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Review Article

Comparative Analysis of Different Inorganic Fillers in Enhancing Bioactivity in Dental Resin – A Review

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Abstract
This review synthesizes research on "Comparative analysis of different inorganic fillers in enhancing bio-active properties of dental composite resin" to address the need for restorative materials that combine mechanical integrity with antibacterial and remineralization functions. The review aimed to evaluate antibacterial and remineralization capabilities, benchmark mechanical enhancements, analyze ion release and cytocompatibility, assess filler characteristics, and compare long-term stability of bioactive dental composites. A systematic analysis of in vitro studies employing diverse bioactive fillers including doped hydroxyapatite, bioactive glasses, calcium phosphate, and fluoride- doped nanoparticles was conducted, focusing on antibacterial efficacy, ion release kinetics, mechanical performance, biocompatibility, and aging under simulated oral conditions. Findings indicate that doped hydroxyapatite and customized bioactive glasses provide significant antibacterial activity and sustained ion release promoting remineralization while maintaining cytocompatibility. Mechanical properties are generally preserved or enhanced with optimized filler type, size, and surface modification, though high filler loadings may reduce strength and polymerization efficiency. Nanoparticle fillers improve bioactivity stability and mechanical performance, but dispersion challenges persist. Aging studies reveal that composites with tailored bioactive fillers exhibit superior mechanical stability and sustained bioactivity compared to conventional materials. These results underscore the critical interplay between filler composition, morphology, and surface treatment in achieving multifunctional dental composites.

Keywords: *Dental Resin, Inorganic Fillers, Bioactivity, Comparative Analysis, Dental Materials, Bioactive Composites, Dental Restoration, Material Science.*

INTRODUCTION
Research on the comparative analysis of different inorganic fillers in enhancing bio-active properties of dental composite resin has emerged as a critical area of inquiry due to the increasing demand for restorative materials that combine mechanical durability with biological functionality [1, 2]. Since the introduction of resin composites over five decades ago, advancements have focused on optimizing filler composition to improve mechanical strength, ion release, and antibacterial effects [3, 4]. The integration of bioactive fillers such as hydroxyapatite, bioactive glass, and calcium phosphate has shown promise in promoting remineralization and preventing secondary caries, which remain leading

causes of restoration failure worldwide [5, 6]. Notably, the prevalence of secondary caries underscores the practical significance of developing composites with enhanced bioactivity and mechanical stability [7, 8].

Despite extensive research on individual fillers, a specific problem persists in balancing bioactivity and mechanical integrity within dental composites [9,10]. While hydroxyapatite and bioactive glasses contribute to ion release and antibacterial properties, their incorporation often compromises mechanical properties such as flexural strength and hardness [11,12]. Moreover, controversies exist regarding the optimal particle size, doping elements, and filler ratios that maximize bioactive effects without degrading polymerization or durability [13,14]. The knowledge gap lies in the lack of comprehensive comparative analyses that systematically evaluate diverse inorganic fillers under standardized conditions, addressing both their bioactive potential and mechanical performance [15,16,17]. This gap limits the translation of promising fillers into clinically viable composites, potentially affecting long-term restoration success [18].

The conceptual framework for this review is grounded in the interplay between filler composition, resin matrix interactions, and resultant composite properties [19, 20]. Key concepts include bioactivity defined as the ability to release therapeutic ions and induce mineral deposition and mechanical performance, encompassing strength, hardness, and polymerization kinetics [21, 2]. Understanding the relationships among filler type, particle size, doping elements, and composite matrix is essential to elucidate mechanisms underlying enhanced bioactivity and mechanical stability [22, 23]. This framework guides the systematic evaluation of fillers to inform material design strategies.

The purpose of this systematic review is to critically compare the effects of various inorganic fillers on the bioactive and mechanical properties of dental composite resins [1, 2]. By synthesizing current evidence, this review aims to identify filler characteristics that optimize antibacterial activity, remineralization potential, and mechanical integrity, thereby addressing the existing knowledge gap [6, 5]. The findings will provide valuable insights for researchers and manufacturers seeking to develop advanced dental composites with balanced functional properties [20, 17].

This review employs a comprehensive literature search and selection of experimental and clinical studies focusing on inorganic fillers in dental composites [1, 2]. Analytical frameworks include comparative assessments of ion release, antibacterial efficacy, mechanical testing, and polymerization behavior [13, 14]. The findings are organized thematically to elucidate filler-specific effects and synergistic interactions, facilitating a nuanced understanding of filler performance in dental composites [22, 15].

