Review

Epoxy resin-based root canal sealers: An integrative literature review

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Abstract

The correct obturation of the root canal system achieved by means of a core and a cement is essential for the success of endodontic treatment. There are several root canal cements (RCCs) on the market; however, because of their excellent characteristics, epoxy resin-based sealers (ERBSs) have been widely used. The main aim of this review was to analyze and integrate the available information on different ERBSs. An electronic search was performed in the PubMed and Scopus databases, using "epoxy resin" AND "root canal treatment", and "epoxy resin" AND "endodontics" as search terms. In general, ERBSs have good flow properties, film thickness, solubility, dimensional stability, sealing capacity, and radiopacity. They are also able to adhere to dentin while exhibiting low toxicity and some antibacterial effects. However, their main disadvantage is the lack of bioactivity and biomineralization capability. A large number of ERBSs are available on the market, and AH Plus keeps being the gold standard RCC. Yet, information on many of them is limited or non-existent, which could be due to the fact that some of them are relatively new. The latter emphasizes the need for relevant research on the physicochemical and biological properties of some ERBSs, with the aim of supporting their clinical use with sufficient evidence via prospective and long-term studies.

Keywords: root canal sealants, root canal filling materials, AH Plus, epoxy resin-based root canal sealer

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Introduction

Three-dimensional obturation of the root space is essential for the long-term success of endodontic treatment. There are various materials and techniques available for obturation of the root space, with most techniques using a central core material and root canal cement (RCC). Regardless of the central core, the use of RCC is essential for hermetic sealing and fluid tightness.[1] Currently, there are several types of endodontic sealers available on the market with different compositions, the most common being RCCs consisting of zinc oxide eugenol, calcium hydroxide ($Ca(OH)_2$), glass ionomers, silicone sealers, calcium silicates, methacrylate resins, and epoxy resins,[2–4] even though they do not comply with all the requirements described by Grossman.[5] Epoxy resin-based sealers (ERBSs) can be considered the RCC of choice[6,7] for obturation of the root canal system because of their adequate physicochemical properties.[7,8] Most recent studies deal with ERBSs on a general basis[2,9] or approach their properties separately,[6,7,10–16] but notably, the present study analyzes, discusses, and integrates the properties of several of these types of RCCs available on the international market, and is the first one to approach their formulation-behavior relationship. This review aimed to analyze and integrate the available data on the different ERBSs, compiling information on the physical, chemical, and biological properties, formulations, and other areas of clinical interest of these RCCs.

Methods

In November 2020, a preliminary search was carried out for literature reviews related to the physicochemical properties of ERBS, and no studies were found that presented an extensive and updated overview of these sealers. In April 2021, an electronic literature search was performed utilizing the PubMed and Scopus databases and the search terms "epoxy resin" AND "root canal treatment", as well as "epoxy resin" AND "endodontics", to find studies that contained these search terms that had been published within the last 10 years. A second search was performed in August 2022, to analyze the information pertaining to the ERBS formulation components.

Only original works published in English were included. A total of 604 and 264 manuscripts were found in PubMed and Scopus, respectively. The search was limited to clinical trials, in vitro studies, literature reviews, systematic reviews, and textbook chapters. Interim reports, abstracts only, letters, brief communications, studies that did not focus on ERBSs, and duplicated works were excluded. Additionally, agar diffusion studies and sealability studies, including linear and volumetric dye penetration assessment methodologies, autoradiographic detection of isotope penetration, radionuclide detection, culture techniques to detect bacterial penetration, salivary penetration models, fluid filtration techniques, fluorometry, intracanal reservoir techniques, and electrochemical techniques were also excluded because such studies have not been considered useful since reliable and reproducible evaluation methods related to clinical outcomes are required.[17] Subsequently, the titles and abstracts of relevant articles were reviewed and a manual search of the references of each selected article was performed to complement the electronic search. Finally, 91 articles and 6 textbook chapters were considered relevant and included in this review.

