

Review

Not peer-reviewed version

Seeking Endurance: Designing Smart Dental Materials for Tooth Restoration

[Tasneem Alluhaidan](#) , Masoumah Qaw , Isadora Garcia , Carolina Montoya , [Santiago Orrego](#) , [MARY MELO](#) *

Posted Date: 29 July 2024

doi: 10.20944/preprints202407.2234.v1

Keywords: Dental caries; Dental resins; stimuli-responsive; smart materials; bioactive



Preprints.org is a free multidiscipline platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This is an open access article distributed under the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Review

Seeking Endurance: Designing Smart Dental Materials for Tooth Restoration

Tasneem Alluhaidan ¹, Masoumah Qaw ¹, Isadora Martini Garcia ², Carolina Montoya ^{3,4}, Santiago Orrego ^{3,4} and Mary Anne Melo ^{1,2,*}

¹ Dental Biomedical Sciences Ph.D. Program, University of Maryland School of Dentistry, Baltimore, MD, 21201, USA.

² Division of Cariology & Operative Dentistry, Department of Comprehensive Dentistry, University of Maryland School of Dentistry, Baltimore, MD, 21201, USA.

³ Department of Oral Health Sciences, Kornberg School of Dentistry, Temple University, Philadelphia, Pennsylvania 19140, United States

⁴ Bioengineering Department, College of Engineering, Temple University. Philadelphia, Pennsylvania 19122, United States

* Correspondence: mmelo@umaryland.edu

Abstract: Smart Dental Materials refer to materials used in dentistry with additional functionality to enhance treatment outcomes, which may improve oral health. Smart materials for dental restorations can react to stimuli such as a specific temperature, a different pH, or mechanical stress, repair small cracks or damage by themselves, and interact beneficially with biological surroundings. For example, they might release ions and promote tooth remineralization or have antibacterial properties to prevent bacterial growth. Others can have enhanced mechanical properties like strength and wear resistance to ensure these materials can withstand the daily masticatory forces. This review presents our current comprehension of smart dental materials designed for tooth restoration. We focused on what these materials need to be effective, like durability, biocompatibility, and aesthetic requests, besides identifying new ideas for their design. A detailed analysis of the current challenges faced in formulating these materials, such as the balance between enough ions released with proper physicochemical properties and achieving the desired biological response, was discussed. We also discussed how these cutting-edge technologies are being leveraged to overcome existing limitations, creating more dental materials with potential clinical translation. The review also discusses the practical challenges in implementation and the prospects for these materials in dentistry.

Keywords: dental caries; dental resins; stimuli-responsive; smart materials; bioactive

1. Introduction

Dental resin composites have become a cornerstone biomaterial in restorative dentistry, offering aesthetic and functional solutions for various dental needs [1]. However, despite their widespread clinical use and ongoing advancements, these materials are not without shortcomings [2].

Failure of resin composite restorations is multi-faceted, influenced by a combination of material properties, clinical application, and patient factors [3]. Secondary caries is one of the primary reasons for the failure of dental composite restorations [4,5]. Composite restorations are subjected to a dynamic and complex oral environment, including an unbalanced microbiome, mechanical stresses, fluctuating temperatures, and chemical exposure [4]. These factors can lead to microcracking, wear, and degradation of the resin matrix, compromising the longevity of restorations [2,3]. The polymerization shrinkage during the curing process can also introduce internal stresses and marginal gaps, making areas more prone to secondary caries [6].

Polymers are susceptible to hydrolysis, and this would not be different for dental resin composites, which are immersed in saliva often exposed to fluctuating pH levels and temperatures,

speeding up the softening, swelling, degradation, and biodegradation processes [7,8]. The degradation of the resin composites over time in the oral environment generates by-products essential for bacterial growth and biofilm development on the teeth/material interface [4,5], which can exacerbate the development of secondary caries.

The inherent challenges resin composites face in the oral environment are illustrated in **Figure 1**. Inadequate handling and placement techniques can lead to voids, poor adhesion, and improper curing, all of which compromise the integrity of the restoration [9]. Additionally, patient factors such as oral hygiene practices, diet, occlusal forces, and parafunctional habits significantly affect the lifespan of these restorations [2]. Systematic reviews have consistently emphasized the multifactorial nature of resin composite failures, underscoring the need for comprehensive material development and clinical application approaches [2,5,10].

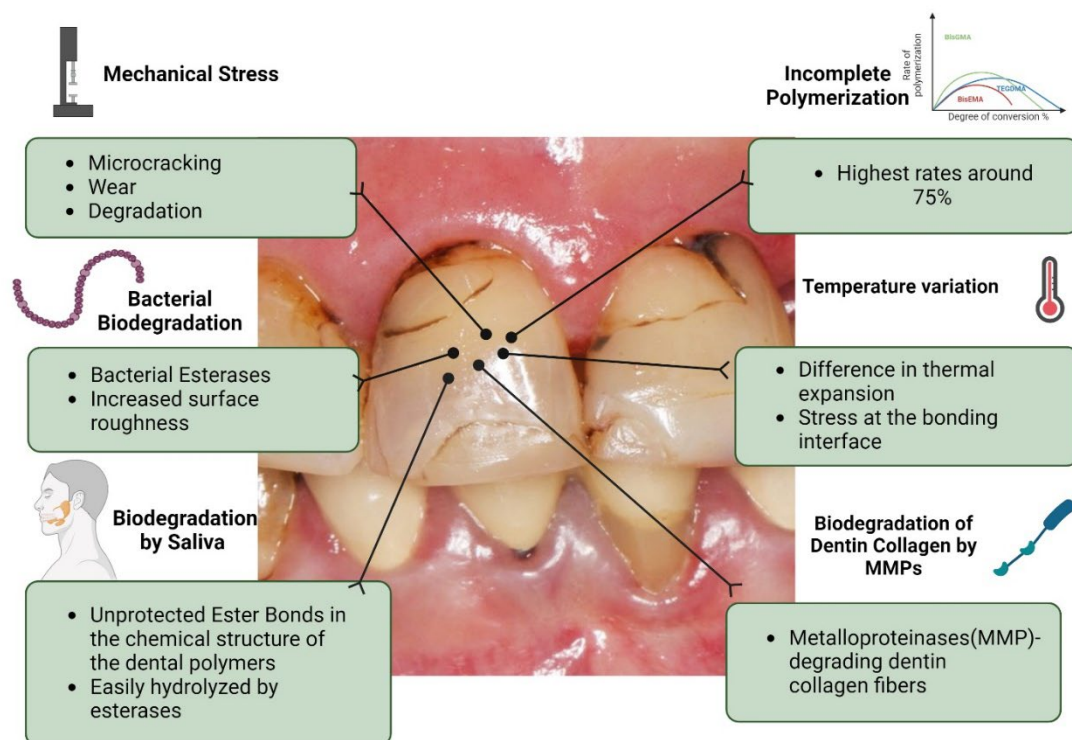


Figure 1. Schematic drawing illustrating the inherent challenges encountered in resin composites, portraying three primary problems: mechanical stress, biodegradation by saliva and bacteria, and incomplete polymerization.

2. The Dental Resin Landscape—What Is on The Horizon?

Despite the steps taken to improve the clinical durability of restorations, prevent hydrolytic degradation, deter bacterial attacks, and enhance the mechanical properties of the hybrid layer, several challenges inherent to resin composites and dentin adhesives persist [11–13]. Together, these challenges impact the material's ability to maintain its functional and aesthetic properties over time when applied directly toward a tooth cavity [14]. In response, the dental research field has seen the proposal of multiple strategies to overcome these barriers, paving the way for developing "smart" dental resin composites [15,16]. The landscape of resin composites is undergoing a significant transformation, marked by the emergence of innovative bioactive biomaterials and approaches seeking to enhance the effectiveness and longevity of restorations [15,17].

The core of dental resin composites comprises a basic formulation of filler particles, a monomeric resin matrix, silane coupling agents, and photoinitiators [1]. The filler particles provide strength and wear resistance [1,18]. At the same time, the resin matrix blends with fillers, providing

the composite with physical properties, such as flexibility and aesthetics [19]. To covalently bond the resin matrix with the fillers, an organosilane is used, acting as a bridge and assisting to distribute the strength within the resin composite better [20,21]

Besides their use in resin composite formulation, monomers are the main components of adhesive systems [22]. These materials penetrate the previously etched enamel and dentin microstructure, forming a micromechanical interlock between the resin composite and the tooth structure [14].

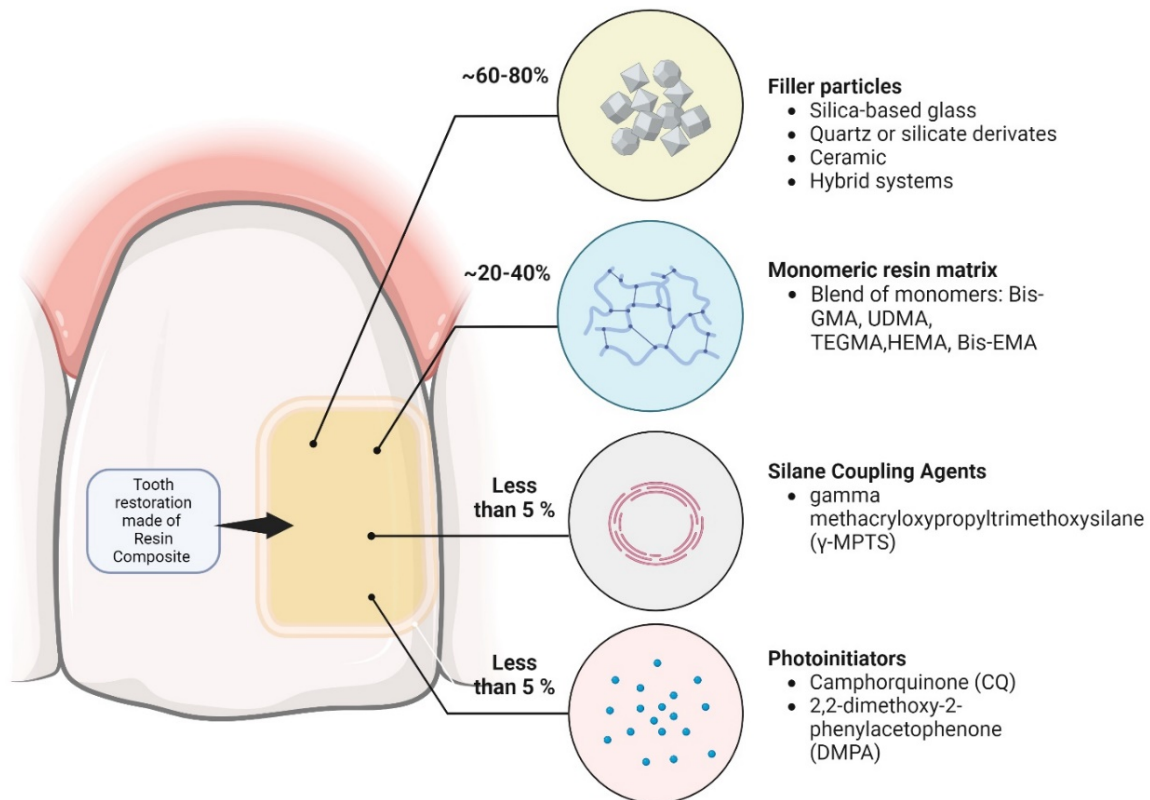


Figure 2. Schematic drawing illustrates the fundamental components constituting the core of dental resin composites comprising filler particles, a monomeric organic resin matrix, silane coupling agents, and photoinitiators. Bis-GMA: Bisphenol A-glycidyl methacrylate, UDMA: Urethane dimethacrylate, TEGDMA: Triethylene glycol dimethacrylate, HEMA: 2-Hydroxyethyl methacrylate, Bis-EMA: Bisphenol A ethoxylate dimethacrylate.

