Journal of Chemical Health Risks

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JCHR (2026) 16(3), 200-207 | ISSN:2251-6727

New Generation Biomaterials in Peri-Implantitis Management: A Paradigm Shift in Therapeutic and Regenerative Strategies - A Narrative Review

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(Received: 16 March 2026 Revised: 14 April 2026 Accepted: 01 May 2026)

KEYWORDS

Peri-Implantitis, Biomaterials, Nanoparticles, Ceramics, Immunomodulation, Drug Delivery Systems, Nanotechnology

ABSTRACT:

Introduction: Peri-implantitis, a biofilm-induced inflammatory condition, leads to progressive peri-implant bone loss and remains a major cause of implant failure. Conventional mechanical and chemotherapeutic approaches show limited success in achieving long-term stability and true tissue regeneration. Advances in biomaterial science have introduced next-generation materials with multifunctional properties that combine antimicrobial action, immunomodulation, and guided bone regeneration.

Objectives: To evaluate the current evidence on the therapeutic and regenerative potential of next-generation biomaterials in peri-implantitis management.

Methods: An electronic literature search was conducted across PubMed, Scopus, and Web of Science databases (2010–2025). Systematic reviews, randomized controlled trials, and preclinical studies on biomaterials with antimicrobial and osteogenic properties were analysed for clinical and regenerative outcomes.

Results: Emerging biomaterials, including ion-releasing ceramics, nanostructured coatings, and bioactive hydrogels, demonstrated significant antimicrobial effects, modulation of host response, and enhanced osseointegration. Smart, stimuli-responsive systems and AI-assisted scaffold designs further improved regenerative predictability.

Conclusions: Next-generation biomaterials mark a paradigm shift from conventional decontamination to biologically driven peri-implant regeneration. Their integration of nanotechnology and digital design offers a promising, evidence-based approach toward personalized and durable peri-implant therapy.

1. Introduction

Dental implants have become the gold standard for oral rehabilitation, offering predictable long-term outcomes and high patient satisfaction. However, the increasing prevalence of peri implant diseases particularly peri implantitis poses a significant biological challenge to implant longevity. Epidemiological studies report peri implantitis prevalence ranging from 12% to 43% at the implant level, with higher susceptibility in patients with a history of periodontitis, poor plaque control, smoking, or systemic conditions such as diabetes [15–18]. The 2017 World Workshop on Periodontology defined peri implantitis as a biofilm induced, host mediated inflammatory condition characterized by progressive peri implant bone loss [16]. Conventional treatment strategies including mechanical debridement, antiseptics, and systemic or local antibiotics often provide only temporary resolution. Limitations include incomplete biofilm removal, restricted access to implant threads, and the inability to regenerate lost bone and soft tissues [3,20]. Moreover, the rise of antibiotic resistance and the unpredictable outcomes of surgical interventions underscore the need for novel, biologically driven therapies.

Recent advances in biomaterials science have introduced multifunctional materials capable of addressing the multifactorial nature of peri implantitis. These include antimicrobial nanoparticles, immunomodulatory agents, bioactive ceramics, and smart hydrogels with controlled drug release [1,2,4–6]. By integrating antimicrobial, regenerative, and immunomodulatory functions, new generation biomaterials represent a paradigm shift in peri

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JCHR (2026) 16(3), 200-207 | ISSN:2251-6727

implantitis management, moving beyond disease control toward true tissue regeneration.

2. Objectives

To evaluate the current evidence on the therapeutic and regenerative potential of next-generation biomaterials in peri-implantitis management.

3. Methodology

A comprehensive literature search was performed in PubMed, Scopus, Web of Science, and Google Scholar using combinations of the keywords 'peri-implantitis,' 'biomaterials,' 'nanoparticles,' 'drug delivery systems,' and 'nanotechnology in implantology.' The search was restricted to English-language articles published between 2018 and 2025. Eligible studies included peer-reviewed original research, systematic reviews, and translational studies focusing on biomaterials for peri-implantitis management.

Narrative reviews, case reports, and non-indexed publications were excluded. Two authors independently screened titles and abstracts, followed by full text evaluation, with disagreements resolved by consensus. A total of 29 articles were included. Data were extracted on biomaterial type, mechanism of action, and reported outcomes, and synthesized qualitatively into thematic categories: antimicrobial nanoparticles, immunomodulatory agents, regenerative bioceramics, smart drug delivery systems, and AI assisted biomaterials. Preference was given to original studies and systematic reviews to ensure reliability and minimize bias

4. Discussion

Pathogenesis and Biological Basis for Regeneration

Peri-implantitis arises from a complex interplay between microbial biofilms and the host immune response.