Since we only searched two electronic databases, this decision could have limited the results with regard to the inclusion of relevant literature in our review, e.g., grey literature was excluded during the literature search stage. Additionally, being an integrative literature review, the present study has inherent limitations, i.e., the complexity of using diverse selected studies, which apply different methods, has the potential to contribute bias and might, therefore, complicate data evaluation and analysis. However, at the same time, this type of review is the broadest of its kind and has the potential to resolve the complexities brought about by varied perspectives.[18]

General characteristics and formulations of ERBSs

Epoxy resin was patented by P. Casta, a Swiss chemist from DeTrey (Zurich, Switzerland), in 1938.[9] ERBSs were introduced into endodontics by Schroeder in 1950, with the market launch of AH 26® (Dentsply Maillefer).[19] Due to its release of formaldehyde, which causes cytotoxicity in periapical tissues, this sealer has been modified to what is now marketed as AH Plus® (Dentsply Sirona).[10,20] This RCC has been extensively evaluated and compared to other alternatives and, based on its physicochemical properties and biological response, is currently considered the gold standard (Fig. 1).[21–24] However, there are other commercially available ERBSs, with different compositions, according to the manufacturer, and are included in Table 1. Based on our performed search, there is no review that integrates information on the characteristics as well as the physicochemical and biological properties of these types of sealers. A compilation of the information on ERBS physical, chemical, and biological properties with highlights of clinical interest is presented in detail below in different sections.

With regard to Table 1, it must be emphasized that all of the listed ERBSs shall finally form an epoxy resin; however, one should take into consideration that the structure of a material results in the formation of its properties, and the latter determines the behavior of the material. In this regard, most commercially available epoxy resins are based on diglycidyl ethers of bisphenol-A, bisphenol-F, or other phenolic compounds,[25] which react with curing agents.