As the field of dental restorative materials has evolved, there has been a notable shift in research focus toward enhancing the longevity of the service of these restorations inside the mouth [15,23]. Over the past decade, this progression has advanced further, with a growing interest in transitioning from materials that prioritize strength alone to the development of "responsive" or "smart" materials [24,25]. Smart materials design aims to achieve optimal conditions that endow dental resins with properties enabling them to maintain high-performance quality over time and positively contribute to maintaining the health status of the restored tooth [24,26].

Starting from the essential pillars of smart dental materials, this review aims to provide a comprehensive overview of the advancements in the field to guide future research directions in developing dental materials that can adapt to and overcome the challenges inherent in dental restorations.

3. Focus on Mechanical Properties

With the shift from mechanically strong amalgam to composite materials in dental restorations, there has been an increased concern over the susceptibility of dental resin restorations to fractures.

This concern has prompted investigations on more mechanically robust resin-based materials. In the last three decades, predominant research in dental resin composites has primarily focused on enhancing mechanical strength and aesthetic properties [27]. Integrating inorganic fillers like glass ceramics, zirconia, and titania into dental resins has significantly improved their mechanical properties and stability [28]. Zirconia was particularly noted for its wear resistance, high toughness, and aesthetic qualities such as natural color and enhanced color matching. By manipulating these inorganic particles' size, distribution, and concentration, dental material scientists have tailored mainly the mechanical, physical, and optical properties described by Ferracane [29]

The evolution of dental composite fillers over the decades highlights a continual trend toward refining the size of these particles to enhance the material's overall properties and clinical effectiveness, as illustrated in **Figure 3**. Starting in the late 1970s, the dental industry saw a significant shift from macrofill composites, which had larger particle sizes, were more prone to wear, and were less aesthetic, to microfill composites. These microfill composites provided a smoother finish and better aesthetic qualities due to their smaller particle sizes [1].

As the industry moved into the 1980s and beyond, the development of hybrid composites combined the durability benefits of macrofills with the aesthetic and polishability advantages of microfills [30]. This combination optimized the physical properties suitable for anterior and posterior applications. Further advancements led to the creation of small particle composites and micro hybrids in the 1990s, which offered further enhancements in handling and finishing.

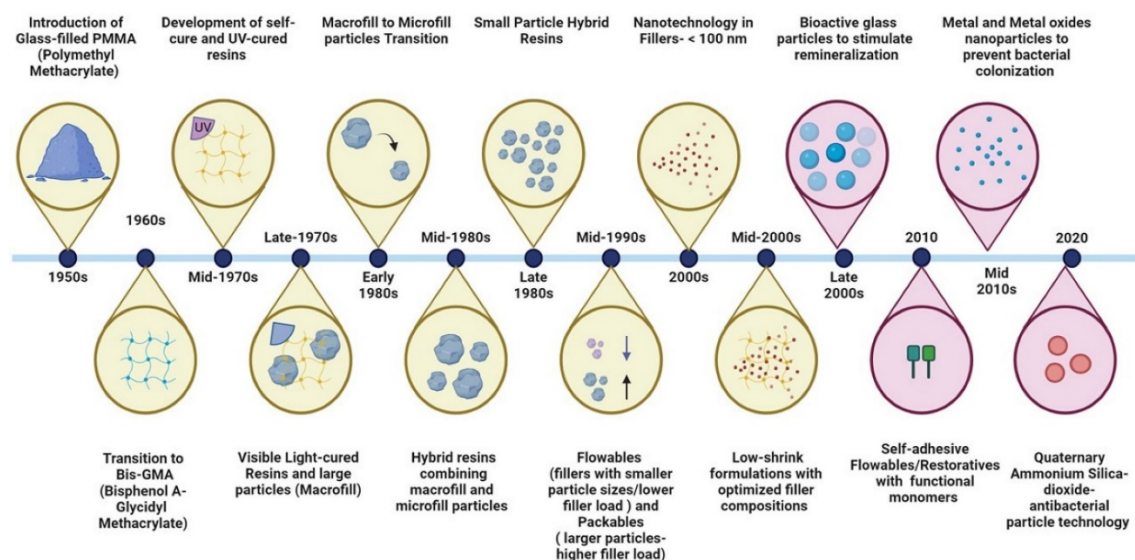


Figure 3. The evolution of dental composite materials from the 1950s to the 2020s. It introduces glass-filled PMMA, highlights advancements in resin technologies such as UV curing and nanotechnology, and transitions into modern developments incorporating bioactive and antibacterial properties over the decades. Each innovation reflects a shift from enhancing mechanical and aesthetic properties to improving oral health outcomes through remineralization and bacterial resistance approaches.

The shift to hybrid particles has been driven by the need for materials that mimic the appearance of natural teeth and withstand the mechanical stresses of daily oral mastication. A significant breakthrough in this area has been the incorporation of nanoparticles (NPs) in dentistry, which have been demonstrated to have various beneficial properties, making them ideal choices for incorporation into dental materials [31,32].

Advances in monomeric organic resin matrices have also targeted improving the mechanical performance of dental composites [33]. Micro-crack formation, polymerization shrinkage, high water absorption, and inadequate stress dissipation can significantly impact mechanical performance [34].

These issues compromise the material's integrity and contribute to its deterioration over time. Specifically, micro-cracks can also allow bacterial infiltration, leading to secondary caries [35]. Studies have focused on reducing these drawbacks by modifying monomer chemistry and polymerization conditions. For instance, developing new monomers such as urethane dimethacrylate (UDMA), thiolene, and thiourethane monomers shows promising reductions in polymerization shrinkage and improved mechanical integrity [36], including novel photoinitiators and alterations in light curing methods that enhance complete monomer conversion [37]. Furthermore, improved filler-matrix interaction through enhanced silanization [38] and nanoparticles [39] has led to better stress distribution and increased fracture toughness.

4. Shift Towards Health-Promoting Restorations

Current dental composites primarily serve as space fillers, restoring form and function to the affected tooth but not contributing to the microenvironmental homeostasis and overall health status [40]. These materials are designed to replace lost tooth substance structurally but lack properties that prevent bacterial buildup or resist the acidic by-products of bacteria [41]. By focusing on making these materials antibacterial or enabling them to release beneficial ions or make them resistant to degradation, researchers aim to restore teeth' form and function and actively contribute to oral health maintenance and microenvironmental homeostasis. This shift in focus seeks to transform dental composites from passive space fillers to active defenders against secondary caries.

5. Dental Materials in the Context of Biomedical Smart Materials

Smart materials are a class of innovative substrates engineered to respond to environmental stimuli, significantly impacting various fields, including biomedical sciences [42]. For example, piezoelectric materials can be used to harvest energy from mechanical vibrations. Due to their distinctive characteristics of responding to environmental stimuli and exhibiting autonomous actions, smart materials have laid the foundation for numerous innovative technological advances [43]. For instance, in robotics, shape memory polymers have seen a swift progression from traditional rigid structures to soft robots made from flexible materials [44].

In biotechnology, smart materials create responsive systems through key properties such as stimuli-responsiveness, shape memory, piezoelectricity, magnetostrictive, photochromic, self-healing, and pH sensitivity that interact dynamically with biological environments. These materials have catalyzed significant progress in areas such as physiological monitoring, minimally invasive procedures, and precision drug delivery [45]. For example, smart hydrogels have been extensively researched for their ability to administer medications in response to specific bodily signals like temperature fluctuations or pH changes [46,47]. This ensures localized drug release, minimizing systemic side effects and enhancing the effectiveness of treatments.

Another application is developing energy harvesting devices for implantable medical devices [48]. Piezoelectric materials can be incorporated into implants where they harvest mechanical energy from body movements, such as heartbeat or muscle motion, and convert it into electrical energy [49]. This energy can then be used to power devices like pacemakers, potentially reducing or eliminating the need for battery replacements in critical medical implants, enhancing such devices' longevity and reliability. Furthermore, smart dressings incorporating chitosan or alginate can adjust their properties based on the moisture content of the wound, facilitating optimal healing environments [50]. These dressings may also include mechanisms for releasing antibacterial substances upon detecting pathogens or physically contracting to aid in closing the wound, thereby exemplifying the integration of smart materials in biotechnological applications [51].

Parallel advancements in Dentistry show how the principles of smart materials—responsiveness to environmental changes, self-healing, and the ability to perform multiple functions—are being applied [52]. In restorative dentistry, this translates to materials that restore the tooth, actively maintain oral homeostasis, and create an environment less susceptible to caries development [25]. Similar to how biotechnological applications of smart materials are designed to interact and integrate with biological systems for enhanced therapeutic outcomes. The term "Smart Dental Materials for

Tooth Restorations " refers to materials used in Restorative/Operative dentistry that are engineered with additional functionalities beyond their core functions. **Figure 4** showcases the innovative use of smart dental materials in tooth restorations, emphasizing their unique properties tailored to assist the maintenance of a health status and durability of the material.