SCOPE OF THE REVIEW

The objective of this report is to examine the existing research on "Comparative analysis of different inorganic fillers in enhancing bio-active properties of dental composite resin" in order to elucidate the roles and efficacies of various inorganic fillers in improving the biological and mechanical performance of dental composites. This review is important as it addresses the critical need for restorative materials that not only restore function but also actively contribute to caries prevention and tissue remineralization. By synthesizing current findings, the report aims to provide a comprehensive understanding of how different filler types influence antibacterial activity, mineralization potential, mechanical integrity, and biocompatibility. Ultimately, this analysis seeks to guide future material development and clinical applications by identifying promising filler candidates and highlighting gaps in knowledge.

SPECIFIC OBJECTIVES:

- To evaluate current knowledge on the antibacterial and remineralization capabilities of diverse inorganic fillers in dental composites.
- Benchmarking of existing approaches to enhance mechanical properties while maintaining bioactivity in resin-based dental materials.
- Identification and synthesis of comparative data on ion release profiles and cytocompatibility associated with various bioactive fillers.
- To deconstruct the influence of filler particle size, composition, and surface modification on composite resin performance.
- Compare the long-term stability and aging effects of dental composites functionalized with different inorganic fillers.

METHODOLOGY OF LITERATURE SELECTION

1. Transformation of Query

We take your original research question — "Comparative analysis of different inorganic fillers in enhancing bio-active properties of dental composite resin"—and expand it into multiple, more specific search statements. By systematically expanding a broad research question into several targeted queries, we ensure that your literature search is both comprehensive (you won't miss niche or jargon-specific studies) and manageable (each query returns a set of papers tightly aligned with a particular facet of your topic).

Below were the transformed queries we formed from the original query:

- Comparative analysis of different inorganic fillers in enhancing bio-active properties of dental composite resin
- Investigating the role of diverse inorganic fillers on the mechanical and bioactive characteristics of dental composite resins
- Investigating the impact of different bioactive fillers on the mechanical properties and remineralization capabilities of dental composite resins
- Exploring the impact of various bioactive fillers on mechanical strength, remineralization, and bioactive properties in dental composite resins
- Assessing the influence of diverse bioactive and inorganic fillers on the mechanical properties and biological performance of dental composite materials

2. Screening Papers

We then run each of your transformed queries with the applied Inclusion & Exclusion Criteria to retrieve a focused set of candidate papers for our always expanding database of over 270 million research papers. during this process we found 359 papers

3. Citation Chaining - Identifying additional relevant works

Backward Citation Chaining: For each of your core papers we examine its reference list to find earlier studies it draws upon. By tracing back through references, we ensure foundational work isn't overlooked.

Forward Citation Chaining: We also identify newer papers that have cited each core paper, tracking how the field has built on those results. This uncovers emerging debates, replication studies, and recent methodological advances A total of 54 additional papers are found during this process.

4. Relevance scoring and sorting

We take our assembled pool of 413 candidate papers (359 from search queries + 54 from citation chaining) and impose a relevance ranking so that the most pertinent studies rise to the top of our final papers table. We found 401 papers that were relevant to the research query. Out of 401 papers, 50 were highly relevant.

RESULTS

1. Descriptive Summary of the Studies

This section maps the research landscape of the literature on Comparative analysis of different inorganic fillers in enhancing bio-active properties of dental composite resin, encompassing a broad spectrum of experimental and comparative studies focused on bioactive fillers such as hydroxyapatite, bioactive glass variants, calcium phosphate, and fluoride-doped nanoparticles. The studies predominantly employ in vitro methodologies assessing antibacterial efficacy, ion release, mechanical performance, biocompatibility, and aging effects under simulated oral conditions. This comprehensive comparison addresses critical research questions by elucidating how filler composition, particle size, and surface modifications influence the multifunctional performance of dental composites, thereby guiding material optimization for clinical applications.

2. Antibacterial Activity:

Approximately 15 studies demonstrated significant antibacterial effects of composites containing zinc/strontium-doped hydroxyapatite, fluoride-doped nano-zirconia, hydrated calcium silicate, and bioactive glass fillers, with reductions in cariogenic bacteria such as *Streptococcus mutans* and *Staphylococcus aureus* [1, 8, 24]. Several studies highlighted the role of ion release (fluoride, calcium, hydroxide ions) and alkaline microenvironments in mediating antibacterial efficacy [8]. Some resin-based bioactive materials showed limited antibacterial activity compared to calcium silicate cements, indicating variability in efficacy depending on filler type and composite formulation [18].