Table 1. Epoxy resin-based sealers (ERBSs) available on the international market

Sealer	Composition*		Manufacturer
AH Plus	paste A: bisphenol A epoxy resin, bisphenol F epoxy resin, calcium tungstate, zirconium oxide, silica and iron oxide pigments	paste B: bibenzyldiamine, aminoadamantane, tricyclodecane-diamine, calcium tungstate, zirconium oxide, silica and silicone oil	Dentsply Maillefer, DeTrey, Germany
Thermaseal Plus			Dentsply Sirona, Becht, Germany
Topseal			Dentsply Maillefer, Ballaigues, Switzerland
AH-26	resin paste: epoxy resin	powder: bismuth oxide, methenamine, silver, titanium dioxide	Dentsply Maillefer, DeTrey, Germany
Acroseal	base: hexamethylene tetramine, bismuth subcarbonate, hydrogenated rosin, paraffin oil, venice terpentine, enoxolone	catalyst: bismuth carbonate, calcium hydroxide, diglycidyl ether bisphenol A, yellow iron oxide	Specialités-Septodont, Saint Maur-des-Fossés, France
Adseal	base: epoxy oligomer resin, ethylene glycol salicylate, calcium phosphate, zirconium oxide, bismuth subcarbonate	catalyst: polyaminobenzoate, triethanolamine, calcium phosphate, bismuth subcarbonate, zirconium oxide, calcium oxide	Meta Biomed Co, Cheongju, Korea
DiaProSeal	paste A: epoxy resin, zirconium oxide, calcium hydroxide	paste B: calcium tungstate, zirconium oxide, calcium hydroxide	Diadent, Cheongju, Korea
EasySeal	diethylenetriamine, amine-epoxy-based no further information		Komet Dental, Lemgo, Germany
Epoxidin	epoxide resin, amine hardening agents, zirconium oxide as a radioopaque filler, a lime component, and a plasticizing agent		TehnoDent, Severnyi, Russia
EZ-Fill Xpress	information not available		Essential Dental Systems, South Hackensack, USA
MM-Seal	base: epoxy resin, ethylene glycol salicylate, calcium phosphate, bismuth subcarbonate, zirconium oxide	catalyst: polyaminobenzoate, triethanolamine, calcium phosphate, bismuth subcarbonate, zirconium oxide, calcium oxide	Micro-Mega, Besançon, France
Obturys	paste A: 4,4′-isopropylidenediphenol, oligomeric reaction products with l-chloro-2,3- epoxypropane, zirconium dioxide, silicon dioxide	paste B: oxirane, 2-methyl-, polymer with oxirane, bis(2-aminopropyl) ether, zirconium dioxide, silicon dioxide	Itena, Paris, France
Obtuseal	base: TCD-diamine, a radiopaque excipient	catalyst: calcium hydroxide, DGEBA (diglycidyl ether of bisphenol A) and radiopaque excipient	A.T.O., Zizine, France
Perma Evolution	paste A: 4-[2-(4-hydroxyphenyl) propan-2-yl]phenol-epichlorohydrineresin, alkylglycidyl ether, barium sulfate, tricalcium phosphate, diphenylolpropan-diglycidyl ether	Paste B: polyalkoxyalkylamine-copolymer, 5-amino-1,3,3- trimethylcyclohexanmethylamin, aqua, barium sulfate, tricalcium phosphate, nanodispersed silicon dioxide, polyhexamethylene biguanides-hydrochloride	Becht, Germany
Radic Sealer	base: poly epoxy resin, zirconium oxide	catalyst: TEA (triethanolamine), zirconium oxide, calcium oxide	KM, Seoul, Korea
Sealer 26	powder: calcium hydroxide, bismuth oxide, hexamethylenetetramine, titanium dioxide	resin: bisphenol epoxy resin	Dentsply, Rio de Janeiro, Brazil
Sealer Plus	base: bisphenol A-coepichlorohydrin, bisphenol F epoxy resin, zirconium oxide, silicone and siloxanes, iron oxide, calcium hydroxide	catalyzer: hexamethylenotetramine, zirconium oxide, silicone and siloxanes, calcium hydroxide, calcium tungstate	MK Life, Porto Alegre, Brazil
Sicura seal	base: epoxy oligomer resin, ethylene glycol salicylate, calcium phosphate, bismuth carbonate, zirconium oxide	catalyst: polyaminobenzoate, triethanolamine, calcium phosphate, bismuth carbonate, zirconium oxide, calcium oxide	Dentalica, Milan, Italy
SimpliSeal	base: epoxy oligomer resin, ethylene glycol mono salicylate, calcium phosphate, bismuth subcarbonate, zirconium oxide	catalyst: poly(1.4-butanediol)bis (4-aminobenzoate), triethanolamine, calcium phosphate, bismuth subcaronate, zirconium oxide, calcium oxide	DiscusDental, Culver City, USA
2Seal	paste A: bisphenol A epoxy resin, bisphenol F epoxy resin, calcium tungstate, zirconium oxide, silica and iron oxide pigments	paste B: dibenzyldiamine, aminoadamantane, tricyclodecane-diamine, calcium tungstate, zirconium oxide, silica and silicone oil	VDW, Munich, Germany

* information obtained from the manufacturers.

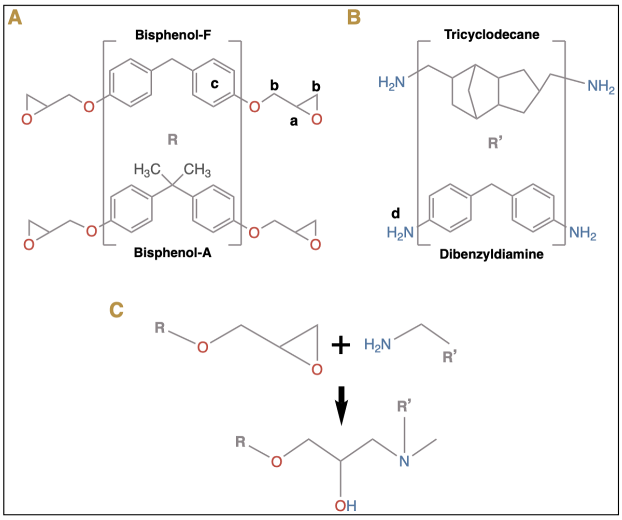

Fig. 1. Molecular structure of the main chemical components of epoxy resin–based endodontic sealer (ERBS) AH Plus

