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Bioceramic versus traditional biomaterials for endodontic sealers according to the ideal properties

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Abstract

Odontology, as a scientific discipline, continuously collaborates with biomaterials engineering to enhance treatment characteristics and patients' satisfaction. Endodontics, a specialized field of dentistry, focuses on the study, diagnosis, prevention, and treatment of dental disorders affecting the dental pulp, root, and surrounding tissues. A critical aspect of endodontic treatment involves the careful selection of an appropriate endodontic sealer for clinical use, as it significantly influences treatment outcomes. Traditional sealers, such as zinc oxide-eugenol, fatty acid, salicylate, epoxy resin, silicone, and methacrylate resin systems, have been extensively used for decades. However, advancements in endodontics have given rise to bioceramic-based sealers, offering improved properties and addressing new challenges in endodontic therapy. In this review, a classification of these materials and their ideal properties are presented to provide evidence-based guidance to clinicians. Physicochemical properties, including sealing ability, stability over time and space, as well as biological properties such as biocompatibility and antibacterial characteristics, along with cost-effectiveness, are essential factors influencing clinicians' decisions based on individual patient evaluations.

Keywords: endodontics; bioceramic-based sealers; traditional sealers; biocompatibility; setting time; stability; antibacterial properties
1. Introduction

Part of the health and well-being of people depends on the complex, specialized organs, known as teeth (Zhai et al., 2019). They are composed of a great variety of highly organized hard and soft tissue types, such as cementum, dentin, and highly calcified enamel, as well as soft tissues like dental pulp and periodontal ligament (Carvalho and Lussi, 2017; Nanci, 2017). Also, teeth are crucial to a person’s capacity to speak and interact successfully, eat and nourish the body, as well as healthy facial aesthetics, and interpersonal and psychosocial health (Zhang and Yelick, 2021). The dental pulp is the soft tissue that covers the tooth’s root and contains connective tissues, blood arteries, and nerves (Balic, 2018). If this pulp becomes infected or inflamed, it can cause severe pain and discomfort and, if left untreated, can lead to tooth loss (Zero et al., 2011).

The study, diagnosis, prevention, and treatment of disorders that affect the dental pulp, root, and tissues surrounding the tooth are the focus of the dental specialty known as endodontics. The objective of this field of knowledge is to investigate the anatomy, physiology, and pathology of human dental pulp and periarticular tissues (Ahmed et al., 2017). Basic and clinical approaches are covered in their study and applications, including the biology of the pulp in a healthy state and the causes, symptoms, and treatments of comorbidities, occurrences, and periarticular disorders that influence this structure (Khandelwal et al., 2022).

Endodontics therapies are designed to safeguard the native tooth while stabilizing its aesthetics and specifications (Chubb, 2019). As part of endodontic therapy, the pulp cavity must be cleaned, sterilized, and filled to facilitate irrigation and allow controlled obturation (Darcey et al., 2015). Indeed, irrigation represents one of the most decisive endodontic processes, due to its objective, which is the elimination of microorganisms, neutralization of endotoxins, dissolving of organic tissue and pulpal remains, whether living or necrotic, and dissolution of certain inorganic components (Darcey et al., 2016a). As a result of the endodontic treatment the mechanical process on its own does not completely eliminate the root canals from bacteria. Hence, the function of the obturation is to avoid reinfection by sealing the cleansed shape as well as sanitized root canal system (Darcey et al., 2016b).
Compared to other medical practices, dental negligence is similar to clinical medicine, mainly because it occurs when a dental professional defies the defined rules for performing dentistry and causes injury to the patient. (Manca et al., 2018). During ordinary clinical procedures, dentists may incur a range of endodontic errors and malpractices, perforation and broken equipment being the most prevalent causes of endodontic malpractice (Pinchi et al., 2013). To aid in clarification, endodontic discrepancies can be split into preoperative, intraoperative, and postoperative errors. Procedural errors that frequently occur during the intraoperative stage include access cavity preparation, instrument fracture, missing canals, ledge, irrigant extrusion through the apical foramen, underfilling, and overfilling of the root canal obturation (Alrahabi et al., 2019).

For endodontic therapy to be more beneficial, an optimum root-end filling is required that has strong root-end sealing potential, biocompatibility with surrounding cells and tissue, superior antibacterial characteristics, and the potential to promote tissue regeneration (Song et al., 2021a). The selection of an endodontic sealer for clinical use has an impact over time, so it is necessary to understand the characteristics and properties of an endodontic sealer to select the appropriate option and application for each clinical situation. (Bodanezi et al., 2012). The use of sealers, a thin sticky substance that acts as a lubricant and luting agent during the obturation process, allows core obturation material, such as gutta-percha points or other hard materials, to slide and cement in the canal (Viapiana et al., 2014). Sealers can cover spaces, lateral canals, and accessory tunnels since core obturation materials cannot penetrate them (Jardine et al., 2016; Kim et al., 2015).

Based on setting reaction and composition, there are multiple traditional endodontic sealers available, such as zinc oxide-eugenol, fatty acid, salicylate, epoxy resin, silicone, and methacrylate resin sealer systems (Komabayashi et al., 2020). Bioceramics are non-metallic, inorganic, and biocompatible materials that are used in the healthcare and dental sectors close to living tissues (Edrees et al., 2019). Additional bioceramic materials have been developed and implemented in endodontic procedures, including pulp capping, obturation, the building of apical barriers, the repair of perforations, and root-end filling. This is because they interact favorably with organic tissues, are chemically stable, and are non-corrosive (Wang, 2015).
Nowadays, endodontists are required to be familiarized with the myriad of sealers available, as doing so allows them to individually tailor patient treatment to match each patient's needs. By selecting the ideal sealer for a certain therapeutic situation and understanding the characteristics of different endodontic sealers, clinicians can maximize the effects of therapy and see the cost-effectiveness, which may improve patient outcomes and predictability. To inform dentists which material is more biocompatible, appropriate, exact, and safe and offers more guarantees to be able to maximize the management of each condition, the present review aims to compare standard sealants with bioceramics.