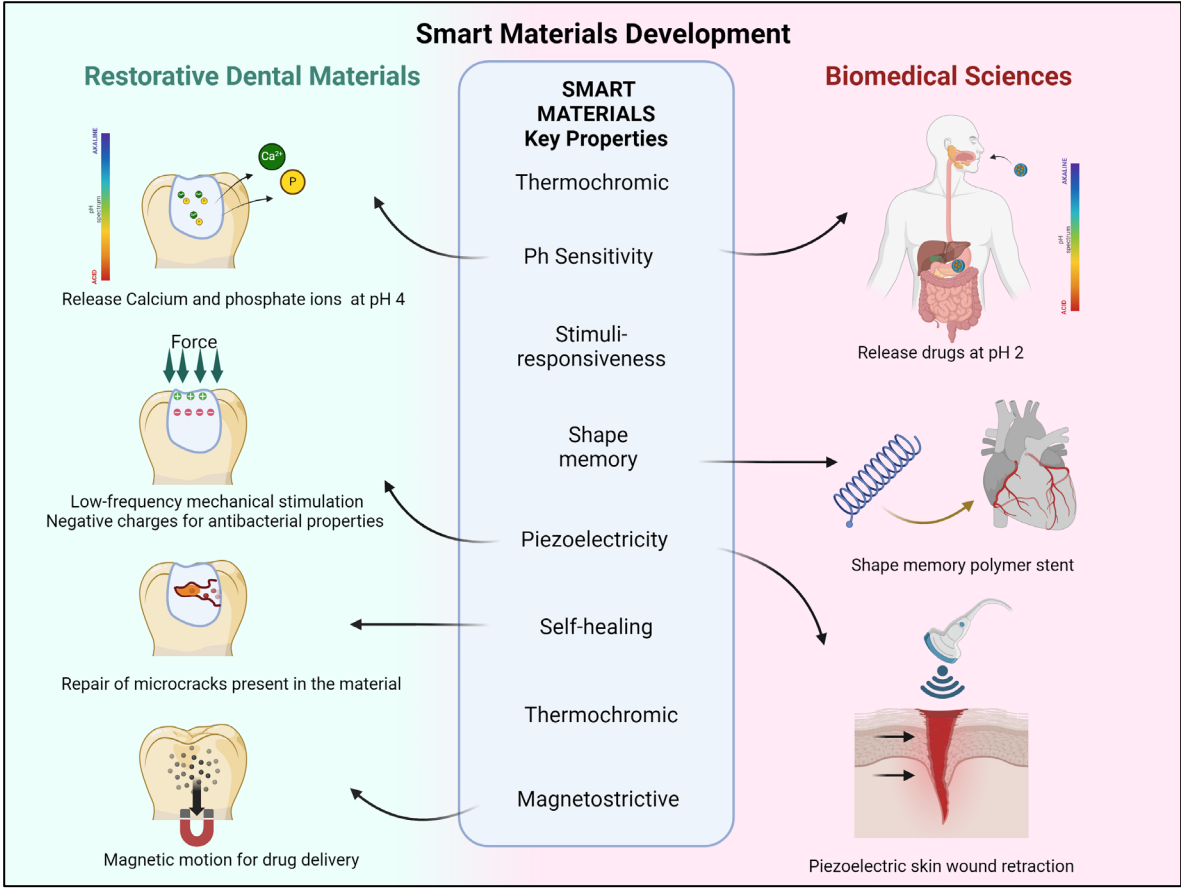


Figure 4. The diagram provides a comprehensive overview of smart materials utilized in restorative dental and biomedical sciences. In dental applications, the materials exhibit properties such as releasing calcium and phosphate ions, antibacterial charges through low-frequency mechanical stimulation, self-repair of microcracks, and targeted drug delivery via magnetic motion. In biomedical contexts, the materials are engineered for specialized tasks such as targeted drug release in acidic environments, adaptive shape memory polymers for stents, and piezoelectric properties to heal skin wounds. These innovative materials leverage key properties like piezoelectricity, pH sensitivity, and magnetostriction to significantly enhance clinical outcomes and material performance in their respective fields.

Below are detailed descriptions of some of the smart dental materials, highlighting their key functionalities:

Self-Healing Dental Composites: These composites are engineered with embedded microcapsules that contain a healing agent. When the composite develops microcracks, these capsules rupture, releasing the agent, which then polymerizes in the presence of an embedded catalyst to repair the crack [53]. This capability is intended to prolong the life of dental restorations by continuously repairing damage caused by normal wear and tear, thus maintaining structural integrity over time. Self-healing agents commonly investigated for dental resin include dibenzoyl peroxide (BPO) and dental tertiary amine accelerator, N, N-dihydroxyethyl-p-toluidine (DHEPT) [54] (**Figure 5A**). They are typically added to the composite material to react with the core material when the microcapsules rupture, facilitating self-healing. However, BPO's reactivity can significantly reduce the shelf life of dental materials. A recent study explored a strategy to address this issue by

encapsulating BPO in poly(urea-formaldehyde) (PUF) microcapsules (MC). This encapsulation aims to isolate BPO until needed, thus mitigating its impact on the shelf life of dental materials [55].

Piezoelectric Dental Composites: Incorporating piezoelectric materials into dental composites allows these materials to convert the mechanical stress from chewing into electrical energy. The electrical charges are used to enable different therapeutic effects, including antimicrobial, mineralization, and bone-tissue regeneration [56,57]. In restorative dentistry, integrating piezoelectric nanoparticles of barium titanate (BaTiO_3) as a bioactive filler in dental resin composites was recently demonstrated by Montoya et al. [58]. This novel approach provided both antibacterial and remineralization effects at the bonded interface. The developed piezoelectric dental composites exhibit enhanced mechanical and physical properties suitable for restorative applications [58], as shown in **Figure 5B**.

pH-Sensitive Composites Containing Nano Amorphous Calcium Phosphate (NACP): These composites are designed to react to fluctuations in the oral environment's pH levels. Under acidic conditions caused by acid-producing bacteria in dental plaque, such as *Streptococcus mutans* and *Lactobacillus* species, the oral environment's pH drops, demineralizing tooth enamel. In these acidic conditions, NACP releases calcium and phosphate ions, which help to neutralize the acidic environment and counteract the effects of acid attacks, thereby slowing down the conditions that favor tooth decay development [59–61].

The optimal concentration of NACP in experimental resin composites is around 20% by weight, balancing both remineralization efficacy and mechanical properties of the intended resin material [62] (**Figure 5C**). Higher concentrations of NACP improve the composite's ability to buffer acids and enhance remineralization but can negatively impact mechanical properties such as strength and wear resistance. Therefore, a trade-off exists between maximizing the bioactive benefits of NACP and maintaining sufficient mechanical integrity [60].

Adhesives with Magnetic Motion as Part of Magnetostrictive Properties: These adhesives leverage magnetostrictive components that respond to external magnetic fields. This response can enhance the bonding process between the dental adhesive and the tooth by improving micro-mechanical interlocking and improving the bond strength [31,63]. As a drawback, the color of the adhesive can be affected by the concentration and type of magnetic particles used, potentially limiting its aesthetic applications. Smaller particles typically have higher surface area-to-volume ratios, which can enhance their magnetic response and exhibit superparamagnetic behavior, where they can rapidly align with an external magnetic field and return to a non-magnetic state when the field is removed [64]. This means they can align more effectively with an external magnetic field, improving the overall performance of the adhesive. Other findings indicate that these adhesives can be designed to respond dynamically to external magnetic fields, offering potential applications in smart materials and responsive systems [65] (**Figure 5D**).

In addition to the abovementioned properties, magnetic particles can be assembled into innovative dental adhesives featuring core-shell structures for drug delivery. These adhesives, part of the array of smart dental materials, are designed to allow the controlled release of therapeutic agents, such as antibiotics or anti-MMPs (matrix metalloproteinases inhibitors) [66]. Engineered with core-shell nanoparticles embedded within the adhesive matrix, the core of these particles can be loaded with specific drugs. The protective shell encapsulating these drugs regulates the rate and timing of their release, ensuring a targeted and sustained therapeutic effect [67]. This multifunctional approach not only enhances the mechanical and magnetic properties of the adhesive but also provides additional health benefits through localized drug delivery, addressing structural and microbial challenges in dental treatments.

The design of smart dental materials aims to integrate multifunctional properties through innovative engineering and material science techniques.

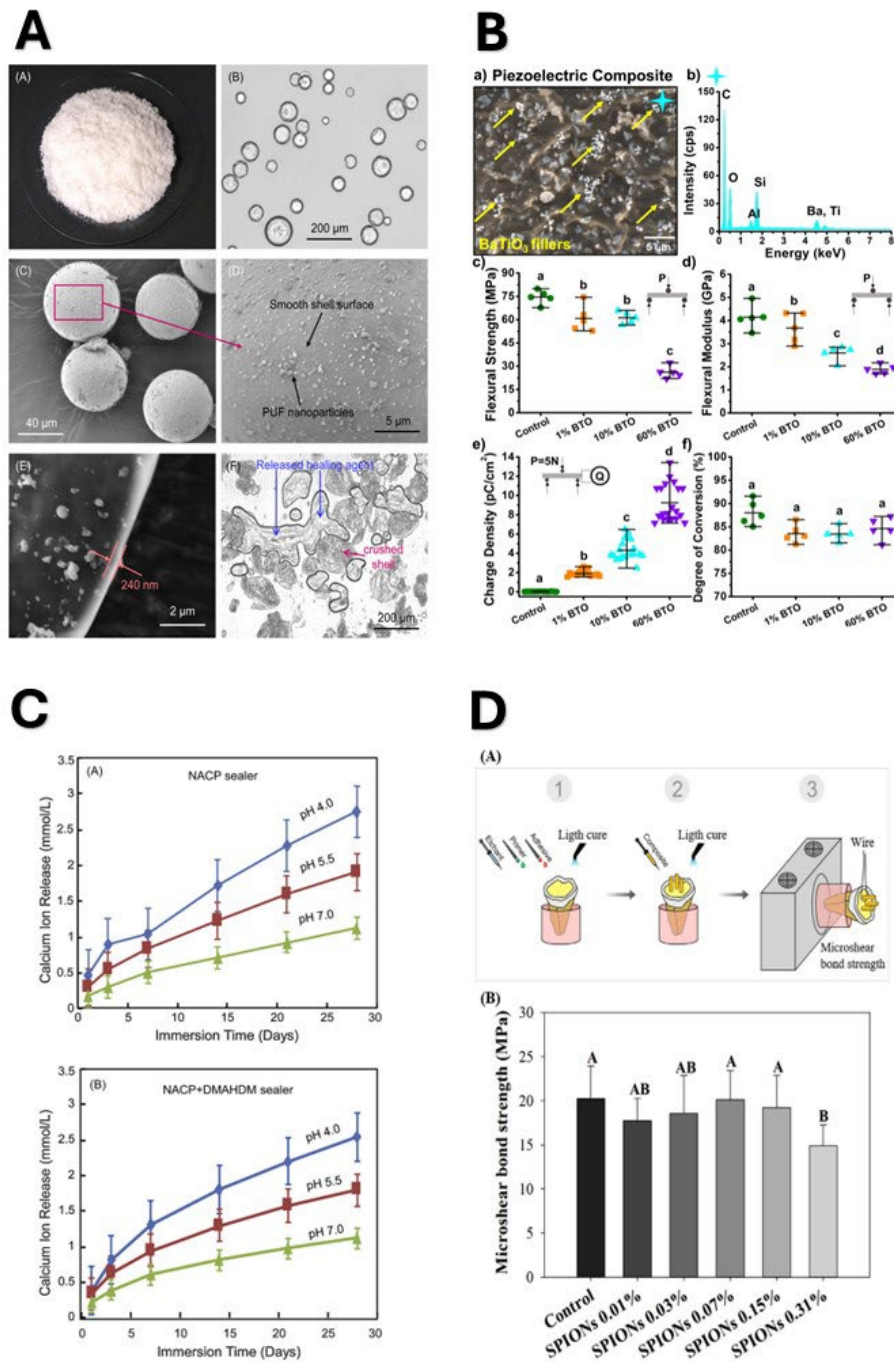


Figure 5. 5A: Microcapsules containing TEGDMA-DHEPT healing liquid within PUF shells were synthesized and characterized. The images display a pile of microcapsules (A), their shell structure (B), SEM images showing typical microcapsules (C) and detailed views of the shell surface (D) and thickness (E), and an optical image of crushed microcapsules releasing the healing liquid (F). Reproduced, with permission, from [54]; 5B: Characterization of piezoelectric composites. The images include a micrograph of a 10% barium titanate (BaTiO₃) nanoparticles composite's fracture surface showing piezoelectric fillers (a), an EDS spectrum highlighting barium and titanium peaks (b), and comparative evaluations of flexural strength (c), flexural modulus (d), electrical charge density under cyclic load (e), and degree of conversion (f) of the composites. Reproduced, with permission, from [58]; 5C: Release of calcium ions from endodontic sealers. The graphs show Ca ion release from nanoparticles of amorphous calcium phosphate (NACP) sealer (A) and NACP + dimethylaminohexadecyl methacrylate (DMAHDM) sealer (B), with mean \pm SD values (n = 4). Reproduced, with permission, from [68]; and 5D: Microshear bond strength assessment of

superparamagnetic iron oxide nanoparticles- loaded dental adhesives. The schematic (A) illustrates the restoration process using conventional adhesive systems on human teeth embedded in acrylic resin. The results (B) present mean and standard deviation values of microshear bond strength, with significant differences among groups indicated by different capital letters ($p < 0.05$). Reproduced, with permission, from [69].