A – epoxy molecules bisphenol-A and bisphenol-F with characteristic epoxy rings on both ends: (a) CH group of epoxide; (b) C–H bond in CH_2; (c) C=C bonds in benzene rings. B – aromatic amine epoxy resin hardeners (dibenzyldiamine and tricyclodecane) with characteristic 2 amine functional groups: (d) N–H bond in aromatic amine. C – epoxy resin setting (curing) reaction induced by the amine hardeners that cross-link the epoxy monomers together after opening epoxy rings to form the resinous matrix. Reproduced with permission from Atmeh and AlShwaimi.[63]

However, almost none of the ERBSs have the same formulation; thus, in the next paragraphs of this section, we will discuss some relevant compounds in the formulations described in Table 1, alongside various other compounds in subsequent sections.

As for the curing agents listed in Table 1 (which are aliphatic and aromatic amines), epoxy resins may be cured with any of them, because they have a labile hydrogen atom or hydroxyl group that reacts with the epoxy rings and initiates the polymerization process, even at room temperature. However, aliphatic amines are strong skin irritants, while aromatic amines impart higher temperature stabilities.[25] AH-26, Sealer 26, Sealer Plus, and Acroseal contain methenamine (hexamethylenetetramine), which releases formaldehyde during the polymerization process, being an inherent disadvantage of these sealers due to its toxicity[26], although the released quantity is considered negligible.[27] Poly(aminobenzoate) is contained in Adseal, MM-Seal, Sicura Seal, and SimpliSeal and is effective in applications where long working times, substrate wettability, and lower heat-build are required,[28] thereby improving the performance in these ERBS. On the other hand, methenamine (which decomposes into formaldehyde and ammonia in an acidic environment) is curiously also used as a food preservative or fraudulently in dairy products.[29] Additionally, formaldehyde is a natural by-product of amino acid metabolism in almost all cells, with the endogenous level known to be 3–12 ng/g in tissues[30] and 2.5 ppm in plasma.[31]

On the other hand, Sealer Plus has silicone and siloxanes (the –Si–O–Si–O– backbone of silicones is referred to as siloxane) added to its composition. In this regard, this backbone confers silicones with a very high thermal stability[25] and results in the enhancement of flexibility, toughness, durability, and chemical and weather resistance.[32] These could be the reasons for their addition to this sealer. AH Plus, Thermaseal Plus, Topseal, Sealer Plus, and 2Seal have silicone oil (polydimethylsiloxane) in their composition, which is hydrophobic in nature, resistant to bacterial degradation, has an extremely low surface tension, and adsorbs strongly to solid surfaces.[33] Additionally, it possesses high heat resistance and lubricant properties.[34] All these properties would certainly favor the clinical behavior of these sealers.

It has been stated that the most important additive in an adhesive composition is the filler (improving thermal stability, bond strength, and flow properties).[25] However, ERBS manufacturers do not specify it in their formulations. In this regard, some sealers (AH Plus, Thermaseal Plus, Topseal, Sealer Plus, 2Seal, and Obturys) contain silica – also defined as silicon dioxide[35] – in their formulations. This is an inorganic filler that has exhibited pivotal effects in relation to reducing shrinkage during curing as well as conferring thixotropic properties and improving the bond strength of epoxy adhesives[25]; it also stimulates osteogenesis by inducing biomineralization.[36] Finally, titanium dioxide is a filler in AH26 and Sealer 26 and is widely used to produce a white color in numerous products.[37]

Acroseal is the only ERBS that contains (three) plant-derived ingredients, i.e., hydrogenated rosin, Venice turpentine, and enoxolone. Hydrogenated rosin (colophony) and Venice turpentine are diterpenic resins with very similar compositions (complex mixtures of resinous acids)[38] that enable cross-linking and polymerization in the polymer matrix.[39] Both of them possess excellent adhesive properties and are often included as additives in adhesive formulations to increase adhesion, brightness, and toughness.[38] Recently, rosin has attracted attention in the formulation of biobased epoxy resins from renewable resources.[40] Furthermore, enoxolone (glycyrrhetinic acid) is a bioactive triterpenoid compound of licorice (*Glycyrrhiza glabra*) that exhibits anti-inflammatory, antioxidant, and anti-nociceptive properties,[41] which are ideal for an endodontic sealer formulation.

