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Innovations in Pain Management Strategies in Endodontics: Review

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Abstract

Background: Pain management in endodontics remains a critical concern, as dental procedures can induce significant discomfort. Recent advancements in bioceramics, particularly calcium silicate-based materials, have shown promise in enhancing treatment outcomes and patient comfort.

Methods: A comprehensive literature review was conducted using PubMed and Web of Science databases from 1993 to 2023, focusing on studies related to bioceramic materials in endodontics. Keywords such as "bioceramics," "pain management," "endodontics," "root canal therapy," and "vital pulp therapy" were utilized to identify relevant research articles.

Results: The review highlighted the evolution of bioceramics, with materials like Mineral Trioxide Aggregate (MTA), Biodentine, and BioAggregate demonstrating superior biocompatibility and bioactivity. These materials facilitate effective pain management by promoting tissue regeneration and reducing inflammation. Innovations such as the incorporation of antibacterial ions into bioceramic formulations further enhance their efficacy against endodontic pathogens, thereby improving patient comfort during and after procedures.

Conclusion: The integration of advanced bioceramics in endodontic practice significantly contributes to pain management and treatment efficacy. These materials not only support biological healing processes but also reduce procedural discomfort. Future research should focus on optimizing mechanical properties and exploring novel bioceramic formulations to address current limitations. Continued clinical studies are essential to establish the long-term benefits of these innovations in routine dental practice.

Keywords: Bioceramics, Pain Management, Endodontics, Calcium Silicate, Regenerative Dentistry.

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1. Introduction

Bioceramics, a novel class of dental materials, were first used in the area of endodontics in the early 1990s. A comprehensive assessment of dental biomaterials indicated that bioceramics were a focal point of research from 2007 to 2019 [1]. Bioceramics are biocompatible ceramic substances or metal oxides, such as alumina, zirconia, bioactive glass, glass ceramics, hydroxyapatite, calcium silicate, and resorbable calcium phosphate. Bioceramics may be categorized as bioinert, bioactive, and biodegradable materials according to their interaction with adjacent tissues [2,3]. Bioceramics used in endodontics are mostly bioactive, with calcium silicate-based cements (CSCs) being the most prevalent. Besides possessing superior physical and chemical qualities, CSCs are significant in endodontic treatment owing to their biocompatibility and bioactivity [5,6].

In the last thirty years, there has been significant interest in creating bioactive dental materials that may engage with and promote the regeneration of adjacent tissue. Mineral trioxide aggregate (MTA) is the foremost bioactive ceramic used in endodontics and is the most extensively researched bioceramic to date. A bibliometric analysis indicated that MTA was a prominent subject in endodontic research throughout the first two decades of the 21st century [7]. MTA was produced from Portland cement and shown excellent biocompatibility and sealing properties [8,9]. Initially launched in dentistry as a root-end filling material in 1993, it received approval from the Food and Drug Administration (FDA) in 1997. ProRoot MTA was the first commercial MTA device introduced in 1999. The first ProRoot MTA product was gray, and all later iterations have enhanced this foundation. The intrinsic drawbacks of MTA include extended curing duration, elevated expense, and the potential for discolouration [10].

In the early 2000s, several customized MTA solutions emerged, addressing the limitations of conventional MTA while preserving its superior performance. White MTA, released in 2002, decreased the likelihood of tooth discolouration relative to gray MTA due to its lowered quantities of iron, aluminum, and magnesium oxides. MTA Angelus was introduced in 2001 and received FDA approval in 2011. MTA Angelus has a reduced setup time and enhanced operability while maintaining the exceptional performance of conventional MTA [11,12].

During the late 2000s and early 2010s, further bioceramics were formulated and used in endodontic treatment, exhibiting biological features similar to MTA, including antibacterial efficacy, little cytotoxicity, and a subdued inflammatory response [13,14]. Products like Biodentine, EndoSequence root repair material (ERRM), BioAggregate, and calcium-enriched mixes (CEM) have been extensively used in clinical practice [15]. Biodentine was launched in the dentistry market in 2009 as a "dentine substitute," enabling its infiltration into exposed dentine tubules [16]. Biodentine is developed using MTA-based cement technology, exhibiting enhanced mechanical strength and expedited solidification due to the absence of calcium aluminate or calcium sulfate [17].