6. Designing Smart Materials Pathways

Developing smart dental materials for tooth restorations involves a multi-faceted approach, primarily in modifying fillers, resin monomers, and other key constituents such as photoinitiators and silanes [17]. Each of these pathways provides distinct opportunities to enhance the properties and performance of dental materials [70]. For instance, modifying the filler can improve the material's mechanical strength and wear resistance. At the same time, modification/addition of the chemical composition of resin monomers can enhance the polymerization process, resulting in a more durable and stable dental material. Optimizing photoinitiators can lead to more efficient curing processes under light activation, and tweaking silanes can improve the bond strength between fillers and the resin matrix. These modifications are crucial for tailoring the material to respond to specific oral challenges, enhancing its functionality and longevity. The various pathways for designing smart materials are detailed in **Figure 6**, illustrating the strategic adjustments made to these components to achieve desired outcomes.

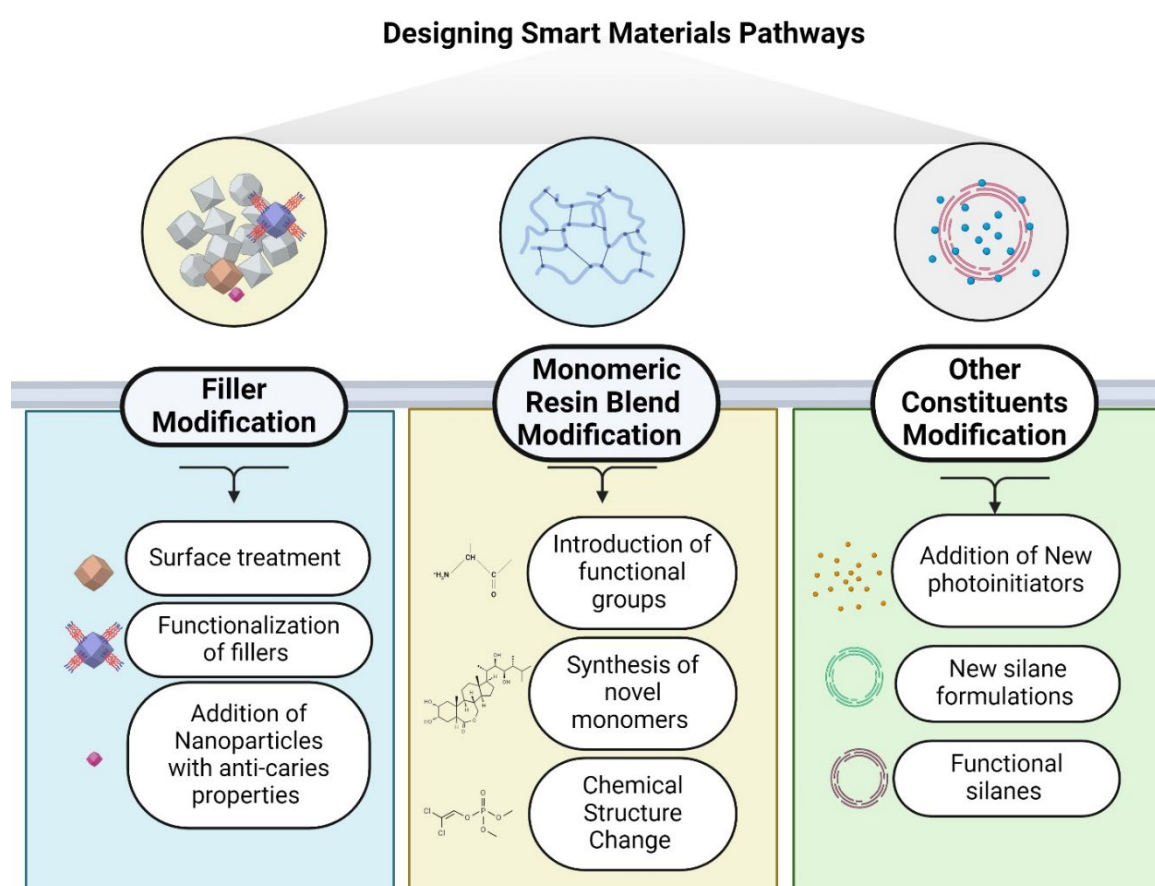


Figure 6. Schematic illustration of the most prevalent pathways for developing smart dental materials, focusing on the strategic modifications of fillers, resin monomers, photoinitiators, and silanes.

7. Filler Modification Pathway:

Several filler modification strategies are employed in designing smart materials to enhance dental composites' performance and therapeutic properties. These modifications are tailored to

improve mechanical properties and integrate functionalities promoting oral health [71]. Nanostructures have been increasingly recognized for their antibacterial and bactericidal properties, making them highly investigated for dental resins [72].

Materials such as silver nanoparticles, zinc oxide, and copper oxide possess intrinsic antibacterial activities that disrupt bacterial cell membranes or interfere with their metabolic processes [73]. When embedded into dental composites, these nanostructures can reduce bacterial colonization and biofilm formation on the surface of dental restorations [69,74,75]. This proactive antibacterial action could potentially help prolong the restorations' lifespan and reduce secondary caries' incidence. Several nanoparticles commonly incorporated in dental materials are assorted in **Table 1**.

Table 1. Summary of the prevalent types of nanoparticles incorporated into restorative dental materials to innovate and improve their properties. Each row represents a different nanoparticle, the intended new properties it conveys to the material, and the base restorative materials with which it is commonly used.

NANOPARTICLE TYPE	INTENDED NEW PROPERTY	BASE RESTORATIVE MATERIAL
SILVER NANOPARTICLES	Antibacterial	- Dental restorative nanocomposite - Dental implants - Dental prosthesis
ZINC OXIDE NANOPARTICLES	Antibacterial	- Dental composite - Dental implant coating material
TITANIUM COMPOUND: TITANIA NANOPARTICLES (TiO ₂)	Antibacterial	- Dental implant - Dental resin
COPPER NANOPARTICLES: COPPER IODIDE, COPPER OXIDE	Antibacterial	- Dental implants - Dental primers - Adhesive systems - Glass ionomer-based materials
NANODIAMONDS	Antibacterial	- Dental resin - Antibiotics drug carrier - Gutta-percha
POLYMERIC/ORGANIC FILLERS		
QUATERNARY AMMONIUM POLYETHYLENIMINE (QAPET) NANOPARTICLES	Antibacterial	- Temporary restorative materials - Root canal sealer - Resin composite
CHITOSAN NANOPARTICLES	Antibacterial /Antifungal	- Dental varnishes - In calcium hydroxide paste for dressing for root canal treatment - Poly methyl methacrylate-based bone cements - Coatings for dental implants
CHLORHEXIDINE RELEASING FILLERS	Antibacterial	- Mouth rinses - Dental composite - Dentin adhesive system - Dental implant coating material

Similarly, nanoparticles capable of releasing fluoride, calcium, and phosphate have been extensively explored to enhance the remineralizing properties of dental resins [76]. Fluoride-releasing nanoparticles, such as calcium fluoride, release fluoride ions in the presence of saliva, promoting the formation of a more acid-resistant fluorapatite layer on the enamel [77]. Additionally, calcium-phosphate nanoparticles release both calcium and phosphate ions, which synergistically contribute to the precipitation of new mineral formation on the tooth surface [78].

Incorporating bioactive ions such as fluoride, calcium, and phosphate into dental resins offers significant remineralizing benefits, while ions such as silver and zinc provide antibacteriostatic and antibacterial effects. However, an important drawback of these bioactive ions is the exhaustion of their release over time. As the restoration ages, the ion release rate diminishes, gradually losing these protective effects [69,79]. This depletion can make the restoration less effective in preventing caries

in the long term. Furthermore, the finite nature of ion release means that the longevity of the restoration's preventive capabilities is inherently limited. To address these challenges, ongoing research is directed toward developing materials that can sustain ion release for extended periods or can be 'recharged' by external sources, such as fluoride treatments, to extend the effectiveness of dental restorations [80].

8. Monomeric Organic Resin Modification Pathway:

This pathway involves incorporating specific additives or modifying the chemical composition of monomers that compose the resin formulation to impart antibacterial, remineralizing, or anti-degradation properties.

Dental resins can be modified with monomers that actively kill bacteria or inhibit their growth on the dental restoration surface to impart antibacterial properties. For example, Quaternary Ammonium Monomers (QAMs) are often integrated into the resin matrix to impart antibacterial surface to restorative materials, such as dental adhesives, resin composites, and cements [81]. These monomers, such as methacryloyloxydodecylpyridinium bromide (MDPB), disrupt bacterial membranes upon contact, effectively reducing bacterial colonization [82].

Enhancing the durability and resistance of dental composites has been a key focus of investigations, driven by the inherent susceptibility of dental monomers to degradation. Ester-free thiol-ene dental resins have been developed to address these challenges. These innovative resins aim to improve mechanical performance, minimize water uptake, and reduce leachables and degradation. They also help lower polymerization shrinkage stress, enhancing dental restorations' overall stability and longevity [83,84].

Furthermore, advancements in monomeric resins have led to modifying these materials with methacrylamide-based QAC (Quaternary Ammonium Compound) monomers, aiming to convey antibacterial and hydrolytic resistance properties. Formulations with 10 wt% methacrylamide-based quaternary ammonium monomer have successfully preserved physical properties and enhanced resin-dentin bond strength [85].

9. Modification of Other Constituents:

Apart from fillers and resin monomers, modifying other constituents, such as photoinitiators and silanes, also plays a crucial role in enhancing the performance of dental materials [86]. Photoinitiators play an essential role in the polymerization process, initiating the curing of resin composites upon exposure to light. Investigations on optimizing photoinitiators have sought improved polymerization efficiency, reduced polymerization shrinkage, enhanced depth cure, and improved color stability [37]. By optimizing the type and concentration of photoinitiators, researchers can achieve faster curing times, improved depth of cure, and enhanced polymerization efficiency [87].