Oxyranes – also known as epoxides[42] – are described in Obturys formulation. They represent one of the new monomers that have been developed to substitute bisphenol A-containing BisGMA dental composites.[43] Oxyranes are cyclic ether compounds that are more hydrophobic than methacrylates, and they polymerize via cationic ring-opening processes, which reduces polymerization shrinkage stress.[42] Although the latter would benefit the clinical behavior of the ERBS, there are no published studies that have evaluated such issues.

Perma Evolution contains poly(hexamethylenebiguanide)-hydrochloride, which is considered an antibacterial agent[44] and could improve the antibacterial properties of this sealer. However, there are no published studies that have evaluated this property. Other ERBS-containing antibacterial agents are described below in the antibacterial section, and those containing $Ca(OH)_2$ are described in the biocompatibility and bioactivity sections.

On the other hand, Sicura seal and SimpliSeal contain ethylene glycol salicylate, also known as 2-hydroxyethyl salicylate, which is formed from the condensation of the carboxyl group of salicylic acid with one of the hydroxyl groups of ethylene glycol.[45,46] Salicylates are very often used in the formulation of topical anti-inflammatory products for the treatment of mild to moderate pain.[45,46] Additionally, derivatives of salicylate resins are used to obtain resins/polymers[47] and it has been shown that the flow ability of some sealers is influenced by the type of salicylate resin and its particle size.[46]

Finally, regarding the ERBS compositions listed in Table 1, it must be taken into consideration that specific processes and/or ingredients for formulating sealers are proprietary of the manufacturer. Moreover, many manufacturers do not provide any information about the composition ratio of these sealers.[46] These issues inherently limit an ample discussion on the above-mentioned structure-properties relationship.

Physicochemical properties

The physicochemical properties of ERBSs are described in the sections that follow, and a condensed table of information regarding these properties is presented in Table 2, including their flow, film thickness, solubility, setting time, dimensional change, and radiopacity.

Flow

According to the American National Standards Institute and American Dental Association (ANSI/ADA) No. 57 and The International Organization for Standardization (ISO) 6876, RCCs should have a minimum flow rate of 17 mm.[48,49] Available evidence shows that the sealers AH Plus,[11,12,20,21,50–58] ThermaSeal Plus,[50] Acroseal,[11] Adseal,[11,20,56,59] EasySeal,[53] EZ-Fill Xpress,[52] MM-Seal,[58] Pherma Evolution,[12] Radic Sealer,[20] Sealer Plus,[21,51] and SimpliSeal[52] meet the established requirements. On the other hand, 1 study evaluated Dia-Proseal and AH Plus (Table 2),[59] which fell short of achieving the required values; this difference may be due to the methodology used since the authors mention that more precise evaluation techniques (rheometer) should be used.[59]

The activation of sealer cements with sonic and ultrasonic protocols has shown an increase in flow values of AH Plus and Adseal, which attained the highest values after ultrasonic activation while still complying with ANSI/ADA No. 57 and ISO 6876 standardizations. The heat generated during this process reduced the viscosity of the sealers, increasing their flow and improving their rheological and mechanical properties, especially their cohesive strength.[63] On the other hand, the manufacturer of EZ Fill Xpress recommends that it be warmed using a heated spatula to improve its fluidity.[64] However, high flow may result in apical extrusion, possibly leading to periapical tissue injury due to RCC cytotoxicity[50] and subsequent postoperative pain.[65]

Film thickness

ANSI/ADA No. 57 and ISO 6876 suggest that this thickness should not exceed 50 μm.[48,49] Resin-based sealers have shown greater adhesion to dentin in thicker layers. On the contrary, in thin layers, there is greater penetration of the RCC into the dentinal tubules. In this regard, the resin matrix of the cement penetrates the dentinal tubules, while the filling particles do not, due to their larger size, thus leaving a layer enriched with particles but without resin in the canal wall, resulting in a lower adhesion strength.[13,14] These findings suggest that the "ideal" thin film for this type of RCC needs to be reconsidered.[14]

The sealers AH Plus,[11,52,53] Easy Seal,[53] EZ-Fill Xpress,[52] and SimpliSeal[52] meet standardizations. On the other hand, 1 study reported values of 85 ±8 μm for the film thickness of AH Plus.[55] Acrosel and Adseal obtained values higher than 50 μm (Table 2). Although the different studies comply with the standardized methodology, the available information does not specify the causes of the variations in the results.