2. **Histological architecture of the tooth**

The teeth are hard, mineralized structures localized in the oral cavity that play important digestive, pronunciation, and aesthetic functions. The crown of the teeth is the portion of the tooth that protrudes from the maxillary or jawbone, and the root anchors to the alveolar bone and supplies vascularization and innervation. The teeth present the same basic cytoarchitecture composed of three layers of specialized tissue, enamel, cementum and dentin, and pulp. Enamel is the external, thin, and translucent layer that covers the crown of the tooth. It is mostly composed of calcium hydroxyapatite, the hardest substance in the entire organism. Approximately, 95% of its composition corresponds to calcium hydroxyapatite whereas the remaining percentage corresponds to water and different organic compounds which are increasingly being studied (Gil-Bona and Bidlack, 2020).

The cementum is a thin layer of material similar to the bone that covers the root of the tooth. The external surface of the cementum is bonded to the periodontal ligament to attach the tooth to the bone (Farci and Soni, 2022). Next, the dentin locates under the enamel and cementum. It is the more abundant tissue, supports the external layers, and contains the pulp. This layer is formed by about 70% of hydroxyapatite, and the remaining 30% is organic component emphasizing collagen type I. Attached to this, predentin is secreted by odontoblasts and contains two exclusive proteins that regulate dentin mineralization: dentin phosphoprotein and dentin sialoprotein (Ritchie, 2018). Odontoblasts secrete predentin and step back while dentin is deposited, leading to the
formation of dentinal tubules and a layer of odontoblasts in the interface pulp-dentin (Tjäderhane and Haapasalo, 2009).

The pulp is a loose connective tissue that contains blood vessels and nerves, that enter through the apical foramen in the root and extend to the crown leading to the formation of vascular and nervous networks under and within the odontoblast layer, and some naked nerve endings penetrate the dentinal tubules. Due to the continuous formation of dentin all through life, the pulp cavity gets smaller (Legge and Hardin, 2015).

Lastly, the periodontium comprises those tissues around the teeth that support them, which are the alveolar bone, gingiva, and periodontal ligament (Nanci and Bosshardt, 2006). A simple schema of tooth structure can be visualized in Figure 2.

3. Biomaterials for sealers in endodontics

3.1. What are sealers in endodontics and which properties define them?

In endodontics, the root canal sealer is the material that fills the empty area between the core obturating material and the dentine. Sealers can infiltrate voids, lateral canals, and accessory canals, where core filling material cannot access, and create micromechanical retention by the interaction with the surface of dentin (Viapiana et al., 2014). The sealer creates an impermeable barrier to the root canal system and prevents bacterial entry.

The ideal properties of biomaterials can vary depending on their specific application and intended use. In general, the ideal properties of biomaterials include biocompatibility, bioactivity, mechanical properties, stability, sterility, ease of use, cost-effectiveness, regulatory compliance, compatibility with imaging techniques, and longevity. Biomaterials used in endodontics, specifically in root canal treatment, have specific requirements due to the unique environment and conditions of the root canal system. According to the recent and available literature (Gasner and Brizuela, 2023; Komabayashi et al., 2020), updated ideal properties of biomaterials used in endodontics can include:

i. Biocompatibility: refers to the ability of a material to interact with living tissues without causing harmful effects on the surrounding tissues in the root canal
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system. Concretely, they should not induce inflammation, toxicity, or immune responses that could lead to complications or failure of the root canal treatment.

ii. **Sealing ability**: Biomaterials used in endodontics should have excellent sealing ability to prevent bacterial leakage and reinfection of the root canal system. They should create a tight seal between the root canal filling material and the canal walls, minimizing the risk of bacterial penetration and promoting healing.

iii. **Antibacterial properties**: to help control and eliminate bacteria in the root canal system. This can include antimicrobial agents or materials that inhibit bacterial growth and reduce the risk of reinfection.

iv. **Setting time**: appropriate timing allows for adequate manipulation and placement in the root canal system. They should have a controlled setting process to ensure proper sealing and stability after placement. It's important to follow the manufacturer's instructions for the specific sealer being used, as the setting time may vary based on the product. The clinician should also consider the clinical situation and patient factors when determining the optimal setting time for a particular case.

v. **Dimensional stability**: these materials should maintain their dimensional stability over time, even in the presence of moisture, saliva, and other oral fluids. They should not undergo significant shrinkage or expansion, which could compromise their sealing ability.

vi. **Radiopacity**: this means that these biomaterials should be visible on dental X-rays. Radiopacity allows for accurate assessment of the placement and performance of the biomaterials in the root canal system using radiographic imaging techniques.

vii. **Ease of use**: Biomaterials used in endodontics should be easy to handle, manipulate, and apply in a clinical setting. They should have appropriate working times, viscosity, and handling characteristics to facilitate their placement by the endodontist.

viii. **Long-term stability**: they should be stable over the long term, maintaining their sealing ability and performance without significant degradation or breakdown.
They should be able to withstand the challenges of the root canal environment and remain effective for an extended period.

ix. **Retrievability**: this means they should allow possible retreatment or reevaluation of the root canal system if needed. They should not bond excessively to the root canal walls, making their removal feasible without causing excessive damage to the tooth structure.

x. **Regulatory compliance**: they should meet applicable regulatory requirements, including safety, efficacy, and quality standards set by relevant regulatory authorities, such as the *Food and Drug Administration* in the United States or the *European Medicines Agency* in Europe.