Silanes, commonly used as coupling agents in dental composites, contribute to filler-matrix adhesion and overall material stability [88]. Modifying silanes allows for better integration of fillers into the resin matrix, resulting in improved mechanical properties and longevity of dental restorations [89]. Recently, Garcia et al. explored the potential of antibacterial and hydraulic resistance of ionic liquid silanes [90]. Ionic liquids prevent degradation in dental resins primarily due to their unique chemical properties. They comprise organic cations and inorganic or organic anions, creating a stable and non-volatile medium [91]. This stability helps resist chemical breakdown and environmental degradation, such as hydrolysis and oxidation [92], which are common in the moist and dynamic environment of the oral cavity. Moreover, ionic liquids can enhance the physical properties of the resins, such as improving their mechanical strength and flexibility, thus contributing to the overall durability of dental restorations.

Modifications must adhere to a structured approach to ensure new smart dental materials' feasibility and potential clinical application. This structured process is represented in **Figure 7**, which outlines a clear sequence of development stages.

10. "SMART FAB" Structured Approach for Smart Restorative Materials

The design of smart dental materials should start with a structured approach focusing on ensuring baseline biocompatibility and enhancing functionality.[93]. Here, we provide a straightforward and user-friendly guide named "SMART FAB." This outline provides a systematic framework to guide the development process, ensuring that each critical aspect of material innovation is addressed comprehensively. The process begins with defining the objectives these new materials must meet, followed by research and development to explore viable materials and additives. The formulation is refined through prototyping and rigorous testing phases to enhance these properties effectively [45]. This process may lead to the eventual scale-up and regulatory approvals necessary for bringing innovative dental materials to market. A systematic approach aims to reduce innovation spans between conceptual and molecular levels and practical application, supporting the development of next-generation dental materials.

"SMART FAB" summarizes a series of steps to rationally create, design, and process restorative materials with specific properties in mind by focusing on specific stages from the initial conception to the final product testing and approval.

Starting with "Specify Application", this approach identifies the specific applications for the smart material, such as resin composites, cement crowns, adhesives, or dental sealants. Each application demands unique properties like strength, flexibility, biocompatibility, and aesthetic qualities to effectively provide the expected performance of the material inside the mouth [26].

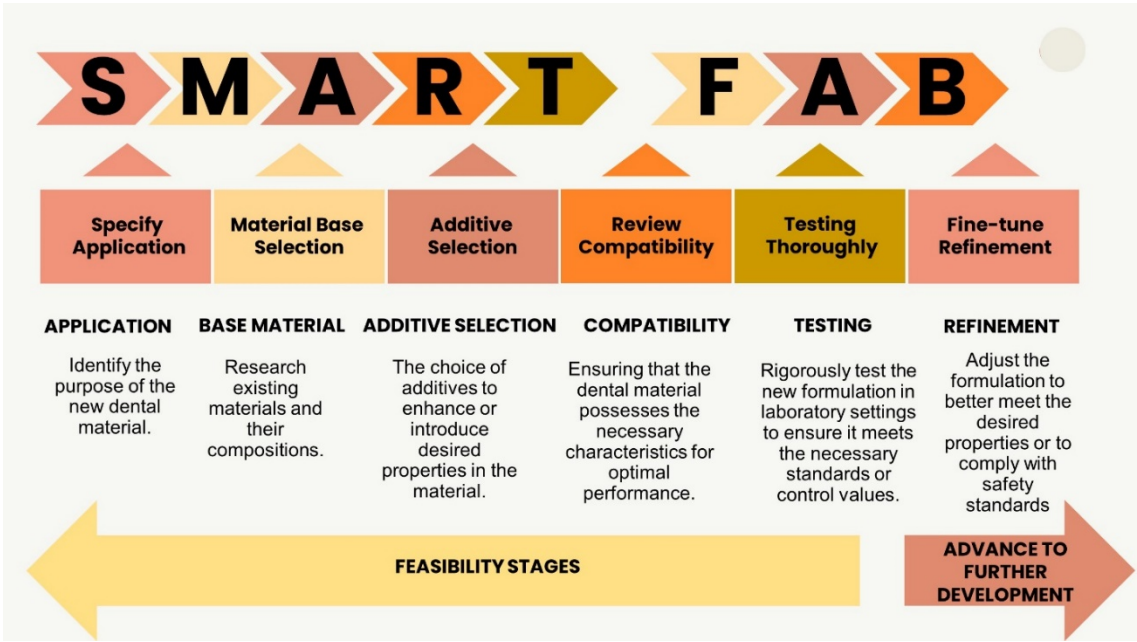


Figure 7. The flowchart illustrates the structured development process for smart dental materials, outlining the key stages from the initial objective setting through research and development, prototyping, and rigorous testing, leading to final refinements.

The next stage is " Base Material Selection". This stage focuses on examining existing materials and their compositions, fully understanding dental materials' chemistry, physics, and biology and their interactions with tooth structures. For example, if the material base is a flowable resin, several properties and attributes are significant, such as low viscosity, strong bonding to tooth enamel and dentin, and high elasticity [60].

The process continues with the "Additive Selection" stage, which involves carefully selecting additives that introduce or enhance desired properties within the dental material. At this critical intersection, specific additives are chosen for their ability to grant new functionalities to the base material. For instance, certain additives are engineered to release beneficial ions that contribute to enamel mineral integrity. Others may be selected to reduce bacterial growth over the material [94].

In the subsequent step, "Review Compatibility," the formulation is meticulously tailored with specifically chosen additives to ensure compatibility and performance. This critical and arduous labor phase involves producing small batches of the material to sift through the innumerable possibilities, find the optimal formulations, and evaluate how the additives interact with the base materials. These preliminary tests are crucial as they provide initial insights into the feasibility of the formulation. This set becomes essential because, while additives can enhance specific properties, they might also negatively impact others. For instance, certain additives might significantly affect the degree of conversion in resin-based dental materials [95]. A high degree of conversion is crucial for achieving optimal mechanical properties and durability; however, some additives can inhibit this process, compromising the material's integrity and functionality. For example, some larger bioactive particle sizes may impair light transmission [96]. This reduction in performance can cease further research and development of the formulation, as materials failing to meet basic performance criteria may not proceed to later stages of development. Consequently, many formulations may be discontinued at this stage if they do not demonstrate the desired compatibility and performance characteristics, underscoring the importance of this phase in developing dental materials.

In the subsequent step, "Test Thoroughly," the new formulation undergoes rigorous laboratory testing to ensure it adheres to established standards and control values. This phase involves comprehensive preclinical assays and in vitro modeling designed to evaluate the material's mechanical strength, biocompatibility, and other specific properties under ISO guidelines [97,98] and conditions that closely mimic the oral environment [99].

This step is critical and must encompass a range of complementary assays to evaluate the material comprehensively. Relying on a single assay or a limited set of tests that only examine one aspect of the material is discouraged. For example, materials with antibacterial properties should not be assessed just using microbiological assays. Still, a multi-faceted testing approach should be employed to assess different characteristics simultaneously, ensuring the material's overall effectiveness and safety. These tests help identify any potential weaknesses in the formulation and confirm that the material meets all necessary specifications for further development and eventual clinical use. This comprehensive testing protocol is vital for advancing the material through the development pipeline, which has the potential to translate to clinical use.

In the "Fine-tune Refinement" phase, the formulation undergoes adjustments based on the results of rigorous testing. This stage aims to align the material with the desired properties better and ensure it adheres to health and safety standards. The refinement process is essential for optimizing the material's performance and suitability for the intended dental application.

Following refinement, the "Finalize Material Properties" phase ensures that the final product meets all specified requirements for dental applications, including safety standards. It is crucial that the material maintains its functional properties over time with shelf-life simulation [100] and manages the release of any components, such as nanoparticles, to avoid potential harm [101]. This step confirms the material's readiness for real-world dental applications and long-term stability and safety.

The "Advance Prototyping" phase involves creating prototype versions of the final product, which are subjected to further testing and evaluation. This may include clinical studies, providing critical data on the material's performance, and gathering user feedback. Depending on the local regulatory agency, clinical data for new dental resins may be recommended in case designs are dissimilar from designs previously cleared, e.g., novel polymer systems [102].

Finally, the "Benchmark Against Standards" stage is crucial before the product can enter the market. During this phase, the material must obtain the necessary approvals from health and safety regulatory bodies, ensuring that the new smart dental materials have met all relevant ISO standard requirements and safety standards of organizations such as the Federal Food, Drug, and Cosmetic Act (the act), in the United States [102]. Similar regulatory bodies in Europe and Asia, such as the European Medicines Agency (EMA) and the China National Medical Products Administration (NMPA), as well as in Latin America, like the Brazilian Health Regulatory Agency (ANVISA), and in the Middle East, such as the Saudi Food and Drug Authority (SFDA), play analogous roles in

ensuring that dental materials meet stringent safety and performance criteria before being allowed on the market.

11. Concluding Remarks and Future Perspectives

Smart dental materials hold significant promise for advancing the field of restorative dentistry by providing enhanced functionality beyond traditional tooth-filling materials. The integration of stimuli-responsive features, self-healing capabilities, and antibacterial/remineralization/acid neutralization properties offers a comprehensive solution to the challenges faced by conventional dental materials, such as polymerization shrinkage, secondary caries, and mechanical degradation. This review highlights cutting-edge technologies and innovative balancing mechanical properties, biocompatibility, and aesthetic considerations in the design of effective smart dental materials. However, several major challenges remain in integrating smart materials into clinical settings and evaluating economic and long-term outcomes.

In the advancing design of smart dental materials, the exploration and integration of advanced technologies such as machine learning (ML) and artificial intelligence (AI) may accelerate the design process. These technologies can significantly contribute to designing and fabricating new smart dental materials by optimizing material formulations and predicting their performance in various clinical scenarios. ML algorithms can analyze vast datasets to identify optimal combinations of fillers, monomers, and additives that enhance dental materials' mechanical, physical, and biological properties. Additionally, AI and ML can develop predictive models that simulate the long-term behavior of smart dental materials in the oral environment. These models can provide insights into material performance, helping researchers identify potential issues and make necessary adjustments before clinical implementation. This interdisciplinary approach can foster innovation and accelerate the development of next-generation smart dental materials.