Water solubility

Solubility indicates the mass loss of the material when immersed in water. RCCs must have a low solubility.[60] The solubility, according to ANSI/ADA No. 57 and ISO 6876, must be less than 3%.[48,49] Conventional methodologies for assessing solubility have some limitations, so micro-computed tomography (micro-CT) imaging methods are currently being used to complement the tests performed by ANSI/ADA No. 57 and ISO 6876.[57]

The difference in material weight before and after immersion in water may not represent the solubility of all RCCs, as some of these materials may absorb water, even though they exhibit solubility.[57] A soluble RCC can degrade and leach chemicals over time, creating voids within the material or at its interface with surrounding tissues/materials.[54] These voids could serve as pathways for microorganisms to transverse the root canal into the periapical tissues, while the leaching of chemicals can irritate periapical tissues.[53,54]

ERBSs have low solubility,[11,55] which may be due to the strong cross-linking of these RCCs.[55,58] This characteristic is desirable if the stability of the material in the intraradicular space is taken into account but may not be the best property when the material is extruded. The fate of the RCC will depend on its solubility in tissue fluids and its susceptibility to phagocytosis.[66,67] According to a solubility evaluation of AH Plus and Obturys, values of 0.0% and 0.2% at 24 h, respectively, were obtained.[60] The solubility studies of AH Plus,[21,51,53–60] Topseal,[61] Acroseal,[11,61] Adseal,[11,56,59] AH-26,[61] Dia-Proseal,[59] EasySeal,[53] MM-Seal,[58] Obturys,[60] Sealer 26,[51] Sealer Plus,[21] and 2Seal[61] meet the standardizations (Table 2).

Setting time

This time should not exceed more than 10% of that indicated by the manufacturer[49]; however, a sufficiently long time is required to allow the placement and adjustment of the sealing material, which provides a clinical advantage.[68] On the other hand, a slow setting time may cause tissue irritation and affect solubility, leading to seal failure,[54] and is therefore considered a critical clinical issue.[57] The setting time of AH Plus can be affected by the portion of the tube from which the paste is dispensed, i.e., the initial, intermediate, or final segment.[15,55] Thus, it is more fluid at the beginning than at the end, since it is not uniform and its consistency changes along the tube; there is incomplete miscibility between the components, which certainly alters the monomer–catalyst ratios.[15] The setting times obtained by different authors are detailed in Table 2. Their high values are probably due to the occurrence of slow polymerization between the amines in the epoxy resin, where the conversion of monomers into polymers occurs gradually.[55,58]

Table 2. Summary of the physicochemical properties of epoxy resin-based sealers (ERBSs)