3.2. **What types of sealers are there?**

Traditional sealers owe their denomination due to their extended use for years in clinical practice. Nevertheless, these have several limitations, including microleakage, lack of bioactivity, and difficulty in achieving complete sealing in complex root canal anatomy. Biomaterial engineering continues addressing these leverages, trying to mimetic the challenges of biomechanical properties and histology of teeth. Some of these newer materials have already been used in dentistry, while others keep improving by relying on nanotechnology.

Newer bioceramic-based sealers are known for their excellent sealing ability and minimal solubility and also improved biocompatibility and antimicrobial properties. They are designed to be durable and stable in the root canal system, providing a reliable and long-lasting seal. However, both kinds of sealers have their advantages and limitations. Some traditional ones are still commonly used in endodontics and can be effective when used appropriately by established clinical guidelines. The choice of the sealer depends on various factors, including the clinical situation, patient characteristics, and the clinician's preference and experience.

In the following sections, this review will provide specific details of each biomaterial used as a sealer in endodontics, describing their particular properties and classifying them as traditional or bioceramic-based.
3.2.1. Traditional sealers

a) Zinc oxide eugenol-based sealers

The zinc oxide eugenol-based (ZOE) sealer was developed in 1931 by Rickert and Dixon (Rickert and Dixon, 1931). Due to their long-term success, they are considered the gold standard in endodontics. ZOE-based sealers are typically composed of two main components: zinc oxide powder and eugenol liquid, an essential oil extracted from clove plants. If both components are mixed, a paste or putty-like consistency is obtained. The setting takes place by a chelation reaction, where zinc chelates two eugenolate molecules and forms a cross-linked network embedded with zinc oxide that hardens into a solid material (Komabayashi et al., 2020).

Eugenol from clove oil has been shown to confer antibacterial properties to the mix, which can help control and eliminate bacteria in the root canal system, which is important in root canal treatment (Marchese et al., 2017; (“Eugenol (Clove Oil),” 2019; Ulanowska and Olas, 2021).

Additionally, ZOE-based sealers are used in combination with gutta-percha (Vishwanath and Rao, 2019; Pandey et al., 2020), which is a rubber-like material that is used to fill the root canal space after the infected pulp has been removed. During the setting process, the eugenol liquid in the sealer reacts with the zinc oxide powder to form a solid mass. ZOE-based sealers work by filling the gaps and irregularities between the gutta-percha points and the root canal walls, creating a hermetic seal that helps prevent bacterial leakage and reinfection of the root canal system. The sealing ability of ZOE-based sealers is generally considered to be moderate to good (Cecchin et al., 2011).

ZOE-based sealers have a relatively long setting time compared to some other types of root canal sealers, which allows for adequate manipulation and placement in the root canal system (Cecchin et al., 2011). The setting time of ZOE-based sealers can vary depending on the specific product and manufacturer, as well as the clinical conditions and application technique used. However, as a general guideline, the setting time of ZOE-based sealers typically ranges from 24 to 48 hours.
They also have good dimensional stability, implying that they do not significantly shrink or expand upon setting, which helps ensure that ZOE-based sealer maintains its integrity and seal over time. Its stability can be affected by certain factors: on one hand, excessive moisture during mixing or application can impair the setting reaction and jeopardize the sealer's durability; on the other hand, high temperatures or chemical reactions with other components used in the root canal therapy procedure (Donnermeyer et al., 2020).

They also offer radiopacity and ease of handling, which make them popular choices for root canal treatment. They also offer other advantages like low cost, but they do have some limitations. They can be brittle and prone to microleakage and deterioration over time, which may affect their sealing ability (Shetty et al., 2015). Biocompatibility in some studies has been reported to cause potential cytotoxic effects in certain circumstances, such as high concentrations or direct contact with periapical tissues (MT et al., 2019; Buurma and Buurma, 2020). The retrievability is generally good, as it is not permanently attached to gutta-percha, therefore by mechanical instruments the odontologist can remove the piece.

However, despite their slow setting time, they slightly contract at this point, because they are slightly soluble. This leverage can cause teeth staining, especially when applying formulas containing silver in the powder (Tomson et al., 2014). Over time, different formulas have been developed to improve the properties, including silver-free formulas or formulas where calcium hydroxide or hydroxyapatite are added (Komabayashi et al., 2020). Some examples of ZOE sealers are *Pulp Canal Sealer* (Kerr, USA), *Proco-Sol* (StarDental, USA), *Tubli-Seal* (Kerr, USA), or *Bioseal* (OGNA Pharmaceuticals, Italy).

b) *Calcium hydroxide-based sealers*

Calcium hydroxide (Ca(OH)₂) is the main component of these sealers and is a well-known biocompatible material that has been used in various medical and dental applications for many years. Calcium hydroxide-based sealers are generally considered to be biocompatible, because they are well tolerated by living tissues and do not cause significant adverse reactions. Nevertheless, high concentrations of Ca(OH)₂ may cause allergies or hypersensitivity reaction (Romano et al., 2011).
The aim of adding Ca(OH)$_2$ to the sealer is to promote osteogenesis, cementogenesis, and antimicrobial activity (Mohammadi and Dummer, 2011; Ibrahim et al., 2020). Sealing ability resides in alkalinity, induction of mineralization, and chemical bonding with dentin. Alkaline properties of Ca(OH)$_2$ -pH 10-12- can help neutralize the acidic environment in the root canal and promote an antibacterial effect against microorganisms that may be present. Calcium hydroxide-based sealers also have been shown to stimulate the formation of mineralized tissue and promote the regeneration of periapical tissues, which can contribute to favorable healing outcomes (Mohammadi and Dummer, 2011). However, to exert its action, solubilization of Ca(OH)$_2$ is necessary, which may be counterproductive because effective sealers should be as stable as possible according to Grossman (Grossman, 1958; Gatewood 2007). Finally, chemical bonding with dentin provides a tight union between the sealer and the dentin helping to prevent microleakage (Mirhadi et al., 2016).