References

1. Aminoroaya, A.; Neisiany, R.E.; Khorasani, S.N.; Panahi, P.; Das, O.; Madry, H.; Cucchiari, M.; Ramakrishna, S. A Review of Dental Composites: Challenges, Chemistry Aspects, Filler Influences, and Future Insights. *Composites Part B: Engineering* **2021**, *216*, 108852, doi:10.1016/j.compositesb.2021.108852.
2. Shah, Y.; Shiraguppi, V.; Deosarkar, B.; Shelke, U. Long-Term Survival and Reasons for Failure in Direct Anterior Composite Restorations: A Systematic Review. *J Conserv Dent* **2021**, *24*, 415, doi:10.4103/jcd.jcd_527_21.
3. Pizzolotto, L.; Moraes, R.R. Resin Composites in Posterior Teeth: Clinical Performance and Direct Restorative Techniques. *Dentistry Journal* **2022**, *10*, 222, doi:10.3390/dj10120222.
4. Cho, K.; Rajan, G.; Farrar, P.; Prentice, L.; Prusty, B.G. Dental Resin Composites: A Review on Materials to Product Realizations. *Composites Part B: Engineering* **2022**, *230*, 109495, doi:10.1016/j.compositesb.2021.109495.
5. Guo, X.; Yu, Y.; Gao, S.; Zhang, Z.; Zhao, H. Biodegradation of Dental Resin-Based Composite—A Potential Factor Affecting the Bonding Effect: A Narrative Review. *Biomedicines* **2022**, *10*, 2313, doi:10.3390/biomedicines10092313.
6. Ferracane, J.L.; Hilton, T.J. Polymerization Stress--Is It Clinically Meaningful? *Dent Mater* **2016**, *32*, 1–10, doi:10.1016/j.dental.2015.06.020.
7. Mokeem, L.S.; Garcia, I.M.; Melo, M.A. Degradation and Failure Phenomena at the Dentin Bonding Interface. *Biomedicines* **2023**, *11*, 1256, doi:10.3390/biomedicines11051256.
8. Guo, X.; Yu, Y.; Gao, S.; Zhang, Z.; Zhao, H. Biodegradation of Dental Resin-Based Composite—A Potential Factor Affecting the Bonding Effect: A Narrative Review. *Biomedicines* **2022**, *10*, 2313, doi:10.3390/biomedicines10092313.
9. Peskersoy, C.; Recen, D.; Kemaloğlu, H. The Effect of Composite Placement Technique on the Internal Adaptation, Gap Formation and Microshear Bond Strength. *eor* **2021**, *0*, 0–0, doi:10.26650/eor.2022897456.
10. Ástvaldsdóttir, Á.; Dagerhamn, J.; van Dijken, J.W.V.; Naimi-Akbar, A.; Sandborgh-Englund, G.; Tranæus, S.; Nilsson, M. Longevity of Posterior Resin Composite Restorations in Adults – A Systematic Review. *Journal of Dentistry* **2015**, *43*, 934–954, doi:10.1016/j.jdent.2015.05.001.

11. Tjäderhane, L.; Nascimento, F.D.; Breschi, L.; Mazzoni, A.; Tersariol, I.L.S.; Geraldini, S.; Tezvergil-Mutluay, A.; Carrilho, M.; Carvalho, R.M.; Tay, F.R.; et al. Strategies to Prevent Hydrolytic Degradation of the Hybrid Layer-A Review. *Dent Mater* **2013**, *29*, 999–1011, doi:10.1016/j.dental.2013.07.016.
12. Frassetto, A.; Breschi, L.; Turco, G.; Marchesi, G.; Di Lenarda, R.; Tay, F.R.; Pashley, D.H.; Cadenaro, M. Mechanisms of Degradation of the Hybrid Layer in Adhesive Dentistry and Therapeutic Agents to Improve Bond Durability--A Literature Review. *Dent Mater* **2016**, *32*, e41-53, doi:10.1016/j.dental.2015.11.007.
13. Saikaew, P.; Sattabanasuk, V.; Harnirattisai, C.; Chowdhury, A.F.M.A.; Carvalho, R.; Sano, H. Role of the Smear Layer in Adhesive Dentistry and the Clinical Applications to Improve Bonding Performance. *Jpn Dent Sci Rev* **2022**, *58*, 59–66, doi:10.1016/j.jdsr.2021.12.001.
14. Mai, S.; Zhang, Q.; Liao, M.; Ma, X.; Zhong, Y. Recent Advances in Direct Adhesive Restoration Resin-Based Dental Materials With Remineralizing Agents. *Front. Dent. Med* **2022**, *3*, 868651, doi:10.3389/fdmed.2022.868651.
15. Montoya, C.; Roldan, L.; Yu, M.; Valliani, S.; Ta, C.; Yang, M.; Orrego, S. Smart Dental Materials for Antimicrobial Applications. *Bioactive Materials* **2023**, *24*, 1–19, doi:10.1016/j.bioactmat.2022.12.002.
16. Cao, W.; Wang, X.; Li, Q.; Ye, Z.; Xing, X. Mechanical Property and Antibacterial Activity of Silver-Loaded Polycation Functionalized Nanodiamonds for Use in Resin-Based Dental Material Formulations. *Materials Letters* **2018**, *220*, 104–107, doi:10.1016/j.matlet.2018.03.027.
17. Yu, K.; Zhang, Q.; Dai, Z.; Zhu, M.; Xiao, L.; Zhao, Z.; Bai, Y.; Zhang, K. Smart Dental Materials Intelligently Responding to Oral PH to Combat Caries: A Literature Review. *Polymers* **2023**, *15*, 2611, doi:10.3390/polym15122611.
18. Syed, M.R.; Bano, N.Z.; Ghafoor, S.; Khalid, H.; Zahid, S.; Siddiqui, U.; Hakeem, A.S.; Asif, A.; Kaleem, M.; Khan, A.S. Synthesis and Characterization of Bioactive Glass Fiber-Based Dental Restorative Composite. *Ceramics International* **2020**, *46*, 21623–21631, doi:10.1016/j.ceramint.2020.05.268.
19. Kolb, C.; Gumpert, K.; Wolter, H.; Seftl, G. Highly Translucent Dental Resin Composites through Refractive Index Adaption Using Zirconium Dioxide Nanoparticles and Organic Functionalization. *Dental Materials* **2020**, *36*, 1332–1342, doi:10.1016/j.dental.2020.07.005.
20. Cavalcante, L.M.; Ferraz, L.G.; Antunes, K.B.; Garcia, I.M.; Schneider, L.F.J.; Collares, F.M. Silane Content Influences Physicochemical Properties in Nanostructured Model Composites. *Dental Materials* **2021**, *37*, e85–e93, doi:10.1016/j.dental.2020.10.022.
21. Sideridou, I.D.; Karabela, M.M. Effect of the Amount of 3-Methacryloxypropyltrimethoxysilane Coupling Agent on Physical Properties of Dental Resin Nanocomposites. *Dental Materials* **2009**, *25*, 1315–1324, doi:10.1016/j.dental.2009.03.016.
22. Cadenaro, M.; Josic, U.; Maravić, T.; Mazzitelli, C.; Marchesi, G.; Mancuso, E.; Breschi, L.; Mazzoni, A. Progress in Dental Adhesive Materials. *J Dent Res* **2023**, *102*, 254–262, doi:10.1177/00220345221145673.
23. Ozimek, J.; Łukaszewska, I.; Pielichowski, K. POSS and SSQ Materials in Dental Applications: Recent Advances and Future Outlooks. *IJMS* **2023**, *24*, 4493, doi:10.3390/ijms24054493.
24. Melo, M.A.S.; Mokeem, L.; Sun, J. Bioactive Restorative Dental Materials—The New Frontier. *Dental Clinics of North America* **2022**, *66*, 551–566, doi:10.1016/j.cden.2022.05.005.
25. Montoya, C.; Roldan, L.; Yu, M.; Valliani, S.; Ta, C.; Yang, M.; Orrego, S. Smart Dental Materials for Antimicrobial Applications. *Bioactive Materials* **2023**, *24*, 1–19, doi:10.1016/j.bioactmat.2022.12.002.
26. Melo, M. a. S.; Garcia, I.M.; Mokeem, L.; Weir, M.D.; Xu, H.H.K.; Montoya, C.; Orrego, S. Developing Bioactive Dental Resins for Restorative Dentistry. *J Dent Res* **2023**, *102*, 1180–1190, doi:10.1177/00220345231182357.
27. Azmy, E.; Al-Kholy, M.R.Z.; Fattouh, M.; Kenawi, L.M.M.; Helal, M.A. Impact of Nanoparticles Additions on the Strength of Dental Composite Resin. *International Journal of Biomaterials* **2022**, *2022*, 1–9, doi:10.1155/2022/1165431.
28. Xia, Y.; Zhang, F.; Xie, H.; Gu, N. Nanoparticle-Reinforced Resin-Based Dental Composites. *J Dent* **2008**, *36*, 450–455, doi:10.1016/j.jdent.2008.03.001.
29. Ferracane, J.L. A Historical Perspective on Dental Composite Restorative Materials. *Journal of Functional Biomaterials* **2024**, *15*, 173, doi:10.3390/jfb15070173.
30. Bapat, R.A.; Yang, H.J.; Chaubal, T.V.; Dharmadhikari, S.; Abdulla, A.M.; Arora, S.; Rawal, S.; Kesharwani, P. Review on Synthesis, Properties and Multifarious Therapeutic Applications of Nanostructured Zirconia in Dentistry. *RSC Adv.* **2022**, *12*, 12773–12793, doi:10.1039/D2RA00006G.

