial and antibiofilm performance. *Colloids Surf B* 255: 114901. <https://doi.org/10.1016/j.colsurfb.2025.114901>
29. Alfieri ML, Panzella L, Oscurato SL, et al. (2018) The chemistry of polydopamine film formation: the amine-quinone interplay. *Biomimetics* 3: 26. <https://doi.org/10.3390/biomimetics3030026>



AIMS Press

© 2026 the Author(s), licensee AIMS Press. This is an open access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0>)