3. Ion Release Profile

Around 20 studies reported sustained release of therapeutic ions including calcium, phosphate, fluoride, and strontium from various fillers such as bioactive glass, calcium phosphate nanoparticles, and fluoride-doped fillers, contributing to remineralization potential [1, 25, 26, 27]. Customized low-sodium fluoride-containing bioactive glasses and core-shell nanoparticles provided more controlled and prolonged ion release compared to conventional fillers [13, 28]. Ion release profiles were influenced by filler composition, particle size, and surface modification, affecting bioactivity and composite stability [12, 24].

4. Mechanical Properties:

Over 30 studies evaluated mechanical properties, with many reporting that incorporation of bioactive fillers can maintain or improve flexural strength, modulus, and hardness when optimized filler types and loadings are used [1, 29, 22,17]. Nano-sized fillers often preserved or enhanced mechanical properties better than micro-sized counterparts, with some exceptions where high filler loading reduced strength [12, 11, 30]. Polymerization kinetics and shrinkage were variably affected by filler type; customized bioactive glasses showed less inhibition of polymerization than conventional 45S5 BG [13, 14].

5. Biocompatibility and Cytotoxicity:

Multiple studies confirmed excellent cytocompatibility and low cytotoxicity of composites containing zinc/strontium-doped hydroxyapatite, fluoride-doped zirconia, and bioactive glass fillers, with cell viability often exceeding 90% [1, 8, 31]. Some fillers, such as borate glass, showed inhibitory effects on cell proliferation, highlighting the importance of filler composition on biocompatibility [32]. Preconditioning of composites and mineralization improved cellular responses in some bioactive glass-containing materials [6].

6. Aging and Stability:

Studies on aging revealed that composites with customized bioactive glasses exhibited better mechanical stability, lower water sorption, and sustained ion release compared to those with conventional fillers [29, 2]. Water sorption and solubility were higher in ion-releasing composites but necessary for bioactivity; surface modifications and filler selection influenced long-term dimensional stability [2, 33]. Artificial aging and thermocycling generally preserved antibacterial and mechanical properties in optimized composites, supporting their clinical potential [10, 34].

CRITICAL ANALYSIS AND SYNTHESIS

The reviewed literature presents a comprehensive examination of various inorganic fillers incorporated into dental composite resins, focusing on their bioactive properties, mechanical performance, and biocompatibility. A recurring theme is the balance between enhancing antibacterial and remineralization capabilities while maintaining or improving mechanical integrity. Studies demonstrate promising advances with doped hydroxyapatite, bioactive glasses, and novel nanoparticle fillers, yet challenges remain in optimizing filler size, surface modification, and long- term stability. Methodological diversity and variability in experimental designs limit direct comparisons, highlighting the need for standardized protocols. Overall, the evidence underscores the potential of multifunctional fillers but also reveals gaps in understanding the interplay between filler characteristics and composite performance under clinical conditions (Table 1).

Table_1: Analysis and synthesis of various inorganic fillers

Aspect	Strengths	Weaknesses
Antibacterial and Remineralization Efficacy	Several studies demonstrate significant antibacterial activity and mineral deposition with doped hydroxyapatite fillers such as Zn/HAp and Sr/HAp, achieving up to 95% bacterial kill rates and rich mineral formation without cytotoxicity1. Bioactive glasses, especially customized low-sodium fluoride-containing variants, show sustained ion release and apatite formation, contributing to remineralization and antibacterial effects [13, 25, 6]. Fluoride-doped nano- zirconia fillers also provide continuous fluoride release correlated with antibacterial properties [8].	While antibacterial and remineralization effects are well documented, many studies focus on short-term in vitro assessments, limiting understanding of long-term efficacy and clinical relevance [18] The variability in filler loading and ion release kinetics complicates direct comparison across studies. Some bioactive materials show diminished biological activity after aging or under simulated oral conditions [2, 18].
Mechanical Properties and Stability	Incorporation of fillers such as hydroxyapatite whiskers, bioactive glasses, and silica-based hybrid fillers has been shown to improve flexural strength, modulus, and hardness, with some composites meeting or exceeding ISO standards [29, 35, 9] Customized bioactive glasses demonstrate less detrimental effects on polymerization and mechanical properties compared to conventional fillers [13 , 29 ,2] Nanoparticle fillers, including $CaF2/SiO2$ core-shell and zirconia-based fillers, enhance mechanical strength and wear resistance while sustaining bioactivity [22, 16,17].	Many bioactive fillers, particularly at higher loadings, cause reductions in mechanical properties such as flexural strength and degree of conversion, often due to agglomeration or poor filler-matrix interaction [11, 35, 15]. Some studies report compromised mechanical integrity with increased bioactive filler content or polylysine incorporation [36] . The long-term aging effects on mechanical stability remain underexplored, with some composites showing significant property degradation after water immersion or thermocycling [2 ,8].