Microbial colonization

The initial colonization of implant surfaces by oral microorganisms particularly anaerobic Gram-negative bacteria such as Porphyromonas gingivalis, Fusobacterium nucleatum, and Tannerella forsythia triggers a cascade of inflammatory events [9,10]. These pathogens form resilient biofilms that are difficult to eradicate and release virulence factors that stimulate host immune cells.

Innate immune response

The innate immune response is initiated by the recognition of pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs) via toll-like receptors (TLRs) on immune cells. This activates transcription factors such as NF-κB and MAPK, leading to the release of pro-inflammatory cytokines (e.g., IL-1β, IL-6, TNF-α) and matrix metalloproteinases (MMPs), which contribute to connective tissue degradation and osteoclastogenesis [11,12].

Stage	Key events	Key cellular and molecular components	Therapeutic targets
Microbial colonization	Biofilm formation on implant surface	Porphyromonas gingivalis; Fusobacterium nucleatum; Tannerella forsythia	Anti-biofilm agents; antimicrobial coatings
Innate immune activation	PAMP/DAMP recognition → TLR signaling → NF-κB/MAPK activation	Neutrophils; macrophages; dendritic cells	TLR modulators; inhibitors of NF-κB/MAPK
Pro-inflammatory mediator release	Elevated IL-1β, IL-6, TNF-α; MMP secretion	M1 macrophages; Th1 and Th17 cells	Cytokine blockers; MMP inhibitors
Tissue breakdown and osteoclastogenesis	Collagen degradation; osteoclast activation → bone loss	MMPs; RANKL; activated osteoclasts	RANKL inhibitors; MMP inhibitors; antiresorptives
Failure of resolution	Predominant M1 polarization; insufficient Treg/Th2 response	M1 macrophages; reduced M2 and Tregs	Macrophage repolarization; boost Treg/Th2 signals
Regenerative shift	Suppress infection and inflammation; recruit osteoprogenitors	M2 macrophages; IL-10; BMP-2; OPG	Immunomodulatory biomaterials; osteoinductive factors

(Table 1: stages of pathogenesis with their key cellular and molecular components and therapeutic targets)

Macrophages play a pivotal role in this process. The predominance of M1-polarized macrophages in peri-implant lesions promotes chronic inflammation and bone resorption, while M2 macrophages support resolution and tissue repair through the secretion of anti-inflammatory cytokines (IL-10, IL-4) and osteogenic factors such as BMP-2 and OPG [13,14]. Similarly, T-helper cell subsets (Th1, Th17) exacerbate inflammation and bone loss, whereas regulatory T cells (Tregs) and Th2 cells contribute to immune homeostasis and regeneration [15].

Regenerative shift

The biological basis for regeneration in peri-implantitis hinges on reversing this inflammatory microenvironment and promoting osteogenesis. This requires materials that can suppress pathogenic biofilms, modulate immune responses, and stimulate the recruitment and differentiation of osteoprogenitor cells. New-generation biomaterials such as ion-releasing bioceramics (e.g., cuprorivaite and hardystonite), antimicrobial hydrogels,

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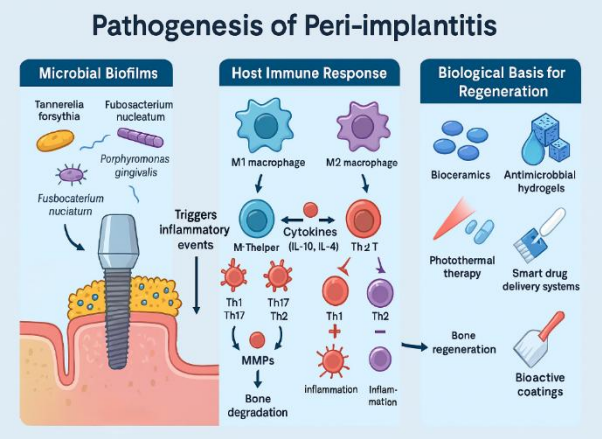
JCHR (2026) 16(3), 200-207 | ISSN:2251-6727

and nano-engineered surfaces have demonstrated the ability to create a favorable niche for bone regeneration while simultaneously controlling infection and inflammation [5,6,16].