The following mechanisms of action have been suggested, although the exact mechanisms remain unclear: free available hydroxy ions are antimicrobial, alkaline pH promotes active calcification and neutralizes lactic acid and Ca(OH)$_2$ denatures proteins of the root canal and arrests external root resorption in the periodontal ligament space (Desai and Chandler, 2009). All of them may contribute to the promotion of healing. Regarding the matrix, Ca(OH)$_2$ is typically added to salicylate-based sealers, which set in a chelation reaction with zinc (Komabayashi et al., 2020), or ZOE or epoxy-based sealers (Gatewood, 2007). Sealapex (Kerr, USA), and Apexit/ Apexit Plus (Ivoclar Vivadent, Lichtenstein) are well-known examples.

Like ZOE-based sealers, the sealing ability is considered good in calcium hydroxide-based ones and is also used with gutta-percha, as it is the most common root filler material. In the same way, calcium hydroxide-based sealers are typically mixed with a vehicle – generally some water or an oil-based solution- to create a paste-like consistency that can be easily applied to the root canal walls. Calcium hydroxide-based sealers have a relatively low film thickness -the thickness of the sealer layer after setting. This low film thickness allows the sealer to flow into irregularities and gaps in the root canal system, ensuring a tight seal between the gutta-percha and the root canal walls. The sealer also sets to form a solid mass, which helps prevent dissolution or disintegration over time and maintains the seal (Srivastava et al., 2016; Brizuela et al., 2017).
This setting time is long compared to other sealers, it can range from several hours to several days. Of course, this period also varies depending on the specific product, as in any material we mention from now. Some sealers of this kind are designed to set slowly, allowing for adequate time for the sealer to penetrate and fill the complex root canal system, while others may have a faster setting time for more efficient clinical use (Abo El-Mal et al., 2019). The setting time of calcium hydroxide-based sealers can be influenced by various factors, such as temperature, humidity, and the specific formulation of the sealer. Higher temperatures and humidity levels can accelerate the setting time of the sealer, while lower temperatures and humidity levels may slow it down (Carvalho et al., 2013).

The radiopacity of the material is low as the number of atomic Calcium units and hydroxide ions is low. The sealer presents light color that is difficult to visualize in radiographic images, but the radiopacity of the gutta-percha helps in visualizing the quality and extent of root canal obturation (Laky et al., 2018).

These sealers exhibit good chemical stability due to the stable component Ca(OH)$_2$ in normal physiological conditions. The quality of mixing will be determinant in guaranteeing stability. They also offer good retrievability when setting steps have been adequate; they are not strongly bonded to gutta-percha (Raghu et al., 2017).

c) **Fatty acid-based sealers**

Being eugenol a cytotoxic agent, some sealers use fatty acid as chelating agents, instead of eugenol, in conjunction with zinc oxide. These sealers consist of a combination of natural or synthetic fatty acids and resins, which are inert biocompatible materials. However, the biocompatibility of fatty acid-based sealers can vary depending on the formulation. Furthermore, fatty acid-based sealers are hydrophobic, meaning they repel water and are resistant to moisture. This property can help to prevent the growth of bacteria and other microorganisms in the root canal system, which can contribute to the overall biocompatibility of the sealer (Komabayashi et al., 2020; Okamoto et al., 2022).

Some studies have shown that fatty acid-based sealers have good retrievability, and a high degree of flow and adaptability, allowing them to effectively fill and seal the root canal system (Komabayashi et al., 2020). Additionally, these sealers have been shown to
exhibit excellent bond strength to both gutta-percha and dentin, further enhancing their sealing ability.

Due to the nature of the heterogeneous composition of fatty acids, their metal complexes are often less well-defined and consistent than those that employ eugenolates and salicylates (Komabayashi et al., 2020). Some examples are Canals-N (Showa Yakuhin Kano, Japan) and Nogenol (GC America, USA). Radiopacity is not a strong point, but bioceramic materials commented on below add other metallic components to these to allow radiographic visibility.

d) Glass ionomer-based sealers

Glass ionomer-based sealers are composed of a mixture of silicate glass powder with polyacrylic and related organic acids and water. They were developed in the late 1960s as a result of an acid-base reaction involving a basic fluoro-alumino-silicate glass powder and polycarboxylic acid in the presence of water (De Bruyne and De Moor, 2004). Glass ionomer-based sealers are not ionomers in the chemical sense, so it is more precise to describe them as glass polyalkenoate cement. Glass ionomer-based sealers are considered safe and biocompatible and present good bonding to dentine because of the interaction between the polyacrylic acid and the hydroxyapatite in the dentin, antimicrobial effects via the sustained release of fluoride, and biocompatibility (Mohammadi and Shalavi, 2012). They release fluoride ions, which can have a protective effect on the tooth structure and prevent the formation of secondary caries. They also have a low pH during setting, which can help to reduce the risk of bacterial colonization and infection. For these properties, glass ionomer-based sealers are also employed in restorative dentistry. However, the antimicrobial activity is minimum, and it is difficult to remove in case of retreatment. An example is Ketac-Endo (3M ESPE, USA).

