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REVIEW ARTICLE

Personalized Nanomedicine for Children's Teeth: Advancing Early Diagnosis, Targeted Therapy, and Remineralization in Pediatric Dentistry

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ABSTRACT

Dental caries, enamel defects, and pulp-related conditions remain important challenges in pediatric dentistry, where developing dentition, behavioral factors, and substantial inter-individual variability can limit the effectiveness of conventional uniform treatment approaches. Personalized nanomedicine has emerged as a promising strategy for improving pediatric oral healthcare by integrating nanotechnology with patient-specific biological, clinical, environmental, and behavioral information. This narrative review summarizes current and emerging nano-enabled approaches for early diagnosis, targeted therapy, and remineralization of children's teeth. Nano-biosensors, nano-enhanced imaging modalities, and chairside diagnostic platforms may facilitate the early detection and monitoring of oral disease through sensitive analysis of salivary biomarkers and structural changes. Therapeutically, antimicrobial nanoparticles, biofilm-disrupting agents, and nanocarrier-based drug-delivery systems may enable localized and controlled treatment while reducing off-target effects. In addition, nano-hydroxyapatite, calcium/phosphate nanocarriers, bioactive nanocomposites, and nanoparticle-enhanced sealants show potential for biomimetic remineralization, prevention of caries progression, and preservation of primary dentition. Regenerative strategies involving self-assembling peptides, hydrogels, nanostructured scaffolds, and stem cell-based approaches may further support enamel and dentin repair. Artificial intelligence can complement these technologies by integrating clinical, genetic, microbiome, and behavioral data for risk stratification, individualized treatment planning, and response monitoring. Nevertheless, translation into routine care requires rigorous pediatric-specific evidence regarding long-term safety, biocompatibility, pharmacokinetics, ethical acceptability, data privacy, and regulatory compliance. Multidisciplinary collaboration and well-designed clinical trials are essential to establish safe, effective, and equitable personalized nanomedicine approaches in pediatric dentistry.

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INTRODUCTION

Dental caries and other tooth-related conditions remain among the most prevalent chronic diseases in children worldwide, affecting their nutrition, growth, school performance, and overall quality of lif [1, 2]. Despite widespread use of fluoride, sealants, and conventional restorative care, a substantial proportion of children continue to experience early childhood caries, enamel defects, and pulp pathology that require repeated interventions throughout growth. These challenges are compounded by behavioral factors, dietary patterns, socio-economic disparities, and unique features of the developing dentition, such as thinner enamel and larger pulp chambers, which render children's teeth more vulnerable to rapid disease progression and invasive treatment [1, 3, 4].

Traditional preventive and therapeutic strategies in pediatric dentistry are largely "one-size-fits-all," with limited adaptation to the individual child's biological, environmental, and behavioral risk profile. However, inter-individual differences in saliva composition, oral microbiome, host response, enamel structure, and genetic susceptibility can substantially influence disease onset, progression, and response to treatment [5]. As a result, some children remain at high risk despite standard preventive measures, while others may be exposed to unnecessary interventions. This reality underscores the need for personalized approaches that integrate diagnostic information, risk stratification, and tailored therapies to maintain and restore oral health in growing patients, ideally with minimally invasive procedures that preserve tooth structure and reduce treatment-related anxiety [6, 7].

Nanomedicine offers a compelling framework to realize such personalization in pediatric dentistry by enabling sensitive early diagnosis, targeted delivery of therapeutic agents, and biomimetic remineralization of enamel and dentin. Nanostructured materials and nanoscale carriers can be engineered to interact selectively with cariogenic biofilms, demineralized tissues, and specific molecular or microbial signatures, thereby enhancing efficacy while limiting systemic exposure and off-target effects [8, 9]. Likewise, nano-enabled diagnostic platforms including salivary biosensors, nano-enhanced imaging, and chairside point-of-care tests have the potential to detect early changes in the oral environment before clinically visible lesions appear [6]. Together, these advances position personalized nanomedicine as a promising paradigm for advancing early diagnosis, targeted therapy, and remineralization in pediatric dentistry, and warrant a comprehensive review of current evidence, challenges, and future directions [2, 3, 8].