Furthermore, the integration of photothermal therapy, smart drug delivery systems, and bioactive coatings enhances the precision and efficacy of these materials. By targeting both the microbial and host-mediated components of peri-implantitis, these biomaterials offer a holistic approach to restoring peri-implant health and achieving long-term implant stability.



(Figure 1: Illustration of pathogenesis of peri-implantitis)

Evolution of Biomaterials in Implantology

The history of implant biomaterials reflects a gradual shift from inert structural supports to multifunctional therapeutic platforms. Early implants were fabricated from commercially pure titanium and titanium alloys, valued for their mechanical strength, corrosion resistance, and biocompatibility [10]. While these materials achieved high osseointegration rates, they lacked intrinsic antimicrobial or regenerative properties, leaving them vulnerable to peri implant infections.

Surface modification techniques such as grit blasting, acid etching, anodization, and plasma spraying were introduced to enhance surface roughness and wettability, thereby improving osteoblast adhesion and bone integration [14]. However, these modifications also created niches for microbial colonization, inadvertently increasing infection risk.

The next phase of innovation focused on bioactivity. Hydroxyapatite and bioactive glass coatings were developed to enhance osteoconduction and bone bonding [2]. Subsequently, antimicrobial coatings incorporating silver, copper, and zinc ions were introduced to reduce bacterial adhesion and biofilm formation [2,10]. More recently, nanostructured surfaces and multifunctional coatings have been engineered to combine antimicrobial, immunomodulatory, and regenerative properties [14]. This evolution underscores the transition from passive implant materials to active participants in peri implant health.

New-Generation Biomaterials

New-generation biomaterials represent a paradigm shift in peri-implantitis management. These materials are designed to perform multiple biological functions simultaneously: suppress microbial colonization, modulate the host immune response, and promote tissue regeneration. Their development is informed by advances in nanotechnology, immunology, and tissue engineering.

Antimicrobial Functionality

Materials such as silver, copper, and zinc nanoparticles exhibit broad-spectrum antibacterial activity by disrupting bacterial membranes and interfering with metabolic pathways. The Cu-Zn-Ag composite hydrogel, for example, combines ion release with photothermal therapy to eliminate pathogens and reduce inflammation without antibiotics [7]. Antimicrobial peptides like LL37, immobilized on implant surfaces, offer targeted bacterial killing while preserving host cell viability [8].

Mechanistic Comparison of Implant Biomaterials

Material Phase	Antimicrobial Action	Immune Modulation	Osteogenesis Support	Clinical Relevance
Titanium / Titanium Alloys	✗ None	✗ Inert	✓ Supports osseointegration via surface contact	Widely used; high mechanical reliability
Surface-Modified Titanium (e.g., grit blasting, acid etching)	✗ May increase microbial niches	✗ No active modulation	✓ Enhanced osteoblast adhesion via roughness	Improved integration; higher infection risk
Bioactive Coatings (Hydroxyapatite, bioactive glass)	✗ Passive	✗ No immune effect	✓ Strong osteoconduction and bone bonding	Used in bone-deficient sites; coating stability varies
Antimicrobial Coatings (Silver, copper, zinc ions)	✓ Disrupts bacterial membranes, biofilm inhibition	✗ May cause cytotoxicity if uncontrolled	⚠ Variable — may impair osteoblasts at high doses	Used in high-risk infection zones; dose-sensitive
Multifunctional Nanostructures (Nano-surfaces, smart coatings)	✓ Targeted antimicrobial release, surface topography limits adhesion	✓ Promotes M2 macrophage polarization, reduces inflammation	✓ Stimulates osteoblasts, BMP-2, OPG pathways	Emerging standard in regenerative implantology

(Table 2: Mechanistic comparison of implant biomaterials)

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JCHR (2026) 16(3), 200-207 | ISSN:2251-6727

Immunomodulatory Potential

Beyond infection control, biomaterials are now engineered to influence immune cell behaviour. Chemically modified tetracyclines inhibit matrix metalloproteinases and reduce inflammatory cytokine production. Statins, bisphosphonates, and specialized pro-resolving mediators (SPMs) promote macrophage polarization toward the M2 phenotype, enhancing tissue repair and bone regeneration [9–11].