Setting times can range from 3-5 minutes for the initial setting and 20-30 minutes for the final setting. The radiopacity of glass ionomer-based sealers is typically higher than that of traditional zinc oxide eugenol-based sealers and calcium hydroxide-based sealers. Glass ionomer-based sealers offer good retrievability due to their ability to dissolve in acidic solutions. This property makes them particularly useful in situations where retreatment may be necessary but also makes them vulnerable to certain foods.
from the perspective of durability (Sidhu and Nicholson, 2016). These can be removed using a combination of mechanical instrumentation and chemical dissolution with an acidic solution, such as 17% EDTA. Additionally, the acidic solution used to dissolve the sealer can also affect the bond strength of any restorative materials placed over the treated tooth.

e) **Resin-based sealers**

This group can be divided according to their constituent elements into epoxy resin-based sealers or methacrylate resin-based sealers. The former is composed of low molecular weight epoxy resins and amines, where an organic addition reaction takes place between the epoxide groups, and amines resulting in the formation of a strong, adhesive, and durable material (Subbiya et al., 2021). They are the group most used in current clinical practice due to their properties: antimicrobial, superior adhesion and sealing capabilities, and are generally well-tolerated by the apical tissues (Pameijer and Zmener, 2010). However, in the case of extrusion into the periapical tissues, they exhibit poor resorption and in the unset state show significant toxicity (Pedrinha et al., 2021). Some examples are apical hydroxyapatite (a mixture of calcium hydroxide, organic resin, and filler particles) (AH) 26/ AH Plus (Dentsply Sirona, Germany), Adseal (Meta Biomed, Korea), or Acroseal (Septodont, France). AH 26 was substituted by AH Plus because it caused tissue response and in 1993 Spångberg et al found that AH 26 releases formaldehyde (Spångberg et al., 1993). Due to its ideal radiopacity, strong bond to dentin, dimensional stability, flow, and low solubility, the AH Plus sealer is widely recognized as the top-performing sealer in endodontics (Garikapati et al., 2020). It is considered to be reliable and effective for long-term success. Besides, this sealer is classified in four generations and polymerizes by radical polymerization. The first one, Hydron (Hydron Technologies, St. Petersburg, FL, USA), introduced by Wichterle and Lim in 1960, was composed of 2-hydroxyethyl methacrylate polymer gel, was designed for en masse root filling and did not require a core filling material (Subbiya et al., 2021). However, its usage ceased during the 1980s due to its brief operational duration, minimal radiopacity, challenges linked to its extraction from canals, and inclination to provoke inflammation in the periapical tissues (Kim et al., 2010). The second generation, EndoRez (Ultradent Products. Inc, Utah, USA), is a
hydrophilic urethane methacrylate resin sealer with a good ability to penetrate dentinal tubules, to achieve a “monoblock”, where the interface between sealer and the core material is completely gapless (Kittur et al., 2018). The third generation comprises *Epiphany Root Canal Sealant* (Pentron Clinical Technologies, Wallingford, Connecticut), in conjunction with the core material Resilon (Resilon Research, LLC, Madison, Connecticut) instead of classic gutta-percha, and improved the bonding to dentin. *Epiphany* sealer is a dual-curable sealer applied after dentin is etched and primed with 17% ethylenediaminetetraacetic acid (EDTA) and *Epiphany Primer*, respectively (Lotfi et al., 2013). *Epiphany* sealer is composed of ethoxylated glycidyl methacrylate and bisphenol A epoxy (*Bis-GMA*), urethane dimethacrylate (*UDMA*), and hydrophilic difunctional methacrylates (Shrestha et al., 2010).

This system also forms a ‘monoblock’ because dentin-sealer and sealer-core materials are covalently bonded. Setting time depends on the specific formulation, ranging from minutes to hours until they reach full polymerization. The last generation of methacrylate-based sealers has the advantage of working as an etchant, primer, and sealer all in one, limiting working time and errors in the bonding steps (Radovic et al., 2008).

The formula includes 4-methacryloyloxyethyl trimellitate anhydride (4-META) as an acidic resin monomer that when polymerizes forms a hybrid layer with dentin (Kim et al., 2010). This type of sealer can be used either with gutta-percha or *Resilon*. However, there is uncertainty regarding the ability of the bond between the core material and sealer to withstand the stresses caused by polymerization shrinkage during the setting of the resin sealer (Tyagi et al., 2013). This uncertainty raises questions about whether the goal of creating a ‘monoblock’ in the root canal system can be achieved by this type of sealer. Some examples are *MetaSEAL* (Hybrid Root SEAL) (Parkell, USA) and *Super-Bond RC Sealer* (Accel) (Sun Medical, Japan).

**f) Silicon-based sealers**

Silicone was first used by Davis et al in 1972 (Davis et al., 1972). Silicone-based sealers are composed of divinyl polysiloxane and polymethylhydrosiloxane which are set by an additional reaction and a platinum salt as the catalyst (Anusavice et al., 2013). Silicone-based sealers have been shown to provide a reliable seal and have good biocompatibility
(De-Deus et al., 2007). However, there is limited research about their biocompatibility properties, which do not display antibacterial activity, and setting time is inconsistent (Silva et al., 2015). *GuttaFlow 2/ RoekoSeal* (Coltene/Whaledent, USA) are the most common silicone-based sealers employed. They have the advantage of presenting a short setting time, around 10 minutes. Nevertheless, these materials do not provide retrievability in all cases, as they form a strong bond to the dentin that requires specialized more complex techniques to remove.

They have good dimensional stability and resistance dissolution, contributing to their long-term sealing ability. They also have the ‘monoblock’ structure that helps in stability and resistance to dislodgement. In table 1, the main traditional endodontic sealers are summarized and compared.

### 3.2.2. Bioceramic-based sealers

In recent years, new materials have arisen denoting interesting features, facing the main challenges in endodontic application: better bioactive materials, improved antimicrobial action and mechanical properties optimized, and reduced setting time (Tahara et al., 2023). Bioceramic materials serve as a superior alternative for various dental procedures, including pulp capping, perforation repair, pulpotomy, root canal filling, and obturation of immature teeth (Chitra et al., 2022). Moreover, dentistry is quickly developing its use of nanoparticles made of natural and manmade materials. These biomaterials have been included in several dental materials for their antibacterial properties and have assisted in the treatment of oral disorders, the removal of smear layers, and the formation of biofilms. When these nanoparticles combine all of their positive qualities, a new paradigm in dentistry will emerge (Raura et al., 2020).