ERRM comprises EndoSequence bioceramic putty (BC Putty) in putty form, analogous to iRoot BP Plus and TotalFill RRM Putty, and EndoSequence bioceramic sealer (BC Sealer) in paste form, comparable to iRoot SP and TotalFill Sealer. ERRM is a hydrophilic calcium silicate compound that generates hydroxyapatite upon solidification. It is a category of pre-prepared bioceramics with excellent operational efficacy and a little risk of dental discolouration [18]. BioAggregate is a bioceramic devoid of aluminum, including additions such calcium phosphate and silica. BioAggregate has shown superior stable bond strength and sealing capabilities, although has comparatively worse mechanical characteristics [19,20]. CEM, first used in dentistry in 2008, comprises several calcium compounds and has comparable superior qualities to MTA at a more economical cost [21]. It has similar physical features and therapeutic applications to MTA, although exhibits a distinct chemical makeup [4]. TheraCal LC was introduced to the market in 2011 as a light-curing resin-modified calcium silicate material intended for use as a liner in both direct and indirect pulp-capping techniques [22].

Over the last decade, the use of bioceramic materials in endodontics has been thoroughly investigated. Certain research focused on assessing the performance and clinical implications of current bioceramics, while others examined updates to older bioceramic products, like EndoSequence fast-set putty and BC Sealer HiFlow. Efforts were made to produce novel bioceramics, including a tricalcium silicate-based repair material combined with 30% calcium tungstate (TCS + $CaWO_4$), despite the absence of clinical evidence to date [23].

The advancement of diverse bioceramics has significantly enhanced the clinical practice of endodontics. This article examines the properties of bioceramics and their clinical uses in endodontics, including root-end filling, root canal therapy, vital pulp therapy, apexification/regenerative endodontic treatment, perforation repair, and root defect repair. Furthermore, we examine existing constraints and potential solutions to enhance the use of bioceramics in endodontic therapy.

2. Methods

We performed an electronic search for relevant studies in the PubMed and Web of Science databases from 1993 to 2023, without any constraints on research type. The MeSH keywords examined were Ceramics, Dental Cements, Biocompatible Materials, and Endodontics. Furthermore, we conducted a manual search of prominent endodontics journals from the last five years, including the Journal of Endodontics, International Endodontic Journal, Australian Endodontic Journal, and Iranian Endodontic Journal. Reference mining was conducted on the identified articles to identify further publications. Keywords such as root-end filling, root canal therapy, vital pulp therapy, apexification, regenerative endodontic treatment, perforation repair, and root defect repair were used to identify bioceramics-related studies in endodontics.

3. Attributes of Bioceramics

To comprehend the distinctions among various materials [4,24-27]. ProRoot MTA, Biodentine, BioAggregate, and CEM are all calcium silicate cements consisting of a powder and liquid component. The powder mostly consists of dicalcium silicate and tricalcium silicate, whereas the liquid's principal component is water. Upon combining the powder with the liquid, a composition mostly consisting of hydrated calcium silicate gels is formed, which ultimately hardens into a solid structure. BC Putty is a pre-mixed calcium silicate cement, a ready-to-use substance mostly composed of calcium silicate and calcium phosphate. TheraCal LC is a light-cured, resin-modified paste composed mostly of type III Portland cement and resin, based on calcium silicate. BC Sealer and EndoSeal MTA are both premixed, injectable calcium silicate-based sealers, differing only in that EndoSeal MTA includes aluminum, whilst BC Sealer does not. MTA Fillapex, BioRoot RCS, and Tech BioSealer are two-component sealers based on calcium silicate, using MTA, tricalcium silicate, and CEM as their active components, respectively.

The biocompatibility and bioactivity of bioceramics are mostly shown by their interactions with adjacent tissues. Bioceramics influence the proliferation, differentiation, migration, and death of stem cells, osteoblasts, osteoclasts, dental pulp cells, periodontal ligament cells, and immune cells. The cellular response to bioceramics influences the efficacy of wound healing and tissue regeneration. Mesenchymal stem cells (MSCs) originating from dental tissue include dental pulp stem cells (DPSCs), stem cells from human exfoliated deciduous teeth (SHED), and stem cells from apical papilla (SCAPs) [28]. Mesenchymal stem cells (MSCs) possess self-renewal capabilities and multidirectional differentiation potential, which are crucial for pulp regeneration and osteogenesis.