Regenerative Capability

Bioceramics such as hardystonite and cuprorivaite release osteogenic ions (Ca^{2+}, Zn^{2+}, SiO_3^{2-}) that stimulate mesenchymal stem cell differentiation and bone matrix formation. Injectable hydrogels and 3D-printed scaffolds provide structural support while delivering bioactive cues. These materials mimic the extracellular matrix and can be tailored to fit peri-implant defects, accelerating healing and osseointegration [12–14].

Smart Delivery Systems

Advanced drug delivery platforms microspheres, nanofibers, and pH-responsive coatings enable localized, sustained release of therapeutic agents. AI-assisted surface design and digital workflows further enhance precision and personalization, allowing clinicians to match biomaterial properties to patient-specific needs [15].

Together, these innovations redefine the role of biomaterials in implantology not as passive supports, but as active participants in healing, defense, and regeneration.

Mechanobiology and Host–Material Interface

The biological performance of an implant is not determined solely by its chemistry but also by its mechanical and structural cues. Mechanobiology explores how cells sense and respond to physical forces at the implant interface. Osteoblasts, fibroblasts, and immune cells interact with implant surfaces through integrins and focal adhesion complexes, which activate mechanotransduction pathways such as YAP/TAZ and MAPK [11]. These pathways regulate gene expression, influencing osteogenic differentiation, angiogenesis, and immune modulation.

The "race for the surface" concept emphasizes the competition between host cells and bacteria for early colonization of implant surfaces [10]. Surfaces with optimized roughness, wettability, and stiffness can favour osteoblast adhesion while discouraging bacterial attachment. However, excessive roughness may paradoxically increase microbial retention [14]. Recent studies show that nano engineered topographies can direct macrophage polarization toward an M2 phenotype, thereby reducing inflammation and enhancing tissue integration [8]. Thus, the host–material interface is not passive but a dynamic battlefield where mechanical and biological signals converge to determine implant success.

Functional Domain	Key Materials / Technologies	Mechanism of Action	Clinical Benefit
Antimicrobial Functionality	Silver, copper, zinc nanoparticles Cu-Zn-Ag composite hydrogel LL37 antimicrobial peptides	Disrupt bacterial membranes Photothermal therapy Targeted bacterial killing	Infection control without antibiotics Preserves host cell viability
Immunomodulatory Potential	Chemically modified tetracyclines Statins, bisphosphonates SPMs	Inhibit MMPs and cytokines Promote M2 macrophage polarization	Reduced inflammation Enhanced tissue repair and bone regeneration
Regenerative Capability	Hardystonite, cuprorivaite bioceramics Injectable hydrogels 3D-printed scaffolds	Release osteogenic ions (Ca^{2+}, Zn^{2+}, SiO_3^{2-}) Stimulate MSC differentiation Mimic ECM structure	Accelerated healing Improved osseointegration Defect-specific customization
Smart Delivery Systems	Microspheres, nanofibers pH-responsive coatings AI-assisted surface design	Localized, sustained drug release Digital personalization of biomaterial properties	Precision therapy Reduced systemic side effects Patient-specific outcomes

(Table 3: New generation biomaterials and technologies with their mechanism of action)

Nanotechnology and Smart Responsive Systems

Nanotechnology has revolutionized implantology by enabling precise control over surface features and drug delivery systems. Nanostructured titanium dioxide, silver, and copper coatings exhibit potent antimicrobial activity by disrupting bacterial membranes and generating reactive oxygen species [2,27]. These coatings also enhance osteoblast proliferation and angiogenesis, creating a dual antimicrobial–regenerative effect.

Smart responsive systems represent the next frontier. pH sensitive hydrogels can release antimicrobials selectively in acidic peri implant pockets, minimizing systemic exposure [6]. Photothermal composites, such as the Cu Zn Si hydrogel, generate mild heat under near infrared light, killing pathogens while simultaneously releasing osteogenic ions [1]. Nanofibers and microspheres allow