Bioceramic sealers are composed of tricalcium and dicalcium silicates which undergo a hydration reaction with the water of dentinal tubules that sets and solidifies the cement (Altan and Tosun, 2016). During the setting reaction, calcium hydroxide is produced and the matrix starts to release calcium and hydroxide ions. These ions induce the formation of hydroxyapatite together with the preformed mineral infiltration zone in the interface dentin-sealer, leading to a chemo-physical bonding (Chellapandian et al., 2022).
Bioceramic sealers have gained recognition as preeminent materials for various clinical applications and they are widely regarded as the optimal reparative, owing to their superior physicochemical and biological attributes: short setting time, high mechanical strength, high alkaline pH and release of calcium ions, high radiopacity, moderate flow, low porosity and solubility, biocompatibility, stimulation of biomineralization, induction of pulp cell differentiation and better antibacterial activity (Wang, 2015).

They provide the advantages of faster healing and reduced inflammation. Radiopacity is provided by the addition of some molecules such as bismuth oxide, zirconia, tantalum oxide, or barium zirconate. However, a significant drawback associated with bioceramic sealers is the heightened adhesion between the material and the dentin wall, thereby presenting considerable challenges in terms of endodontic retreatment and post-preparation procedures (Jitaru et al., 2016).

Bioceramic-based sealers can be subclassified according to their capacity of reactivity with surrounding tissues, as recently reviewed and defined by Tahara et al. (Tahara et al., 2023): bioinert, bioactive, and biodegradable. From these three, only functional bioactive and biodegradable are considered in endodontics.

- **Bioinert**: They are chemically stable in vivo and have excellent resistance to corrosion, wear, and resistance to strength forces (Ivanova et al., 2014). They do not interact with biological systems. This group includes alumina and zirconia which are commonly used in orthopedics and dentistry, e.g.: femoral heads or dental implants, but not in endodontics (Schierano et al., 2015).

- **Bioactive**: Because of the bioactivity and capacity of bioactive ceramics to interact with the biological environment, bioactive ceramic sealers in endodontics have the potential to increase tissue regeneration, healing, and sealing (Chellapandian et al., 2022). Calcium silicate sealers, bioactive glass, bioactive glass ceramics, and hydroxyapatite are members of this category. Among these materials, calcium silicate sealers are the most employed due to their properties (Dawood et al., 2015). Mineral trioxide aggregate (MTA) was the first of this kind, introduced in the 1990s by Torabinejad and White (Torabinejad and White, 1993).
Biodegradable: Biodegradable bioceramics are a class of ceramic materials that can degrade or break down over time when exposed to physiological conditions. These materials are designed to be gradually resorbed by the body or incorporated into the tissue [35]. The most employed are calcium phosphate and bioactive glasses.

a) **Calcium silicate-based bioceramics: Mineral Trioxide aggregate (MTA)**

Successful calcium silicate-based bioceramics have been introduced into endodontics due to their superior biological characteristics, which has also boosted the success rate of endodontic therapy (Song et al., 2020).

Mineral Trioxide Aggregate (MTA) is the top calcium-silicate sealer. It contains *Portland cement*, calcium silicates, calcium aluminate, and bismuth oxide and sets in the presence of water. *Portland cement* was traditionally used in construction materials, it is a type of hydraulic cement used as a binder in dentistry. It has been used as an alternative to traditional root canal sealers and is bioinert (Parirokh and Torabinejad, 2010). Bismuth oxide allows the release of calcium ions, promoting osteogenesis and hard-tissue formation. These components do not cause significant inflammation and present low toxicity. *In vitro* studies demonstrated excellent biocompatibility, although the selection of repair bioceramic materials or MTA based on biocompatibility should be the professional's decision (Gomes Cornélio et al., 2011; de Oliveira et al., 2018).

The first MTA product available was *ProRoot MTA Gray* (Dentsply Sirona, Johnson City, TN, USA) in 1997, but it was used as a core filling material, not as a sealer. Then, *Grey & NeoMTA Plus* (NuSmile Avalon Biomed, Houston, TX, USA) was introduced followed by other powder-liquid sealers: *BioRoot RCS* (Septodont, France) and *Endo CPM Sealer* (EGEO, Buenos Aires, Argentina) (Tyagi et al., 2013). Currently, single paste sealers are gaining popularity because of their easy manipulation despite the high cost, e.g.: *iRoot SP*/*EndoSequence BC*/*Total Fill BC*/*Edge Endo Sealer* (Innovative Bioceramix, Canada), these are the same products under different brand names, *Bio-C Sealer* (Angelus, Brazil), *Endoseal MTA* (Maruchi, Korea) or *Ceraseal* (MetaBiomed, Korea). The setting of single-paste sealers consists of the direct absorption of water
from the dentinal tubules, leading to the formation of hydroxyapatite in the interface (Koch et al., 2010). *MTA Fillapex* (Angelus, Brazil) is a two-paste sealer that contains calcium silicates, but it is embedded in a matrix of salicylate.

These type of sealers offers a tight seal with dentin as it can set in the presence of moisture and its hydraulic properties, which allow it to expand and fill gaps between the material and the surrounding dentin (Song et al., 2021b). Setting times vary on product formulation, generally, they take 4-6 hours at 37°C (*EndoSequence BC*). This long setting time helps stability, ensuring a durable seal; nevertheless, it can also be seen as a limitation, since it may affect clinical performance. The radiopacity is good due to the presence of metallic particles, e.g. *EndoSequence BC* has zirconium oxide which offers high contrast on radiography (Bilvinaite et al., 2022).

MTA has been shown to have antibacterial activity against various bacteria commonly found in infected root canals, including *Enterococcus faecalis* and *Porphyromonas gingivalis*. It presents high pH and the release of calcium ions creates an alkaline environment inhibiting bacterial growth. However, organic components can lessen this ability (Stuart et al., 2006; Elreash et al., 2019). Conversely, retrievability is not simple and requires experienced action, and can cause damage to surrounding tissues.