Filler Particle Size and Morphology	Downsizing bioactive glass particles to the nanoscale improves alkalizing potential and uniform hydroxyapatite layer formation without negatively affecting degree of conversion or hardness [12,14]. Novel 3D structured fillers like fluorinated urchin-like hydroxyapatite exhibit enhanced remineralization and antibacterial properties due to their morphology [8].	Despite advantages, nanoparticle fillers may pose challenges in dispersion and agglomeration, potentially affecting composite homogeneity and mechanical properties [11, 35]. The influence of particle size on polymerization kinetics and shrinkage stress is not consistently addressed, with some fillers inhibiting polymerization [13,14]. Morphological complexity may complicate manufacturing scalability and reproducibility.
Surface Modification and Polymerization Behavior	properties, suggesting morphology-driven benefits [4]. Surface modification of fillers, such as methacrylate-functionalized hydroxyapatite, enhances filler-matrix compatibility, improving composite stability and balanced ion release [23] Customized bioactive glasses show negligible adverse effects on polymerization kinetics and light transmittance, supporting their use in light- curable composites [13, 25].	Conventional bioactive glasses like 45S5 can reduce polymerization rate and degree of conversion, potentially compromising mechanical properties [13, 25]. Some studies lack detailed analysis of how surface treatments affect polymerization shrinkage and stress, which are critical for clinical performance [14] The impact of filler surface chemistry on long-term biocompatibility and degradation is insufficiently explored.
Ion Release Profiles and Cytocompatibility	Ion release from fillers such as amorphous calcium phosphate, bioactive glasses, and fluoride-doped fillers is linked to remineralization and antibacterial effects, with some materials demonstrating sustained release over weeks [26, 27, 31]. Cytocompatibility is generally maintained, with fibroblast viability exceeding 99% in several studies [1 , 8 ,31].Hybrid fillers combining silica and hydroxyapatite balance mechanical and bioactive properties effectively [9].	Ion release rates vary widely depending on filler type, size, and surface treatment, complicating optimization for clinical use [26, 27]. Some composites exhibit increased water sorption and solubility, potentially leading to filler leaching and compromised mechanical integrity [11 ,37]. Limited in vivo or long-term cytotoxicity data restrict conclusions about safety and efficacy.
Long-Term Stability and Aging Effects	Customized bioactive glasses and certain filler combinations demonstrate improved resistance to mechanical degradation and water sorption after artificial aging, suggesting better long-term stability [29, 2]. Some composites maintain antibacterial activity and mechanical properties after thermocycling [10].	Many studies focus on initial or short-term properties, with insufficient data on aging under oral-like conditions [18]. Water-induced microhardness reduction and increased solubility are common with conventional bioactive fillers [2]. The durability of ion release and antibacterial effects over extended periods remains uncertain.
Methodological Rigor and Comparability	The body of research employs diverse analytical techniques including FTIR, SEM- EDS, mechanical testing, and biological assays, providing multifaceted insights [1, 13,33] Some studies utilize standardized testing protocols and ISO benchmarks, enhancing reliability [29, 22].	Heterogeneity in experimental designs, filler concentrations, resin matrices, and testing conditions limits direct comparison and meta-analysis [38]. Many studies rely on in vitro models that may not fully replicate clinical environments. The lack of standardized aging protocols and long-term clinical data constrains the translation of findings.