FOUNDATIONS OF PERSONALIZED NANOMEDICINE IN PEDIATRIC DENTISTRY

Personalized nanomedicine in pediatric dentistry represents a transformative approach that leverages nanotechnology to address the unique challenges of children's oral health. This field aims to enhance early diagnosis, targeted therapy, and remineralization of children's teeth by tailoring treatments to individual needs. The integration of precision medicine principles with nanotechnology offers promising solutions for pediatric dental care, although it also presents specific challenges due to the distinct physiological and developmental characteristics of children. This response explores the foundational concepts of personalized nanomedicine in pediatric dentistry, focusing on precision medicine and the challenges in children's oral environments.

Personalized medicine in dentistry involves tailoring treatments based on a child's unique genetic, environmental, and clinical profile. This approach is facilitated by advancements in molecular tools and genomic sequencing, allowing for highly precise healthcare interventions [10]. Nanotechnology enhances the precision of dental treatments by utilizing nanoparticles for targeted drug delivery, improving drug solubility and stability, and enabling controlled release. These properties are particularly beneficial in pediatric dentistry, where traditional formulations often fall short [8, 11]. The application of nanotechnology in pediatric dentistry requires careful consideration of safety and regulatory standards. The unique properties of nanomaterials necessitate thorough evaluation to ensure their safe use in children [8, 11]. Children's growth and physiological differences from adults pose challenges in pharmacokinetics and pharmacodynamics, necessitating pediatric-specific formulations. Nanotechnology offers solutions by improving drug delivery and reducing dosing frequency, but these must be adapted to children's unique needs [12, 13]. Pediatric dentistry faces challenges such as poor taste and dosage flexibility of traditional medications, which can lead to non-compliance. Nanotechnology can address

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these issues by enhancing the palatability and effectiveness of treatments [11]. Nanotechnology enables the development of advanced therapies, such as nanorobots for precise dental procedures and nanocomposites for rapid tooth restoration. These innovations promise to improve oral health outcomes in children by providing more effective and less invasive treatments [14].

While personalized nanomedicine holds significant potential for advancing pediatric dentistry, it is essential to consider the broader implications and challenges. The integration of nanotechnology in dental care requires interdisciplinary collaboration to overcome regulatory hurdles, ensure long-term safety, and address ethical considerations in pediatric clinical trials. Additionally, the focus on adult markets often overshadows the specific needs of children, highlighting the need for dedicated research and development in pediatric nanomedicine [11, 12].

NANOTECHNOLOGY FOR EARLY DIAGNOSIS OF PEDIATRIC DENTAL DISEASES

Nanotechnology is revolutionizing pediatric dentistry by enabling early diagnosis and personalized treatment of dental diseases in children. This approach leverages advanced nanoscale technologies to enhance diagnostic accuracy and therapeutic outcomes. The integration of nanotechnology in pediatric dentistry is particularly promising in areas such as nano-biosensors, enhanced imaging techniques, and point-of-care diagnostic platforms. These innovations are paving the way for more precise and effective dental care for children, ensuring early intervention and improved oral health outcomes.

Nano-biosensors are highly sensitive and selective, capable of detecting minute quantities of analytes in saliva, which is a non-invasive and easily accessible diagnostic fluid. These sensors can identify biomarkers for dental caries, periodontal disease, and other oral conditions, facilitating early diagnosis and monitoring of disease progression. The integration of wireless technology with nanosensors enhances their potential for real-time, point-of-care applications, making them suitable for pediatric use [15, 16].

Nanotechnology enhances imaging modalities by improving resolution and contrast, which is crucial for detecting early-stage dental diseases in children. Techniques such as nano-enhanced optical and fluorescence imaging provide detailed visualization of dental structures, aiding in the accurate assessment of dental caries and other conditions [14, 17]. Radiographic imaging benefits from nanotechnology through the development of materials that reduce radiation exposure while maintaining image quality, ensuring safer diagnostic procedures for children [17].