**b) Biodentine**

*Biodentine* was introduced in the market in 2009 (Septodont, Saint Maur des Fosses, France) as a “dentin substitute” based on the MTA sealing composition (Rajasekharan et al., 2018). However, its composition was slightly modified to improve its physicochemical properties, i.e.: *Biodentine* shows a faster setting time (the initial setting time is around 12-14 minutes, and the final setting time is around 20-30 minutes) and increased mechanical strength (Kaur et al., 2017). *Biodentine* formula includes a setting accelerator (CaCl₂). The enhanced compressive strength and surface hardness observed in *Biodentine* can be attributed to its low water-to-powder ratio. This characteristic is potentially influenced by the presence of a water-soluble polymer in the liquid component of the material (Jang et al., 2014). *Biodentine* uses zirconium oxide instead of bismuth oxide as a non-inducing discoloration radiopacifier (Grech et al., 2013). For these reasons, even being a new material with no long-term results, all *Biodentine* is considered an alternative to the tricalcium materials used in endodontics.
Studies have revealed that Biodentine is biocompatible with pulp cells, periodontal ligament cells, and bone cells, proving that it has good biocompatibility. It has been discovered that Biodentine can cause the development of a mineralized tissue resembling dentin, demonstrating its biocompatibility and capacity to encourage tissue regeneration. Furthermore, research has demonstrated that Biodentine is not cytotoxic and not genotoxic, supporting its biocompatibility. This biomaterial can offer antibacterial activity against bacteria commonly associated with endodontic infections, but further research is still required in this field. Finally, for retrievability, not enough research has been done. This may be due to its design to be a permanent material as it cannot be removed easily.

c) Calcium phosphate-based sealers

Calcium phosphate-based sealers are highly biocompatible materials due to their composition, which is very similar to the mineral component of human bone and tooth structure (Bae et al., 2010). It has found success in different biomedical applications too, such as dental implants and grafts, besides endodontics. These sealers are primarily valued for their biocompatibility and ability to promote the formation of hydroxyapatite, rather than their antibacterial properties.

Recently developed Capsel based on tetracalcium phosphate, dicalcium phosphate dehydrate, Portland cement and zirconium oxide showed good biocompatibility, lower cytotoxicity, and tissue response. Indeed, Capsel releases a greater number of calcium ions than Sealapex and Sankin Apatite Root Sealer III (Bae et al., 2011). Bioagreggate (Verio Dental Co. Ltd., Vancouver, Canada) is a sealer that contains both nanoparticle sized tricalcium silicates and calcium phosphates with better performance than MTA (Zhu et al., 2014).

The sealing ability is considered optimal as it can penetrate dentinal tubules, and this property is improved by the ability of mineralization. Due to the low solubility and minimal setting shrinkage, dimensional stability is optimal as it maintains its shape over time (Al-Haddad and Aziz, 2016).

Setting time from these type of sealers can take a few minutes to many hours (Yong et al., 2022). For instance, certain calcium phosphate cements may require 8-10 minutes of
working time and 20–30 minutes of setting time, whereas other calcium phosphate
cements may require 2-3 minutes of working time and 10-15 minutes of setting time.  
However, some manufacturers have developed fast-setting versions of calcium
phosphate sealers that can set in less than a minute. To guarantee correct handling and
setting times, it is crucial to adhere to the manufacturer's recommendations for the
specific product being used, as must be considered in any material. Although there is
limited knowledge, this newer biomaterial is being thought of as not being removed,
therefore retrievability is not contemplated as its strong bond with dentin would be
difficult. Finally, regarding radiopacity, Zirconium oxide, tantalum oxide, and calcium
tungstate are a few radiopacifiers that can be utilized in calcium phosphate-based
sealers. The manufacturer and sealer's formulation may affect the particular
radiopacifier that is employed.

All properties here mentioned can be summarized in Table 2 for a better understanding
and comparison of the different biomaterials used as sealers in endodontics.

Conclusions

Bioceramic-based sealers are improving limitations that traditional sealers may have.
Biomaterial engineering keeps innovating and trying to reach the challenging nature of
teeth.

What we know so far is that novel bioceramic-based sealers are not being designed to
be retrievable due to their optimized biocompatibility with natural teeth.

Moreover, dentistry is quickly developing its use of new nanoparticles and components
to include several endodonic materials for their antibacterial properties. When these
biomaterials combine all of their strengths, a new paradigm in dentistry will emerge.

For the moment, we should not forget that the choice of biomaterials should be made
after giving careful attention to each material's characteristics, clinical evidence, and
appropriate application by established guidelines and protocols, as well as the specific
requirements and conditions of each patient. The clinician should also be prepared to
manage any adverse reactions or complications that may arise during or after root canal
treatment and monitor the patient's response to the sealer closely.
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**Figure Legends**

**Table 1.** Summary of properties of the principal biomaterials for traditional endodontic sealers. For any biomaterial, it is of note that to guarantee correct handling and setting times, it is crucial to adhere to the manufacturer's recommendations for the specific product being used.

**Table 2.** Summary of properties of the principal biomaterials for bioceramic-based endodontic sealers. For any biomaterial, it is of note that to guarantee correct handling and setting times, it is crucial to adhere to the manufacturer's recommendations for the specific product being used.