LIMITATIONS OF THE LITERATURE

Table_2: This table contains limitations of the literature

Area of Limitation	Description of Limitation	Papers which have limitation
Limited Long-Term Clinical Data	Most studies focus on in vitro or short-term evaluations, limiting the external validity regarding long-term performance and durability of bioactive fillers in dental composites. This gap restricts understanding of aging effects and clinical longevity.	[1, 13, 29, 8, 2, 5]
Variability in Filler Types and Compositions	The heterogeneity in inorganic filler types, doping elements, particle sizes, and surface modifications across studies introduces methodological constraints, complicating direct comparisons and synthesis of findings. This variability affects the generalizability of conclusions.	[1, 13, 12,11, 23, 10, 17]
Insufficient Standardization of Testing Protocols	Differences in experimental conditions such as resin matrices, curing methods, aging simulations, and measurement techniques reduce reproducibility and comparability, thereby weakening the robustness of evidence on filler efficacy.	[13 , 2, 33, 37]
Limited Investigation of Biocompatibility and Cytotoxicity	While some studies assess cytotoxicity, comprehensive biocompatibility evaluations remain sparse, limiting confidence in the safety profile of novel inorganic fillers for clinical use. This gap affects the translational potential of findings.	[1, 35, 8, 12 , 6]
Focus on Mechanical Properties Over Multifunctionality	Many studies prioritize mechanical enhancements, often neglecting simultaneous evaluation of bioactivity, ion release kinetics, and antibacterial effects. This narrow focus restricts understanding of holistic performance needed for clinical success.	[29, 7, 30, 15, 16]
Limited Comparative Studies Among Filler Types	Few investigations directly compare multiple inorganic fillers under identical conditions, hindering definitive conclusions about relative efficacy in enhancing bioactive properties and mechanical performance.	[1, 12, 11, 10 , 5]
Predominance of Laboratory-Based Studies	The reliance on laboratory models, including simulated body fluids and artificial aging, limits external validity as these conditions may not fully replicate the complex oral environment and clinical challenges.	[13, 39, 2,18]

SUMMARY AND CONCLUSION

The collective evidence from the reviewed literature underscores the critical role of inorganic fillers in enhancing the bioactive properties of dental composite resins. Diverse filler types—including doped hydroxyapatite (zinc and strontium), bioactive glasses (conventional and customized formulations), calcium phosphate nanoparticles, fluoride-doped zirconia, and hydrated calcium silicate—have demonstrated the capacity to impart antibacterial effects and promote remineralization through sustained ion release. These fillers contribute to creating alkaline microenvironments and releasing therapeutic ions such as calcium, phosphate, fluoride, and strontium, which collectively inhibit cariogenic bacteria and facilitate mineral deposition on tooth surfaces. Notably, customized low- sodium fluoride-containing bioactive glasses and fluorinated hydroxyapatite with unique morphologies offer more controlled ion release and enhanced antibacterial efficacy, bridging the gap between bioactivity and mechanical performance.

Mechanical integrity remains a pivotal consideration in filler integration. The literature reveals that while many bioactive fillers maintain or improve flexural strength, modulus, and hardness when optimally loaded and surface-modified, excessive filler content or poor dispersion—especially with nano-hydroxyapatite and polysine additives—may compromise mechanical properties. Nanoparticle fillers often provide superior mechanical reinforcement and bioactivity compared to their micro-sized counterparts, although challenges related to agglomeration and polymerization kinetics persist. Surface modification strategies, such as methacrylate functionalization of hydroxyapatite, improve filler-matrix compatibility, thereby enhancing mechanical stability and sustaining ion release without adversely affecting polymerization behavior.

Biocompatibility profiles across the studies are generally favorable, with many composites exhibiting excellent cytocompatibility and minimal cytotoxicity. However, certain filler compositions, such as borate glass, may inhibit cellular proliferation, emphasizing the necessity of careful filler selection. Aging studies demonstrate that composites containing customized bioactive glasses or hybrid fillers show improved resistance to water sorption, solubility, and mechanical degradation over time, preserving antibacterial and remineralization functions under simulated oral conditions.

Despite these advances, methodological heterogeneity and a predominance of in vitro assessments limit direct comparisons and extrapolation to clinical settings. Long-term clinical data and standardized aging protocols remain sparse, posing challenges for definitive conclusions on the durability and sustained efficacy of these composites. Nonetheless, the synthesis of current research highlights the promise of multifunctional inorganic fillers in developing dental composites that not only restore mechanical function but also actively participate in caries prevention and tissue remineralization. Future investigations should prioritize standardized evaluation frameworks and in vivo validation to optimize filler formulations for enhanced clinical outcomes.

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Nil.

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