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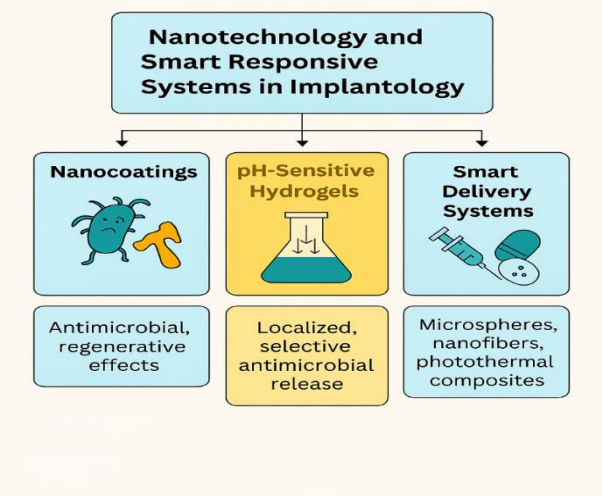
sustained release of antibiotics, growth factors, or immunomodulators directly at the implant site [21,24]. Together, these technologies transform implants from inert devices into active therapeutic platforms capable of adapting to the peri implant microenvironment.

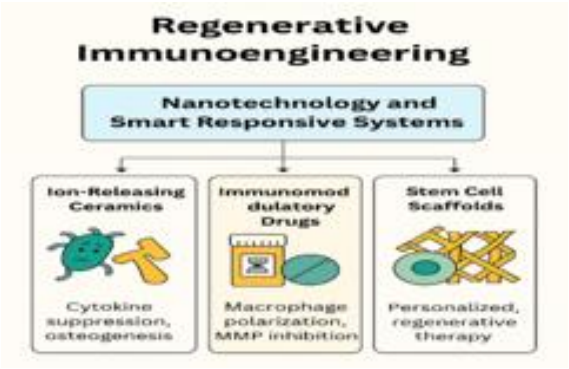


(Figure 2: Illustration of nanotechnology and smart responsive systems in implantology)

Regenerative Immunoengineering

Traditional regenerative approaches focused on scaffolds and growth factors, but current strategies recognize the immune system as a central player in tissue healing. Chronic inflammation in peri implantitis is driven by M1 macrophages and Th17 cells, which perpetuate cytokine release and osteoclast activation [7]. Regenerative Immunoengineering seeks to reprogram this hostile environment into one conducive to healing.

Ion releasing ceramics such as hardystonite and cuprorivaite release Zn^{2+}, Cu^{2+}, and SiO_3^{2-} ions that not only stimulate osteoblast differentiation but also suppress pro inflammatory cytokines [4,5]. Statins and chemically modified tetracyclines inhibit matrix metalloproteinases and promote M2 macrophage polarization [7,8]. Specialized pro resolving mediators (SPMs) further enhance resolution pathways, reducing tissue destruction while supporting regeneration [8]. Scaffold based delivery of stem cells combined with immunomodulatory agents represents a promising avenue for personalized regenerative therapy. This dual focus on immune modulation and tissue regeneration marks a paradigm shift in peri implantitis management.

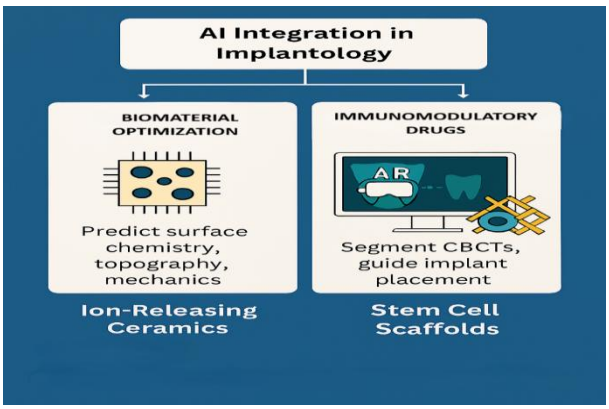


(Figure 3: Illustration of regenerative Immunoengineering)

AI and Computational Biomaterial Design

Artificial intelligence (AI) and computational modelling are increasingly applied to biomaterial design and implant planning. Machine learning algorithms can predict biomaterial performance based on surface chemistry, topography, and mechanical properties, accelerating the discovery of optimal compositions [28]. Computational simulations also model drug release kinetics and host–material interactions, reducing reliance on trial-and-error experimentation.

In clinical practice, AI driven segmentation of CBCT scans enables precise virtual modelling of peri implant defects and guides the design of patient specific scaffolds [29]. Augmented reality (AR) and AI assisted surgical navigation further enhance precision in implant placement. By integrating digital workflows with biomaterial science, clinicians can tailor therapies to individual patients, moving toward a future of personalized implantology.