Nanotechnology enables the development of compact, efficient diagnostic platforms that can be used chairside, providing immediate results and facilitating timely intervention.

These platforms utilize lab-on-chip technologies and nanosensors to perform comprehensive analyses of salivary biomarkers, offering a practical solution for pediatric dental diagnostics. The portability and ease of use of these platforms make them ideal for pediatric settings, where quick and non-invasive diagnostics are essential [15].

While nanotechnology holds great promise for advancing pediatric dental care, challenges such as the need for long-term clinical trials and standardized regulations remain. Addressing these issues is crucial for the widespread adoption and integration of nanotechnology in clinical practice, ensuring safe and effective dental care for children.

TARGETED NANO-THERAPIES FOR CHILDREN'S TEETH

The integration of nanotechnology into pediatric dentistry offers promising advancements in the diagnosis, treatment, and prevention of dental diseases in children. Personalized nanomedicine, particularly through targeted nano-therapies, is poised to revolutionize pediatric dental care by enhancing early diagnosis, delivering targeted therapies, and promoting remineralization. This approach leverages the unique properties of nanoparticles to address specific dental conditions in children, offering more effective and less invasive treatment options. The following sections explore the key areas where targeted nano-therapies are making significant impacts in pediatric dentistry.

Biofilm Disruption: Nanoparticles have shown significant potential in disrupting oral biofilms, which are major contributors to dental caries and periodontal diseases. Their small size and unique properties allow them to penetrate biofilms and target bacteria in otherwise inaccessible areas, enhancing antimicrobial efficacy [18, 19].

Antimicrobial Properties: Various nanoparticles, such as silver and chitosan, exhibit strong antimicrobial properties. Silver

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nanoparticles, for instance, have been shown to reduce biofilm formation by up to 85%, although they may pose cytotoxicity risks at higher concentrations [14]. Chitosan nanoparticles, on the other hand, offer antibacterial, antifungal, and anti-inflammatory properties, making them suitable for pediatric applications [20].

Nanodrug delivery systems, such as liposomes and polymeric nanoparticles, are being developed to target dental caries and periodontal diseases. These systems enhance drug bioavailability and provide controlled release, improving therapeutic outcomes while minimizing side effects [21, 22]. Polysaccharide-based nanoparticles, such as those made from chitosan and alginate, are particularly promising for pediatric dentistry due to their biocompatibility and low toxicity. These materials can be tailored for specific drug delivery applications, offering a safer alternative to synthetic polymers [23].

Nanotechnology facilitates minimally invasive treatments by enabling precise targeting of diseased tissues, reducing the need for extensive surgical interventions. This is particularly beneficial in pediatric patients, where preserving healthy tissue is crucial [6]. Nanoparticles, such as hydroxyapatite, are used to promote remineralization of enamel and repair of dental tissues. These particles can integrate with the tooth structure, enhancing its strength and resistance to deca [6].

While the potential of targeted nano-therapies in pediatric dentistry is immense, there are challenges and considerations that must be addressed. The long-term safety of nanomaterials in developing organisms remains a concern, as does the need for scalable manufacturing and regulatory approval [11]. Additionally, ethical considerations in pediatric clinical trials must be carefully managed to ensure the safety and efficacy of these innovative treatments. Despite these challenges, the continued research and development in this field hold promise for significantly improving pediatric dental care outcomes.

NANOMATERIALS FOR REMINERALIZATION AND ENAMEL/DENTIN REGENERATION

Nanomaterials have emerged as a promising avenue for the remineralization and regeneration of enamel and dentin, particularly in pediatric dentistry. These materials offer unique properties that enable them to mimic natural dental tissues and provide targeted therapeutic effects. This review explores the role of nano-hydroxyapatite, bioactive nanocomposites, and strategies for guided repair in the context of personalized nanomedicine for children's teeth.