Bioceramics markedly enhance the adhesion and viability of stem cells, with their impact varying according to cell type [28-30]. Biodentine, NeoMTA Plus, and TheraCal LC have excellent biocompatibility and may promote the odontogenic and osteogenic development of mesenchymal stem cells (MSCs) [31]. Mesenchymal stem cells (MSCs) may be used in bone regeneration and tissue engineering when integrated with calcium phosphate bioceramics [32]. ProRoot MTA and Biodentine have biological properties that promote the activity of DPSCs in vitro [33]. Biodentine promotes the odontoblastic development of dental pulp stem cells (DPSCs) via mitogen-activated protein kinase (MAPK) and calcium/calmodulin-dependent protein kinase II (CaMKII) pathways [34].

MTA-HP and ERRM promote the proliferation, mineralization, and adhesion of DPSCs [35]. MTA and ERRM have excellent biocompatibility and osteogenic characteristics, facilitating the proliferation, adhesion, and migration of SHED [36]. MTA, Biodentine, and ERRM have favorable cytocompatibility and bioactivity when cultivated with SHED [37]. ProRoot MTA, Biodentine, and ERRM may facilitate the mineralization of SCAPs and promote odontogenic/osteogenic differentiation, hence endorsing their use in pulp regeneration [38,39]. SCAPs co-cultured with ProRoot MTA and Biodentine exhibited superior adhesion capacity and vitality compared to BioRoot RCS and calcium hydroxide [40]. BC Sealer markedly improves the cell migration of SCAPs and stimulates alkaline phosphatase activity as well as the development of mineralized nodules [41].

The restoration of bone tissue around impaired teeth relies on the quantity and equilibrium of osteoblasts and osteoclasts [42]. The interaction between bioceramics and cells is essential for regulating inflammation and facilitating wound healing during perforation repair and root-end filling [43]. MTA markedly suppresses RANKL-induced osteoclastogenesis and osteoclast function, therefore reducing bone resorption in periapical lesions [44]. BioAggregate promotes osteoblastic development, suppresses osteoclast formation in vitro, and has significant inhibitory effects on osteoclastic differentiation and inflammatory bone resorption in vivo [45-47]. BC Sealer and ProRoot ES exhibit superior biocompatibility compared to traditional root canal sealers and facilitate osteoblastic development [48].

DPCs and PDLCs participate in wound healing and the regeneration of dental and periapical tissues [49]. Bioceramics engage with DPCs/PDLCs during pulp capping, perforation repair, and root-end filling procedures. MTA, Biodentine, BioAggregate, and ERRM stimulate the expression of genes associated with mineralization and odontoblastic development in DPCs [50-54]. BioAggregates enhance the adhesion, migration, and attachment of DPCs [55]. Biodentine, MTA Angelus, and ERRM exhibit minimal cytotoxicity and high cell survival for DPCs in vitro, making them suitable as biocompatible materials in crucial pulp treatment [56,57]. Bioceramics like ProRoot MTA, Biodentine, and ERRM have beneficial effects on the odontogenic differentiation of DPCs in vitro and may efficiently facilitate the development of high-quality dentine bridges [58]. MTA Fillapex and BC Sealer promote reduced expression of inflammatory mediators and improved osteoblastic development of PDLCs via integrin-mediated signaling pathways [59].

Upon the introduction of a biomaterial into the tissue, immune cells, including monocytes and macrophages, react promptly. Macrophages secrete proinflammatory cytokines, including TNF-α, IL-1, and IL-12, during the initiation of the acute inflammatory response; anti-inflammatory cytokines, such as IL-4, are produced during tissue regeneration and repair. MTA alters the release of inflammatory cytokines, facilitates leukocyte recruitment and extravasation, and modulates inflammatory regulation and tissue repair in pulpitis and periapical conditions [60,61]. MTA and BC Sealers have favorable biocompatibility with macrophages, facilitating M1 and M2 polarization in RAW 264.7 and enhancing the secretion of proinflammatory cytokines. Biphasic calcium phosphate ceramics facilitate CaSR-mediated polarization of M2 macrophages for bone induction via the sustained release of calcium ions [62].

Numerous research studies have examined the biocompatibility and bioactivity of bioceramics in endodontics. MTA is the most extensively studied material and is regarded as the "gold standard." Insufficient research exists to assess other bioceramics in comparison to MTA, and discrepancies are evident in the methodologies and outcomes of several in vitro models. Consequently, further extensive studies are required to provide robust data for the use of these materials in endodontic procedures.