31. Mokeem, L.S.; Garcia, I.M.; Shahkarami, Y.; Blum, L.; Balhaddad, A.A.; Collares, F.M.; Williams, M.A.; Weir, M.D.; Melo, M.A.S. Core-Shell Nanostructures for Improving Dental Restorative Materials: A Scoping Review of Composition, Methods, and Outcome. *Smart Materials in Medicine* **2023**, *4*, 102–110, doi:10.1016/j.smaim.2022.08.002.
32. Moraes, G.; Zambom, C.; Siqueira, W.L. Nanoparticles in Dentistry: A Comprehensive Review. *Pharmaceuticals* **2021**, *14*, 752, doi:10.3390/ph14080752.
33. Antonucci, J.M.; Regnault, W.F.; Skrtic, D. Polymerization Shrinkage and Stress Development in Amorphous Calcium Phosphate/Urethane Dimethacrylate Polymeric Composites. *Journal of Composite Materials* **2010**, *44*, 355–367, doi:10.1177/0021998309345180.
34. Naebe, M.; Abolhasani, M.M.; Khayyam, H.; Amini, A.; Fox, B. Crack Damage in Polymers and Composites: A Review. *Polymer Reviews* **2016**, *56*, 31–69, doi:10.1080/15583724.2015.1078352.
35. Khvostenko, D.; Salehi, S.; Naleway, S.E.; Hilton, T.J.; Ferracane, J.L.; Mitchell, J.C.; Kruzic, J.J. Cyclic Mechanical Loading Promotes Bacterial Penetration along Composite Restoration Marginal Gaps. *Dent Mater* **2015**, *31*, 702–710, doi:10.1016/j.dental.2015.03.011.
36. Lewis, S.H.; Fugolin, A.P.P.; Bartolome, A.; Pfeifer, C.S. Relaxation Mechanisms in Low-Stress Polymer Networks with Alternative Chemistries. *JADA Foundational Science* **2024**, *3*, doi:10.1016/j.jfscie.2024.100033.
37. Lima, A.F.; Salvador, M.V.O.; Dressano, D.; Saraceni, C.H.C.; Gonçalves, L.S.; Hadis, M.; Palin, W.M. Increased Rates of Photopolymerisation by Ternary Type II Photoinitiator Systems in Dental Resins. *Journal of the Mechanical Behavior of Biomedical Materials* **2019**, *98*, 71–78, doi:10.1016/j.jmbbm.2019.06.005.
38. Chen, H.; Wei, S.; Wang, R.; Zhu, M. Improving the Physical-Mechanical Property of Dental Composites by Grafting Methacrylate-Polyhedral Oligomeric Silsesquioxane onto a Filler Surface. *ACS Biomater Sci Eng* **2021**, *7*, 1428–1437, doi:10.1021/acsbomaterials.1c00152.
39. Azhar, S.; Rana, N.F.; Kashif, A.S.; Tanweer, T.; Shafique, I.; Mena, F. DEAE-Dextran Coated AgNPs: A Highly Blendable Nanofiller Enhances Compressive Strength of Dental Resin Composites. *Polymers (Basel)* **2022**, *14*, 3143, doi:10.3390/polym14153143.
40. German, M.J. Developments in Resin-Based Composites. *Br Dent J* **2022**, *232*, 638–643, doi:10.1038/s41415-022-4240-8.
41. Chen, L.; Suh, B.I.; Yang, J. Antibacterial Dental Restorative Materials: A Review. *American Journal of Dentistry* **2018**, *31*.
42. Chen, F.; Dong, J.; Sun, W.; Di Iorio, D.; Wegner, S.V.; Zeng, W. Editorial: Construction of Smart Materials for Biomedical Application. *Front Bioeng Biotechnol* **2023**, *11*, 1278243, doi:10.3389/fbioe.2023.1278243.
43. Yin, Y.; Rogers, J.A. Introduction: Smart Materials. *Chem. Rev.* **2022**, *122*, 4885–4886, doi:10.1021/acs.chemrev.2c00074.
44. Kim, Y.; Zhao, X. Magnetic Soft Materials and Robots. *Chem. Rev.* **2022**, *122*, 5317–5364, doi:10.1021/acs.chemrev.1c00481.
45. Yildirim, M.; Candan, Z. Smart Materials: The next Generation in Science and Engineering. *Materials Today: Proceedings* **2023**, doi:10.1016/j.matpr.2023.10.116.
46. Zeng, N.; He, L.; Jiang, L.; Shan, S.; Su, H. Synthesis of Magnetic/PH Dual Responsive Dextran Hydrogels as Stimuli-Sensitive Drug Carriers. *Carbohydrate Research* **2022**, *520*, 108632, doi:10.1016/j.carres.2022.108632.
47. El-Husseiny, H.M.; Mady, E.A.; Hamabe, L.; Abugomaa, A.; Shimada, K.; Yoshida, T.; Tanaka, T.; Yokoi, A.; Elbadawy, M.; Tanaka, R. Smart/Stimuli-Responsive Hydrogels: Cutting-Edge Platforms for Tissue Engineering and Other Biomedical Applications. *Materials Today Bio* **2022**, *13*, 100186, doi:10.1016/j.mtbio.2021.100186.
48. Fan, R.; Lee, S.; Jung, H.; Melo, M.A.; Masri, R. Piezoelectric Energy Harvester Utilizing Mandibular Deformation to Power Implantable Biosystems: A Feasibility Study. *J Mech Sci Technol* **2019**, *33*, 4039–4045, doi:10.1007/s12206-019-0749-4.
49. Dong, L.; Jin, C.; Closson, A.B.; Trase, I.; Richards, H.C.; Chen, Z.; Zhang, J.X.J. Cardiac Energy Harvesting and Sensing Based on Piezoelectric and Triboelectric Designs. *Nano Energy* **2020**, *76*, 105076, doi:10.1016/j.nanoen.2020.105076.
50. Dong, R.; Guo, B. Smart Wound Dressings for Wound Healing. *Nano Today* **2021**, *41*, 101290, doi:10.1016/j.nantod.2021.101290.
51. Yang, J.; He, Y.; Li, Z.; Yang, X.; Gao, Y.; Chen, M.; Zheng, Y.; Mao, S.; Shi, X. Intelligent Wound Dressing for Simultaneous *in Situ* Detection and Elimination of Pathogenic Bacteria. *Acta Biomaterialia* **2024**, *174*, 177–190, doi:10.1016/j.actbio.2023.11.045.

52. Lee, S.; Lee, C.; Bosio, J.A.; Melo, M.A.S. Smart Flexible 3D Sensor for Monitoring Orthodontics Forces: Prototype Design and Proof of Principle Experiment. *Bioengineering (Basel)* **2022**, *9*, 570, doi:10.3390/bioengineering9100570.
53. Wu, J.; Weir, M.D.; Melo, M.A.S.; Xu, H.H.K. Development of Novel Self-Healing and Antibacterial Dental Composite Containing Calcium Phosphate Nanoparticles. *J Dent* **2015**, *43*, 317–326, doi:10.1016/j.jdent.2015.01.009.
54. Wu, J.; Weir, M.D.; Zhang, Q.; Zhou, C.; Melo, M.A.S.; Xu, H.H.K. Novel Self-Healing Dental Resin with Microcapsules of Polymerizable Triethylene Glycol Dimethacrylate and *N,N*-Dihydroxyethyl-*p*-Toluidine. *Dental Materials* **2016**, *32*, 294–304, doi:10.1016/j.dental.2015.11.014.
55. Fadel, V.S.; Furtado, P.R.P.; Meier, M.M. Benzoyl Peroxide Encapsulation in Poly(Urea-Formaldehyde) Microcapsules for Use in Dental Materials. *Polymer Engineering & Science* *n/a*, doi:10.1002/pen.26831.
56. Montoya, C.; Kurylec, J.; Baraniya, D.; Tripathi, A.; Puri, S.; Orrego, S. Antifungal Effect of Piezoelectric Charges on PMMA Dentures. *ACS Biomater. Sci. Eng.* **2021**, *7*, 4838–4846, doi:10.1021/acsbiomaterials.1c00926.
57. Roldan, L.; Montoya, C.; Solanki, V.; Cai, K.Q.; Yang, M.; Correa, S.; Orrego, S. A Novel Injectable Piezoelectric Hydrogel for Periodontal Disease Treatment. *ACS Appl. Mater. Interfaces* **2023**, *15*, 43441–43454, doi:10.1021/acsami.3c08336.
58. Montoya, C.; Jain, A.; Londoño, J.J.; Correa, S.; Lelkes, P.I.; Melo, M.A.; Orrego, S. Multifunctional Dental Composite with Piezoelectric Nanofillers for Combined Antibacterial and Mineralization Effects. *ACS Appl. Mater. Interfaces* **2021**, *13*, 43868–43879, doi:10.1021/acsami.1c06331.
59. Ibrahim, M.S.; AlQarni, F.D.; Al-Dulaijan, Y.A.; Weir, M.D.; Oates, T.W.; Xu, H.H.K.; Melo, M.A.S. Tuning Nano-Amorphous Calcium Phosphate Content in Novel Rechargeable Antibacterial Dental Sealant. *Materials (Basel)* **2018**, *11*, 1544, doi:10.3390/ma11091544.
60. Ibrahim, M.S.; Balhaddad, A.A.; Garcia, I.M.; Collares, F.M.; Weir, M.D.; Xu, H.H.K.; Melo, M.A.S. PH-Responsive Calcium and Phosphate-Ion Releasing Antibacterial Sealants on Carious Enamel Lesions in Vitro. *J Dent* **2020**, *97*, 103323, doi:10.1016/j.jdent.2020.103323.
61. Balhaddad, A.A.; Kansara, A.A.; Hidan, D.; Weir, M.D.; Xu, H.H.K.; Melo, M.A.S. Toward Dental Caries: Exploring Nanoparticle-Based Platforms and Calcium Phosphate Compounds for Dental Restorative Materials. *Bioact Mater* **2019**, *4*, 43–55, doi:10.1016/j.bioactmat.2018.12.002.
62. Melo, M.A.S.; Weir, M.D.; Passos, V.F.; Powers, M.; Xu, H.H.K. Ph-Activated Nano-Amorphous Calcium Phosphate-Based Cement to Reduce Dental Enamel Demineralization. *Artif Cells Nanomed Biotechnol* **2017**, *45*, 1778–1785, doi:10.1080/21691401.2017.1290644.
63. Garcia, I.M.; Balhaddad, A.A.; Lan, Y.; Simionato, A.; Ibrahim, M.S.; Weir, M.D.; Masri, R.; Xu, H.H.K.; Collares, F.M.; Melo, M.A.S. Magnetic Motion of Superparamagnetic Iron Oxide Nanoparticles- Loaded Dental Adhesives: Physicochemical/Biological Properties, and Dentin Bonding Performance Studied through the Tooth Pulpal Pressure Model. *Acta Biomater* **2021**, *134*, 337–347, doi:10.1016/j.actbio.2021.07.031.
64. Li, X.; Wei, J.; Aifantis, K.E.; Fan, Y.; Feng, Q.; Cui, F.-Z.; Watari, F. Current Investigations into Magnetic Nanoparticles for Biomedical Applications. *J Biomed Mater Res A* **2016**, *104*, 1285–1296, doi:10.1002/jbm.a.35654.
65. Li, Y.; Hu, X.; Xia, Y.; Ji, Y.; Ruan, J.; Weir, M.D.; Lin, X.; Nie, Z.; Gu, N.; Masri, R.; et al. Novel Magnetic Nanoparticle-Containing Adhesive with Greater Dentin Bond Strength and Antibacterial and Remineralizing Capabilities. *Dent Mater* **2018**, *34*, 1310–1322, doi:10.1016/j.dental.2018.06.001.
66. Mokeem, L.S.; Martini Garcia, I.; Balhaddad, A.A.; Lan, Y.; Seifu, D.; Weir, M.D.; Melo, M.A. Multifunctional Dental Adhesives Formulated with Silane-Coated Magnetic Fe₃O₄@m-SiO₂ Core-Shell Particles to Counteract Adhesive Interfacial Breakdown. *ACS Appl Mater Interfaces* **2024**, *16*, 2120–2139, doi:10.1021/acsami.3c15157.
67. Zhou, K.; Li, J.; Li, W.; Zhang, Y.; Wang, K.; Xiong, X.; Li, S.; Chen, X.; Cheng, H.-W.; Qiu, J.; et al. Preparation and Magnetic Manipulation of Fe₃O₄/Acrylic Resin Core-Shell Microspheres. *Langmuir* **2023**, *39*, 11459–11467, doi:10.1021/acs.langmuir.3c01474.
68. Baras, B.H.; Wang, S.; Melo, M.A.S.; Tay, F.; Fouad, A.F.; Arola, D.D.; Weir, M.D.; Xu, H.H.K. Novel Bioactive Root Canal Sealer with Antibiofilm and Remineralization Properties. *Journal of Dentistry* **2019**, *83*, 67–76, doi:10.1016/j.jdent.2019.02.006.
69. Garcia, I.M.; Balhaddad, A.A.; Lan, Y.; Simionato, A.; Ibrahim, M.S.; Weir, M.D.; Masri, R.; Xu, H.H.K.; Collares, F.M.; Melo, M.A.S. Magnetic Motion of Superparamagnetic Iron Oxide Nanoparticles- Loaded