**Figure 1.** Main basic steps and objectives of endodontic intervention.

**Figure 2.** Histological structure of the tooth. As represented, the tooth is composed of an outer membrane (enamel), mostly composed by hydroxyapatite (95%) and other organic molecules and water. The next layer, dentin, is also composed of 70% hydroxyapatite, occurred after mineralization of predentin thanks to two proteins, dentin phosphoprotein and dentin sialoprotein. Pulp cavity, composed of connective tissue and cementum, are also components of the cytoarchitecture of the tooth. Anatomically, the tooth is composed by a crown, the visible part of this organ and a root,
<table>
<thead>
<tr>
<th>Biocompatibility</th>
<th>Sealing ability</th>
<th>Antibacterial properties</th>
<th>Setting time</th>
<th>Dimensional stability</th>
<th>Radiopacity</th>
<th>Ease of use</th>
<th>Long-term stability</th>
<th>Retrievability</th>
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<tbody>
<tr>
<td><strong>Traditional</strong></td>
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<tr>
<td>Zinc oxide eugenol-based sealers</td>
<td>Potential cytotoxic effects when applied in high concentrations or with direct contact with periapical tissues</td>
<td>Moderate to good</td>
<td>✔️</td>
<td>Long (24-48h, depending on the manufacturer)</td>
<td>✔️</td>
<td>✔️</td>
<td>By zirconium oxide</td>
<td>Good</td>
</tr>
<tr>
<td>Calcium hydroxide -based sealers</td>
<td>Well tolerated. But high concentrations of Ca(OH)₂ may cause allergies or hypersensitivity reactions and lessen biocompatibility</td>
<td>Good</td>
<td>By Ca(OH)₂</td>
<td>Long (hours-days). Higher temperatures and humidity levels can accelerate it</td>
<td>✔️</td>
<td>Low. Gutta-percha reveals the status of the root canal in radiographic images.</td>
<td>✔️</td>
<td>The main component Ca(OH)₂ is chemically stable in physiological conditions</td>
</tr>
<tr>
<td>S E A L E R S</td>
<td>Fatty acid-based sealers</td>
<td>Generally good. Variable: Resin is inert but fatty acids formulation determines biocompatibility</td>
<td>High. Good flow and adaptability, effectively fill and seal the root canal system.</td>
<td>✓</td>
<td>Variable (hours)</td>
<td>✓</td>
<td>Due to their hydrophobic nature, they do not change shape during setting or over.</td>
<td>✓</td>
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</tr>
<tr>
<td>Glass ionomer-based sealers</td>
<td>Good, safe, no significant adverse reactions</td>
<td>Good</td>
<td>✓</td>
<td>Besides their low pH, they release fluoride ions, which prevent the formation of secondary caries</td>
<td>✓</td>
<td>Better than ZOE-based and calcium hydroxide-based sealers</td>
<td>✓</td>
<td>Vulnerable to acidic solutions (certain foods)</td>
</tr>
<tr>
<td>Resin-based sealers:</td>
<td>✓</td>
<td>AH: Well tolerated by apical tissues Other epoxy and methacrylate show</td>
<td>AH: Superior adhesion and sealing Methacrylate based:</td>
<td>✓</td>
<td>AH’s better sealing ability prevent the advance of</td>
<td>Depends on the formulation (from minutes to hours)</td>
<td>AH: strong bond to dentin, dimensiona stability, flow, and low</td>
<td>✓</td>
</tr>
</tbody>
</table>
- epoxy-based (Apical hydroxyapatite, AH)
- methacrylate based

<table>
<thead>
<tr>
<th></th>
<th>toxicity</th>
<th>‘monoblock’: great sealing core-sealer and sealer-dentin, covalently. Gutta-percha or Resilon as core materials.</th>
<th>bacteria.</th>
<th>solubility</th>
<th>sealer all-in-one limits working time and errors in the bonding steps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silicon-based sealers</td>
<td>Not well recognized yet</td>
<td>‘monoblock’, tight seal</td>
<td>Not display antibacterial activity</td>
<td>Short, around 10 minutes</td>
<td>Good. Resistance to dissolution</td>
</tr>
</tbody>
</table>
For any biomaterial, it is of note that to guarantee correct handling and setting times, it is crucial to adhere to the manufacturer's recommendations for the specific product being used.
Table 2. Summary of properties of the principal biomaterials for bioceramic-based endodontic sealers

<table>
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<th>Long-term stability</th>
<th>Retrievability</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Calcium silicate-based bioceramics:</strong></td>
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<td></td>
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<td></td>
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<tr>
<td>Mineral Trioxide aggregate (MTA)</td>
<td>MTA: Excellent Low toxicity</td>
<td>MTA: Excellent Tight seal. Combined with gutta-percha</td>
<td>It creates an alkaline environment inhibiting bacterial growth. But organic components can lessen this ability.</td>
<td>Long. Vary on product formulation, generally, 4-6 hours at 37ºC</td>
<td></td>
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</tr>
<tr>
<td><strong>Biodentine</strong></td>
<td>Great. Not cytotoxicity</td>
<td>Great. Optimal mechanical strength</td>
<td>✓ Not fully understood</td>
<td>Faster than other biocermics. The initial setting time is around 12-14 minutes and the final setting time is around 20-</td>
<td>✓ Low shrinkage</td>
<td>✓ by zirconium oxide</td>
<td>✓</td>
<td>Suitable for long periods</td>
<td>✓</td>
</tr>
<tr>
<td>Calcium phosphate-based sealers</td>
<td>Great. The most similar to the natural mineral component of teeth.</td>
<td>Great</td>
<td>Not fully understood</td>
<td>Several minutes to a few hours. Some even a minute.</td>
<td>Optimal Due to low solubility and minimal setting shrinkage</td>
<td>Different radiopacifiers depending on manufacturer and formulation (zirconium oxide, tantalum oxide, and calcium tungstate).</td>
<td>Limited research</td>
<td>Not contemplated retrievability</td>
<td></td>
</tr>
</tbody>
</table>
**Irrigation**

Elimination of microorganisms, neutralization of endotoxins, dissolution of organic tissue and pulpal remains, living or necrotic, and dissolution of certain inorganic components.

**Obturation**

Prevent re-infection by sealing the clean and disinfected root canal system.
Hydroxyapatite = 95%

Water and organic compounds

Enamel

Dentin

Predentin+dentin phosphoprotein and dentin sialoprotein

Pulp cavity

Connective tissue

Cementum