4. Clinical Applications in Endodontics

Bioceramics have been extensively used in several endodontic therapeutic applications (Figure 1). Bioceramic putties, including MTA, Biodentine, BioAggregate, BC Putty, and CEM, are often used for root-end filling, vital pulp treatment (VPT), apexification/regenerative endodontic therapy, perforation repair, and root defect repair. Bioceramic pastes, including BioRoot RCS and BC Sealer, are often used as sealing agents in root canal obturations.

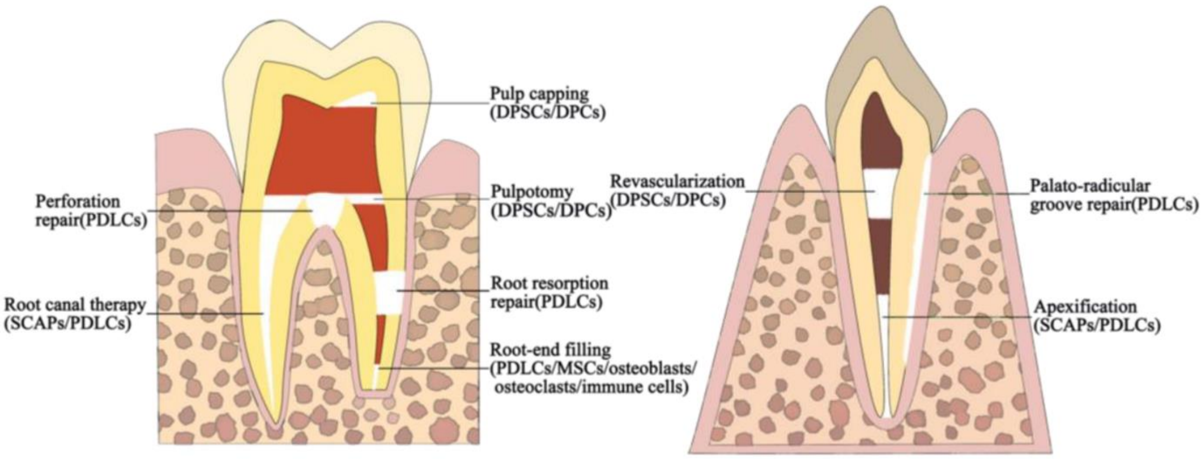

Figure 1. Diagrammatic representation of clinical bioceramics use in endodontics.

Currently, MTA is the most extensively researched bioceramic in endodontics. MTA has shown a reliable clinical result in treating endodontic disorders and is acknowledged as the benchmark for the development of new bioceramics. At now, several innovative bioceramics have been created to enhance their physical and chemical characteristics while minimizing procedure sensitivity and the risk of tooth discoloration. Comparable biocompatibility, bioactivity, and clinical results of numerous new bioceramics have been shown. Nonetheless, the antibacterial efficacy, mechanical characteristics, setting duration, and solubility of bioceramics need improvement in the future.

Bacteria are the primary etiological agents of endodontic disorders. Antimicrobial qualities are a crucial need for the use of bioceramics in endodontics. Nevertheless, only a limited number of bioceramics have shown significant antibacterial efficacy against intracanal biofilms [63]. Recent advancements in bioceramic-based scaffolds exhibiting antibacterial properties include drug-induced, ion-mediated, and physically activated techniques, as well as their synergistic applications tailored to particular antibacterial mechanisms [64]. Incorporating antibacterial ions, such as silver, copper, and zinc, into bioceramic scaffolds may enhance their antimicrobial efficacy. Silver (Ag) is a well-recognized antibacterial agent that may be included in various ways in different bioceramics. The integration of silver ions into hydroxyapatite (HA) yields remarkable antibacterial efficacy against Pseudomonas aeruginosa [65]. β-tricalcium phosphate (β-TCP) enhanced with silver as a bone grafting material may reduce the risk of infections. Copper (Cu) is a widely used therapeutic substance known for its significant angiogenic and antibacterial properties, with the release of Cu2+ being modulated by strategic design and efficient techniques. Cu2+ is incorporated into silicon-based bioceramics to concurrently improve their mechanical and antibacterial characteristics [66].