Nano-hydroxyapatite is structurally similar to natural enamel, making it an effective agent for biomimetic remineralization. It can replace lost mineral content in enamel, enhancing its hardness and resistance to demineralization [24]. Studies have shown that nHAp can significantly improve the hardness and calcium/phosphate ratio of demineralized enamel, outperforming other agents like bioactive glass and calcium phosphate nanoparticles [25]. Calcium/Phosphate Nanocarriers: These nanocarriers are designed to deliver calcium and phosphate ions directly to the demineralized areas, promoting remineralization. They maintain a supersaturated environment of these ions, which is crucial for the remineralization process. Eggshell-derived hydroxyapatite nanoparticles, for instance, have demonstrated effectiveness in dentin remineralization by releasing essential ions and buffering against acidic conditions [26].

Bioactive nanocomposites and nanotechnology-enhanced sealants represent promising preventive and restorative approaches in pediatric dentistry. Bioactive nanocomposites can release therapeutic ions that interact with dental tissues, supporting remineralization and potentially promoting pulp healing. Their application is particularly valuable for preserving primary dentition and limiting caries progression during early oral development [27]. Moreover, incorporating nanoparticles into restorative materials may improve mechanical performance and biocompatibility, providing potential advantages over conventional composite materials [28]. Similarly, nanoparticle-based sealants create a protective barrier against cariogenic challenges while releasing remineralizing ions. By helping preserve the structural integrity of primary teeth, these sealants may contribute to appropriate oral function and development in pediatric patients [27].

Biomimetic and regenerative strategies are emerging as innovative approaches for the repair of enamel and dentin in pediatric dentistry. Biomimetic methods, including self-assembling peptides and hydrogel-based systems, are designed to replicate aspects of enamel's hierarchical architecture and provide scaffolds that guide mineral deposition during hard-tissue repair. In parallel, stem cell-based regeneration remains largely experimental but may offer a long-term restorative strategy by employing stem or progenitor cells to regenerate damaged dental

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tissues, including enamel and dentin. However, translation of these approaches into routine clinical practice is constrained by important challenges, particularly reproducing the complex mechanical properties and structural organization of natural enamel. Further research and interdisciplinary collaboration will therefore be essential to optimize these systems and establish clinically effective regenerative therapies for children [29].

While nanomaterials offer significant advantages for dental regeneration, there are challenges related to their clinical application. Issues such as batch heterogeneity, rapid oral clearance, and biosafety need to be addressed to ensure the safe and effective use of these materials in pediatric dentistry [30]. Additionally, integrating these technologies with advancements in AI and bioprinting could further enhance their efficacy and personalization in dental treatments.

PERSONALIZATION STRATEGIES AND CLINICAL INTEGRATION

Personalized nanomedicine in pediatric dentistry is an emerging field that aims to enhance early diagnosis, targeted therapy, and remineralization of children's teeth. This approach leverages advanced technologies such as AI, genetic profiling, and nanotechnology to tailor dental care to the unique needs of each child. By integrating these technologies, pediatric dentistry can move towards more precise, effective, and individualized treatment plans. The following sections explore key strategies for personalization and clinical integration in this context. The principal nano-enabled diagnostic, therapeutic, regenerative, and AI-assisted strategies relevant to personalized pediatric dental care are summarized in Table 1.

Personalized pediatric dental care relies on stratifying patients according to individual biological, environmental, and behavioral risk factors. This process may incorporate genetic predispositions, environmental exposures, and lifestyle habits to identify children who are more susceptible to specific dental conditions and may benefit from early, tailored preventive interventions [32]. Genetic profiling can further support treatment selection by identifying markers associated with a child's likely response to

Table 1. Nano-enabled platforms and personalization strategies for early diagnosis, targeted therapy, and remineralization in pediatric dentistry.