- Dental Adhesives: Physicochemical/Biological Properties, and Dentin Bonding Performance Studied through the Tooth Pulpal Pressure Model. *Acta Biomater* **2021**, *134*, 337–347, doi:10.1016/j.actbio.2021.07.031.
70. Nathanael, A.J.; Oh, T.H. Biopolymer Coatings for Biomedical Applications. *Polymers* **2020**, *12*, 3061, doi:10.3390/polym12123061.
 71. Tigmeanu, C.V.; Ardelean, L.C.; Rusu, L.-C.; Negrutiu, M.-L. Additive Manufactured Polymers in Dentistry, Current State-of-the-Art and Future Perspectives-A Review. *Polymers* **2022**, *14*, 3658, doi:10.3390/polym14173658.
 72. Garcia, I.M.; Mokeem, L.S.; Shahkarami, Y.; Blum, L.; Sheraphim, V.; Leonardo, R.; Balhaddad, A.A.; Melo, M.A.S. Tube-Shaped Nanostructures for Enhancing Resin-Based Dental Materials: A Landscape of Evidence and Research Advancement. *Smart Materials in Medicine* **2023**, *4*, 504–513, doi:10.1016/j.smaim.2023.03.002.
 73. Adeniji, O.O.; Ojemaye, M.O.; Okoh, A.I. Antibacterial Activity of Metallic Nanoparticles against Multidrug-Resistant Pathogens Isolated from Environmental Samples: Nanoparticles/Antibiotic Combination Therapy and Cytotoxicity Study. *ACS Appl. Bio Mater.* **2022**, *5*, 4814–4826, doi:10.1021/acsabm.2c00527.
 74. Melo, M.A.S.; Cheng, L.; Zhang, K.; Weir, M.D.; Rodrigues, L.K.A.; Xu, H.H.K. Novel Dental Adhesives Containing Nanoparticles of Silver and Amorphous Calcium Phosphate. *Dent Mater* **2013**, *29*, 199–210, doi:10.1016/j.dental.2012.10.005.
 75. Collares, F.M.; Garcia, I.M.; Klein, M.; Parolo, C.F.; Sánchez, F.A.L.; Takimi, A.; Bergmann, C.P.; Samuel, S.M.W.; Melo, M.A.; Leitune, V.C. Exploring Needle-Like Zinc Oxide Nanostructures for Improving Dental Resin Sealers: Design and Evaluation of Antibacterial, Physical and Chemical Properties. *Polymers (Basel)* **2020**, *12*, 789, doi:10.3390/polym12040789.
 76. Balhaddad, A.A.; Kansara, A.A.; Hidan, D.; Weir, M.D.; Xu, H.H.K.; Melo, M.A.S. Toward Dental Caries: Exploring Nanoparticle-Based Platforms and Calcium Phosphate Compounds for Dental Restorative Materials. *Bioact Mater* **2019**, *4*, 43–55, doi:10.1016/j.bioactmat.2018.12.002.
 77. Mitwalli, H.; AlSahafi, R.; Alhussein, A.; Oates, T.W.; Melo, M.A.S.; Xu, H.H.K.; Weir, M.D. Novel Rechargeable Calcium Fluoride Dental Nanocomposites. *Dent Mater* **2022**, *38*, 397–408, doi:10.1016/j.dental.2021.12.022.
 78. AlSahafi, R.; Mitwalli, H.; Alhussein, A.; Balhaddad, A.A.; Alquria, T.A.; Melo, M.A.S.; Lynch, C.D.; Oates, T.W.; Zhang, K.; Xu, H.H.K.; et al. Novel Rechargeable Nano-Calcium Phosphate and Nano-Calcium Fluoride Resin Cements. *J Dent* **2022**, *126*, 104312, doi:10.1016/j.jdent.2022.104312.
 79. Garcia, I.M.; Balhaddad, A.A.; Ibrahim, M.S.; Weir, M.D.; Xu, H.H.K.; Collares, F.M.; Melo, M.A.S. Antibacterial Response of Oral Microcosm Biofilm to Nano-Zinc Oxide in Adhesive Resin. *Dent Mater* **2021**, *37*, e182–e193, doi:10.1016/j.dental.2020.11.022.
 80. Bhadila, G.; Baras, B.H.; Weir, M.D.; Wang, H.; Melo, M.A.S.; Hack, G.D.; Bai, Y.; Xu, H.H.K. Novel Antibacterial Calcium Phosphate Nanocomposite with Long-Term Ion Recharge and Re-Release to Inhibit Caries. *Dent Mater J* **2020**, *39*, 678–689, doi:10.4012/dmj.2019-203.
 81. Liang, X.; Yu, B.; Ye, L.; Lin, D.; Zhang, W.; Zhong, H.-J.; He, J. Recent Advances in Quaternary Ammonium Monomers for Dental Applications. *Materials (Basel)* **2024**, *17*, 345, doi:10.3390/ma17020345.
 82. Thongthai, P.; Kitagawa, H.; Kitagawa, R.; Hirose, N.; Noree, S.; Iwasaki, Y.; Imazato, S. Development of Novel Surface Coating Composed of MDPB and MPC with Dual Functionality of Antibacterial Activity and Protein Repellency. *J Biomed Mater Res B Appl Biomater* **2020**, *108*, 3241–3249, doi:10.1002/jbm.b.34661.
 83. Fugolin, A.P.; Dobson, A.; Mbiya, W.; Navarro, O.; Ferracane, J.L.; Pfeifer, C.S. Use of (Meth)Acrylamides as Alternative Monomers in Dental Adhesive Systems. *Dental Materials* **2019**, *35*, 686–696, doi:10.1016/j.dental.2019.02.012.
 84. Fugolin, A.P.; Lewis, S.; Logan, M.G.; Ferracane, J.L.; Pfeifer, C.S. Methacrylamide–Methacrylate Hybrid Monomers for Dental Applications. *Dental Materials* **2020**, *36*, 1028–1037, doi:10.1016/j.dental.2020.04.023.
 85. Saiprasert, P.; Tansakul, C.; Pikulngam, A.; Promphet, P.; Naorungroj, S.; Ratanasathien, S.; Aksornmuang, J.; Talungchit, S. Novel Hydrolytic Resistant Antibacterial Monomers for Dental Resin Adhesive. *Journal of Dentistry* **2023**, *135*, 104597, doi:10.1016/j.jdent.2023.104597.
 86. Pratap, B.; Gupta, R.K.; Bhardwaj, B.; Nag, M. Resin Based Restorative Dental Materials: Characteristics and Future Perspectives. *Japanese Dental Science Review* **2019**, *55*, 126–138, doi:10.1016/j.jdsr.2019.09.004.
 87. Kowalska, A.; Sokolowski, J.; Bociong, K. The Photoinitiators Used in Resin Based Dental Composite—A Review and Future Perspectives. *Polymers* **2021**, *13*, 470, doi:10.3390/polym13030470.

88. Thadathil Varghese, J.; Cho, K.; Raju; Farrar, P.; Prentice, L.; Prusty, B.G. Influence of Silane Coupling Agent on the Mechanical Performance of Flowable Fibre-Reinforced Dental Composites. *Dental Materials* **2022**, *38*, 1173–1183, doi:10.1016/j.dental.2022.06.002.
89. Thadathil Varghese, J.; Cho, K.; Raju; Farrar, P.; Prentice, L.; Prusty, B.G. Effect of Silane Coupling Agent and Concentration on Fracture Toughness and Water Sorption Behaviour of Fibre-Reinforced Dental Composites. *Dental Materials* **2023**, *39*, 362–371, doi:10.1016/j.dental.2023.03.002.
90. Garcia, I.M.; Souza, V.S. de; Balhaddad, A.A.; Mokeem, L.; Melo, M.A.S. de; Scholten, J.D.; Collares, F.M. Ionic Liquid-Based Silane for SiO₂ Nanoparticles: A Versatile Coupling Agent for Dental Resins. *ACS Appl Mater Interfaces* **2024**, doi:10.1021/acsami.4c04580.
91. Cuppini, M.; Garcia, I.M.; de Souza, V.S.; Zatta, K.C.; Visioli, F.; Leitune, V.C.B.; Guterres, S.S.; Scholten, J.D.; Collares, F.M. Ionic Liquid-Loaded Microcapsules Doped into Dental Resin Infiltrants. *Bioact Mater* **2021**, *6*, 2667–2675, doi:10.1016/j.bioactmat.2021.02.002.
92. Singh, S.K.; Savoy, A.W. Ionic Liquids Synthesis and Applications: An Overview. *Journal of Molecular Liquids* **2020**, *297*, 112038, doi:10.1016/j.molliq.2019.112038.
93. Tibbitt, M.W.; Rodell, C.B.; Burdick, J.A.; Anseth, K.S. Progress in Material Design for Biomedical Applications. *Proc Natl Acad Sci U S A* **2015**, *112*, 14444–14451, doi:10.1073/pnas.1516247112.
94. Zhang, R.; Jones, M.M.; Moussa, H.; Keskar, M.; Huo, N.; Zhang, Z.; Visser, M.B.; Sabatini, C.; Swihart, M.T.; Cheng, C. Polymer–Antibiotic Conjugates as Antibacterial Additives in Dental Resins. *Biomater. Sci.* **2018**, *7*, 287–295, doi:10.1039/C8BM01228H.
95. Al-Dulaijan, Y.A.; Balhaddad, A.A. Prospects on Tuning Bioactive and Antimicrobial Denture Base Resin Materials: A Narrative Review. *Polymers (Basel)* **2022**, *15*, 54, doi:10.3390/polym15010054.
96. Souza, A.F.; Souza, M.T.; Damasceno, J.E.; Ferreira, P.V.C.; Alves de Cerqueira, G.; Baggio Aguiar, F.H.; Marchi, G.M. Effects of the Incorporation of Bioactive Particles on Physical Properties, Bioactivity and Penetration of Resin Enamel Infiltrant. *Clin Cosmet Investig Dent* **2023**, *15*, 31–43, doi:10.2147/CCIDE.S398514.
97. ISO 4049:2019 Dentistry — Polymer-Based Restorative Materials 2019.
98. ISO 3990:2023 Dentistry — Evaluation of Antibacterial Activity of Dental Restorative Materials, Luting Materials, Fissure Sealants and Orthodontic Bonding or Luting Materials 2023.
99. Ibrahim, M.S.; Garcia, I.M.; Kensara, A.; Balhaddad, A.A.; Collares, F.M.; Williams, M.A.; Ibrahim, A.S.; Lin, N.J.; Weir, M.D.; Xu, H.H.K.; et al. How We Are Assessing the Developing Antibacterial Resin-Based Dental Materials? A Scoping Review. *Journal of Dentistry* **2020**, *99*, 103369, doi:10.1016/j.jdent.2020.103369.
100. Cuevas-Suárez, C.E.; Ramos, T.S.; Rodrigues, S.B.; Collares, F.M.; Zanchi, C.H.; Lund, R.G.; da Silva, A.F.; Piva, E. Impact of Shelf-Life Simulation on Bonding Performance of Universal Adhesive Systems. *Dental Materials* **2019**, *35*, e204–e219, doi:10.1016/j.dental.2019.05.023.
101. Karunakaran, H.; Krithikadatta, J.; Doble, M. Local and Systemic Adverse Effects of Nanoparticles Incorporated in Dental Materials- a Critical Review. *The Saudi Dental Journal* **2024**, *36*, 158–167, doi:10.1016/j.sdentj.2023.08.013.
102. Health, C. for D. and R. Dental Composite Resin Devices - Premarket Notification [510(k)] Submissions - Guidance for Industry and FDA Staff Available online: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/dental-composite-resin-devices-premarket-notification-510k-submissions-guidance-industry-and-fda> (accessed on 3 July 2024).

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.