Zinc (Zn) has osteogenic, angiogenic, and antimicrobial characteristics. Bioactive glass scaffolds infused with Zn2+ demonstrate cytocompatibility and antibacterial properties [67]. The incorporation of antibiotics or pharmaceuticals into bionic bone scaffolds, together with the use of bioceramics and scaffolds for controlled release, might enhance antibacterial efficacy. Microspheres composed of lactic-co-glycolic acid (PLGA) covered with chitosan and loaded with hyaluronic acid (HA) and doxycycline hyclate complexes have been formulated for periodontal delivery [68]. Endodontic sealers using innovative, highly concentrated antimicrobial drug-silica coassembled particles (DSPs) exhibit significant antibacterial efficacy [69]. The physical antibacterial properties of bioceramics represent a significant approach. Nanomaterials and nanostructures possess distinctive physical and chemical features that may effectively induce antibacterial activity, especially against drug-resistant bacteria [70]. Consequently, conventional bioceramics in endodontics are anticipated to be enhanced by the incorporation of ions, the loading of antibiotics, and the activation of nanomaterials to tackle the issues of infection management in endodontics.

Optimal mechanical qualities are essential in certain endodontic therapeutic procedures; unfortunately, contemporary bioceramics have not met the requisite standards [3]. Additional investigation is necessary to enhance the mechanical characteristics of bioceramics while preserving their biological functionality. Various methods have been used to enhance the mechanical characteristics of calcium phosphate scaffolds, including structural optimization, ink modification, sintering refinement, and the creation of ceramic-polymer composite scaffolds [71]. Calcium phosphate silicate (CPS) is a potential bioceramic for bone grafting, whereas iron (Fe) is a beneficial ingredient that may augment the mechanical strength of CPS ceramics [72]. Iron-doped akermanite ceramic is an appropriate formulation for future bone substitution materials due to its adequate mechanical strength and favorable bioactivity [73].

Three-dimensional (3D) printing has revitalized the production of bioceramic scaffolds by enabling customizable porosity and intricate form design. Calcium silicate bioceramic scaffolds produced by 3D printing, including suitable pore diameters, show potential for enhancing mechanical characteristics [74]. Polymer-bioceramic composites serve as scaffolds for bone tissue engineering, integrating bioceramics with biocompatible polymers. This approach may enhance the mechanical characteristics of bioceramics. The use of silica-based bioglass enables HA-based bioceramics to sustain elevated compressive strength [75]. Polyether-ether-ketone (PEEK) is augmented with bioactive silicate-based bioceramics as nanofillers, resulting in markedly enhanced elastic modulus, flexural strength, and microhardness [76]. Iron doping, 3D printing, and polymer composites are the primary techniques for improving the mechanical characteristics of bioceramics, anticipated to provide favorable results in endodontics.

Bioceramics used for root-end filling come into direct touch with blood. Consequently, the capacity to withstand wash-out is a crucial determinant of sealing efficacy in this therapeutic context. The setting time is a crucial element in preventing the wash-out of bioceramics [15]. At present, many fast-setting bioceramics have been developed, including EndoSequence fast-set putty and iRoot FS. Further optimization of the solidification time of bioceramics for endodontic applications is essential. Nanomaterials, including multiwalled carbon nanotubes (MWCNTs), titanium carbide (TiC), and boron nitride (BN), may be included in BioRoot RCS to reduce its setting time. MTA Repair HP with nanostructure may achieve rapid setup and effective bioactive action [77]. The incorporation of ions is a prevalent technique for modifying materials, particularly in bioceramics, to enhance their solidification characteristics. Calcium silicates infused with zinc and magnesium have been produced by the sol-gel process, demonstrating a significant reduction in setting time relative to white MTA [78]. HPO42- ions are incorporated into calcium sulfate dihydrate crystals during the setting process, significantly influencing the rheological properties and setting characteristics of the CSC paste. Bi2O3, a widely used radiopacifier, may extend both the initial and ultimate setup periods while inhibiting the degree of hydration [79].

Consequently, the use of a radiopacifier like barium titanate (BT), which does not influence the curing duration, serves as a method to decrease the setting time of bioceramics. The self-setting property of bone cement is intact despite the addition of BT [80]. The incorporation of nanoparticles and ions, together with the substitution of components influencing solidification, are promising ways to decrease the setting time of bioceramics, hence potentially enhancing their applicability in endodontics.

The elevated solubility of bioceramic materials raises concerns, as it may create voids between the dentinal wall and the filling substance, so undermining the integrity of the seal. Calcium silicate-based sealers have much greater solubility compared to epoxy-resin sealers (AH Plus) [81]. Ionic doping is an effective approach to mitigate the limitations (high solubility) of bioceramic materials. Y2O3 and CeO2-doped SiO2–SrO–Na2O glass ceramics exhibit reduced release of Si4+ and Na+ ions [82]. The use of nano-phase materials in bioceramics may enhance their physicochemical characteristics, microstructure, and compressive strength. Composites with reduced solubility are achieved by including nanomaterials such as MWCNTs, TC, or BN in BioRoot RCS [83]. The incorporation of ions and nanoparticles is anticipated to diminish the solubility of bioceramics, therefore enhancing their sealing properties in endodontics.