Clinical objective	Platform/strategy	Main pediatric use	Main limitation	References
Early diagnosis	Salivary nano-biosensors; lab-on-chip devices	Early caries and biomarker detection	Validation and cost	
Imaging	Nano-enhanced optical and radiographic imaging	Detection of early lesions	Standardization and safety	[14, 17]
Biofilm control	Silver and chitosan nanoparticles	Antimicrobial and antibiofilm therapy	Cytotoxicity and resistance	[18-20]
Drug delivery	Liposomes; polymeric nanoparticles	Local drug delivery and controlled release	Oral retention and safety	[21-23, 31]
Remineralization	Nano-hydroxyapatite; calcium/phosphate carriers	Enamel and dentin remineralization	Long-term effectiveness	[24-26]
Prevention/restoration	Bioactive nanocomposites; nano-sealants	Caries prevention and primary-tooth preservation	Material durability	[27, 28]
Regeneration	Peptides, hydrogels, and nanoscaffolds	Guided enamel/dentin repair	Limited clinical translation	[29, 30]
AI personalization	AI imaging and decision-support systems	Risk assessment and treatment planning	Data privacy and validation	[32-34]
Clinical translation	Multidisciplinary care workflow	Personalized treatment delivery	Regulation and pediatric trials	[11, 35-41]

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particular dental therapies or preventive strategies [33]. In addition, the oral microbiome has a central role in oral health and disease; nanomedicine-based approaches aimed at modulating microbial communities may enable personalized prevention and treatment based on each child's distinct microbial profile. Behavioral and psychological factors should also be considered, as they influence anxiety, cooperation, and adherence to care. In this context, artificial intelligence enabled tools may assist clinicians in behavior management, reduce treatment-related anxiety, and improve compliance with individualized treatment plans [34].

Artificial intelligence is increasingly being incorporated into pediatric dentistry to support diagnosis, individualized treatment planning, and longitudinal monitoring of therapeutic outcomes. AI-based image-analysis systems can assist in detecting dental abnormalities from radiographic and other clinical images, potentially enabling earlier identification of disease and more accurate treatment planning than conventional assessment alone [34]. In addition, AI-driven platforms can integrate multidimensional patient data including genetic, oral microbiome, and behavioral information to generate personalized treatment plans tailored to each child's clinical needs and thereby optimize therapeutic outcomes [33]. AI systems may also facilitate continuous monitoring of treatment responses by providing real-time feedback to dental professionals, allowing timely modifications to treatment protocols and supporting improved outcomes in pediatric patients [37].

Nanoparticle-based therapies offer a promising route for delivering therapeutic agents directly to affected oral sites, potentially improving treatment efficacy while limiting off-target effects. In pediatric dentistry, these systems may be especially valuable for remineralization strategies and antimicrobial interventions, where localized delivery can support the prevention and management of caries-related disease [31]. However, clinical implementation requires a structured workflow encompassing comprehensive patient assessment, appropriate therapy selection, and continuous monitoring of treatment responses. Successful adoption also depends on adequate training of dental professionals in nanotechnology- and AI-enabled tools to support the delivery of personalized care [35]. Furthermore, the integration of personalized nanotherapies must address regulatory and ethical considerations, including patient privacy, data protection, and informed consent, particularly because pediatric patients represent a vulnerable population. Compliance with these requirements is essential for the responsible and effective translation of these technologies into clinical pediatric dentistry [32].

While personalized nanomedicine offers significant potential for improving pediatric dental care, challenges remain in its widespread implementation. These include the need for robust clinical evidence, cost considerations, and the development of standardized protocols for integrating these advanced technologies into everyday practice. Addressing these challenges will be essential for realizing the full benefits of personalized nanomedicine in pediatric dentistry.

SAFETY, ETHICAL, AND REGULATORY CONSIDERATIONS IN CHILDREN

The integration of nanotechnology into pediatric dentistry, particularly for personalized nanomedicine targeting children's teeth, presents significant opportunities for advancing early diagnosis, targeted therapy, and remineralization. However, this innovative approach also necessitates careful consideration of safety, ethical, and regulatory aspects. These considerations are crucial to ensure that the benefits of nanotechnology are realized without compromising the well-being of young patients. The following sections delve into the biocompatibility and long-term safety of nanomaterials, ethical issues including parental consent, and the regulatory landscape for pediatric nanodental products.