(Figure 4: Illustration of AI integration in implantology)

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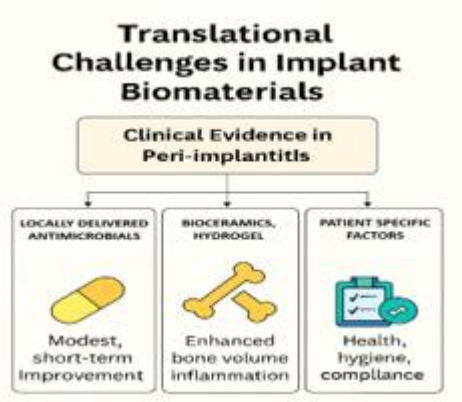
JCHR (2026) 16(3), 200-207 | ISSN:2251-6727

Translational and Clinical Evidence

Despite promising preclinical results, clinical translation remains challenging. Randomized controlled trials (RCTs) evaluating locally delivered antimicrobials such as minocycline and doxycycline have shown modest improvements in probing depth and bleeding indices, but long-term stability is inconsistent [21,24,25]. Chlorhexidine chips and tetracycline fibers have demonstrated short term benefits but limited regenerative potential [22,23].

Animal studies with bioceramic scaffolds and multifunctional hydrogels report enhanced bone volume and reduced inflammation [1,4]. However, large scale human trials are scarce. Patient specific factors including systemic health, oral hygiene, and compliance with maintenance therapy significantly influence outcomes [19]. Thus, while biomaterials hold great promise, robust clinical validation is essential before widespread adoption.

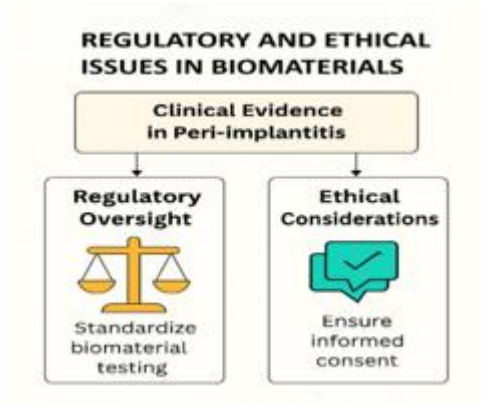


(Figure 5: Illustration of translation challenges in implant biomaterials)

Regulatory and Ethical Perspectives

The introduction of advanced biomaterials raises important regulatory and ethical considerations. Nanoparticles and ion releasing ceramics must undergo rigorous biocompatibility and toxicity testing to ensure long term safety [20]. Regulatory frameworks vary globally, creating challenges for standardization and approval.

Ethically, clinicians must ensure informed consent when offering novel therapies, particularly those involving AI assisted planning or experimental biomaterials [27]. Cost and accessibility remain major barriers, as advanced biomaterials and digital workflows may be prohibitively expensive for many patients [19]. Equitable access and transparent reporting of outcomes are essential to prevent disparities in care.



(Figure 6: Illustration of regulatory and ethical issues in biomaterials)

Knowledge Gaps and Future Directions

Despite rapid progress, several gaps remain:

•Limited long-term clinical data on multifunctional biomaterials

•Incomplete understanding of host–material immune interactions

•Need for scalable, cost-effective manufacturing of smart systems

•Lack of personalized biomaterial platforms tailored to patient risk profiles

Future research should focus on:

•Multi-omics approaches to understand host responses

•AI-guided biomaterial optimization

•Integration of immunotherapy with regenerative scaffolds

•Development of bio responsive materials for real-time feedback

5. Conclusion

New generation biomaterials represent a transformative approach to peri implantitis management. By combining antimicrobial, immunomodulatory, and regenerative functions, these materials address the multifactorial nature of the disease. Advances in nanotechnology, smart

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responsive systems, and regenerative Immunoengineering have redefined implants as active therapeutic platforms rather than passive devices [1,2,4,7,8].

The integration of AI and computational modelling further enhances personalization and precision [28,29]. However, challenges remain in clinical validation, regulatory approval, and equitable access. Future progress will depend on interdisciplinary collaboration, robust clinical trials, and ethical implementation. Ultimately, biomaterial driven strategies hold the potential to shift peri implantitis therapy from disease control to true regeneration and long-term implant stability.

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