Commercially accessible bioceramics consist of various compounds, and even identical materials may exhibit subtle variations in chemical composition based on the producer. Presently, the majority of comparison investigations on various bioceramic materials use commercial items. Laboratory investigations involving active chemicals remain necessary to provide reliable results. Further, well-controlled laboratory and clinical investigations are necessary to elucidate the structure-function connection of diverse bioceramics, which is crucial for advancing material development, and this area requires ongoing research efforts.

5. Conclusions

Bioceramics, including MTA, have shown remarkable bioactivity and biocompatibility, leading to their extensive use in endodontic clinical practice. Nonetheless, no bioceramic material is entirely optimal, since each has certain limits in practical applications. As materials have advanced, other bioceramics beyond MTA have emerged, including Biodentine, ERRM, BioAggregate, CEM, and BioRoot RCS. These innovative materials are used in root-end filling, root canal treatment, vital pulp therapy, apexification/revascularization, perforation repair, and root defect repair. Numerous clinical studies, in vitro investigations, and case reports have shown that they provide equivalent or superior therapeutic results than MTA. Nevertheless, robust clinical trials with extended follow-ups and well-controlled laboratory investigations remain limited. To enhance the trust in the clinical use of these bioceramics in endodontics, more high-quality research data is required in the future. Bioceramics are significant in the treatment of endodontic disorders and provide extensive potential for development. We anticipate the development of other novel or enhanced bioceramics in the future.

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الابتكارات في استراتيجيات إدارة الألم في علاج جذور الأسنان: مراجعة

الملخص

الخلفية :تظل إدارة الألم في علاج جذور الأسنان قضية حاسمة، حيث يمكن أن تتسبب الإجراءات السنية في قدر كبير من الانزعاج. أظهرت التطورات الأخيرة في المواد البيوسيراميكية، وخاصة المواد القائمة على سيليكات الكالسيوم، وعودًا بتحسين نتائج العلاج وراحة المرضى.

المنهجية :تم إجراء مراجعة شاملة للأدبيات باستخدام قواعد بيانات PubMed و Web of Scienceمن 1993 إلى 2023، مع التركيز على الدراسات المتعلقة بالمواد البيوسيراميكية في علاج جذور الأسنان. تم استخدام كلمات مفتاحية مثل "المواد البيوسيراميكية"، "إدارة الألم"، "علاج جذور الأسنان"، "علاج قنوات الجذور"، و"علاج اللب الحيوي" لتحديد المقالات البحثية ذات الصلة.

النتائج :أبرزت المراجعة تطور المواد البيوسيراميكية، حيث أظهرت مواد مثل **MTA (Mineral Trioxide Aggregate)**، وBiodentine، و BioAggregateتفوقًا في التوافق الحيوي والنشاط الحيوي. تسهم هذه المواد في إدارة الألم بشكل فعال من خلال تعزيز تجدد الأنسجة وتقليل الالتهاب. كما أن الابتكارات مثل إدخال أيونات مضادة للبكتيريا في تركيبات المواد البيوسيراميكية عززت فعاليتها ضد مسببات الأمراض في علاج الجذور، مما حسّن من راحة المرضى أثناء الإجراءات وبعدها.

الاستنتاج :يسهم دمج المواد البيوسيراميكية المتقدمة في ممارسة علاج جذور الأسنان بشكل كبير في إدارة الألم وفعالية العلاج. لا تدعم هذه المواد العمليات البيولوجية للشفاء فحسب، بل تقلل أيضًا من الانزعاج الناتج عن الإجراءات. يجب أن تركز الأبحاث المستقبلية على تحسين الخصائص الميكانيكية واستكشاف تركيبات بيوسيراميكية جديدة لمعالجة التحديات الحالية. تظل الدراسات السريرية المستمرة ضرورية لإثبات الفوائد طويلة الأمد لهذه الابتكارات في الممارسات السنية الروتينية.

الكلمات المفتاحية :المواد البيوسيراميكية، إدارة الألم، علاج جذور الأسنان، سيليكات الكالسيوم، طب الأسنان التجديدي.