The unique physiological characteristics of children, such as their developing organs and systems, make them particularly sensitive to the potential toxicological effects of nanomaterials. This necessitates rigorous safety evaluations of engineered nanoparticles (ENPs) used in pediatric dentistry [36]. Long-term safety concerns include the potential for nanoparticles to accumulate in the body, leading to unforeseen health issues. Preclinical studies are essential to assess these risks before clinical application [38]. The biocompatibility of nanomaterials, such as polymer-based drug delivery systems, is critical. These systems must be designed to minimize adverse reactions while maximizing therapeutic efficacy [8].

Ethical considerations in pediatric research are complex due to the vulnerability of children

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as research subjects. Ensuring informed consent from parents or guardians is paramount, alongside assent from the child when appropriate [39, 40]. A thorough risk-benefit analysis tailored to the pediatric population is necessary. This involves evaluating the potential benefits of nanodental products against the risks, considering the unique physiological and developmental stages of children. Ethical frameworks must be adhered to, ensuring that research and clinical applications respect the autonomy and rights of child participants [41].

The regulatory environment for nanomedicine in pediatrics is evolving, with guidelines emphasizing the need for safety and efficacy testing specific to children. This includes adherence to FDA mandates for pediatric testing [40]. Regulatory challenges include establishing clear pathways for the approval of nanodental products, which must address both the innovative nature of nanotechnology and the specific needs of pediatric patients [11]. Collaboration between regulatory bodies, researchers, and industry stakeholders is essential to develop comprehensive guidelines that ensure the safe integration of nanotechnology into pediatric dentistry [38].

While the potential of nanotechnology in pediatric dentistry is vast, it is crucial to address these safety, ethical, and regulatory considerations to ensure that the benefits outweigh the risks. The development of robust ethical frameworks and regulatory guidelines will be instrumental in facilitating the safe and effective use of nanodental products for children. This approach not only protects young patients but also fosters trust and acceptance of nanotechnology in pediatric healthcare.

FUTURE DIRECTIONS AND CONCLUSIONS

The future of personalized nanomedicine in pediatric dentistry is expected to be driven by advances in smart nanomaterials, theranostic systems, and AI-based personalization. Smart nanomaterials can respond to oral environmental stimuli, such as pH fluctuations and bacterial metabolites, enabling targeted antimicrobial activity, biofilm control, localized drug delivery, and enhanced remineralization. In parallel, nanostructured scaffolds and bioactive materials may support the regeneration and repair of dental tissues. Theranostic platforms, which combine diagnostic and therapeutic functions, could further enable early disease detection, real-time treatment monitoring, and adaptive interventions for dental caries and other oral conditions in children.

AI is likely to play a central role in optimizing these technologies by integrating clinical, genetic, microbiome, behavioral, and other multi-omics data to generate individualized treatment strategies. Machine-learning models may help predict patient responses, optimize nanocarrier properties, and support the selection of appropriate preventive or therapeutic interventions. However, important research gaps remain, particularly regarding the long-term safety, biocompatibility, pharmacokinetics, and pharmacodynamics of nanomaterials in pediatric populations. Because children differ substantially from adults in terms of physiological development and metabolism, pediatric-specific evidence is essential before these technologies can be widely implemented.

Future translation into clinical practice will require well-designed randomized clinical trials comparing nanotechnology-based treatments with established conventional approaches. Collaboration among dental clinicians, nanomaterials scientists, AI specialists, ethicists, and regulatory authorities will be necessary to develop standardized protocols, safety-evaluation methods, and appropriate regulatory frameworks. Although personalized nanomedicine has substantial potential to improve early diagnosis, targeted therapy, tissue regeneration, and preventive care, its successful adoption will also depend on addressing ethical concerns, informed consent, patient-data privacy, regulatory compliance, and equitable access to advanced pediatric dental technologies.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest related to the research, authorship, or publication of this manuscript. All authors have disclosed any financial or personal relationships that could potentially influence or bias the work presented.

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