ERBSs	Flow [mm]	Film thickness [μm]	Solubility [%]	Setting time [min]	Dimensional change [%]	Radiopacity [mm Al]
AH Plus	39.16 ±3.85[11] 21.87 ±1.40[20] 21.2 ±0.27[50] 32.25[54] 19.81 ±1.58[21] 23[55] 36.80 ±0.57[36] 34.48 ±0.07[56] 21.3 ±1.1[57] ≈14[59] 36.42 ±0.40[58] 21.94 ±0.74[51] 23[52] 18 ± 1.0[53]	43.65 ± 0.49[11] 85 ± 8[55] 21–30[52] 8 ± 1[53]	0.30 ± 0.02[11] 0.001[54] −0.25 ±0.10[55] 0.212 ±0.046[21] 0.73 ±0.76[56] 0.2 ±0.4[57] ≈ 0.00001[59] 0.41 ±0.21[58] 7 days: 0.20 ±0.08[51] 30 days: 0.21 ±0.07[51] 24 h: 0.0 ±0.0[60] 4 weeks: 0.1 ±0.1[60] 0.1 ±0.1[53]	711.33 ±95.03[11] 1,345 ±16[55] 617–869[54] 437 ±7–849 ±15[21] 463.0 ±1.45[56] 385.0 ±4.5[57] 463.60 ±13.22[58] 497 ±19[51] ≈1,440[52] 1,440[53]	0.50 ±0.36[56] −0.4 ±0.2[57] ≈1.9[59] 2.2 ±2.1[53]	14.50 ±1.69[11] 8.05[54] 15.74 ±0.25[55] 18.4[62] 7.58 ±0.14[21] 7.65 ±0.54[56] 9.2 ±0.5[57] ≈14[59] 7.52 ± 1.59[58] 9.50 ± 0.30[51]
Topseal	–	–	24 h: 0.07[61] 28 days: 0.082[61]	–	–	–
ThermaSeal Plus	21.3 ±0.47[50]	–	–	–	–	–
Acroseal	39.66 ±2.51[11]	65.50 ±6.36[11]	24 h: 0.36[61] 28 days: 0.746[61]	1,230.00 ±42.42[11]	–	5.86 ±0.73[11]
Adseal	37.66 ±2.08[11] 21.87 ±1.40[11] 55.16 ±0.01[56] ≈ 22.5[59]	65.00 ±7.07[11]	0.24 ±0.00[11] −1.68 ±1.96[56] ≈−0.00009[59]	70.00 ±9.00[11] 241.33 ±9.71[56]	8.84 ±4.05[56] ≈1.9[59]	5.84 ±0.66[11] 4.34 ±0.67[56] ≈7[59]
AH-26	–	–	24 h: 0.28[61] 28 days: 1.75[61]	–	–	–
DiaProSeal	≈16.5[59]	–	≈−0.00009[59]	–	≈1.9[59]	≈7.5[59]
EasySeal	17.3 ±0.8[53]	6 ±2[53]	2.7 ±0.3[53]	246[53]	3.4 ±1.4[53]	–
EZ-Fill Xpress	20[52]	31–40[52]	–	≈120–180[52]	–	–
MM-Seal	52.75 ±0.60[58]	–	0.94 ±0.17[58]	47.60 ±4.39[58]	–	3.32 ±0.90[58]
Perma Evolution	35.78 ±0.46[12]	–	–	–	–	–
Radic Sealer	20.80 ±0.84[11]	–	–	–	–	–
Obturys	–	–	24 h: 0.2 ±0.0[60] 4 weeks: 0.6 ±0.2[60]	–	–	–
Sealer 26	–	–	7 days: 0.45 ±0.20[51] 30 days: 0.95 ±0.21[51]	–	–	–
Sealer Plus	19.19 ±0.52[21] 18.95 ±0.74[51]	–	0.266 ±0.027[21]	138 ±10–210 ±18[21] 196 ±14[51]	–	5.42 ±0.20[21] 4.00 ±0.90[51]
SimpliSeal	23[52]	1–10[52]		≈110[52]	–	–
2Seal	–	–	24 h: 0.037[61] 28 days: 0.04[61]	–	–	–

Data presented as mean ± standard deviation (*M* ±*SD*). Cements without available information were excluded from the table.

One study evaluated how sonic and ultrasonic activation influences the setting times. AH Plus increased its time from 7.71 ±0.02 to 8.63 ±0.24 and 16.52 ±0.12 h, respectively, as these procedures can raise the temperature inside the root canals by up to 2°C. The ultrasonic devices may generate radicals in the organic portion (catalysts) due to increases in temperatures and pressures, generating a slow polymerization reaction.[56] On the contrary, Adseal showed the opposite behavior, decreasing the setting time from 4.02 ±0.16 to 2.60 ±0.19 h with sonic and to 2.36 ±0.12 h with ultrasonic activation, which may be related to the different percentages and types of polymerizing agents present in the compositions of these sealers.[11,56]

Dimensional change after setting

ANSI/ADA No. 57 standardizations recommend that this value should range from −1% (linear shrinkage) to +0.1% (expansion).[48] ERBSs are considered "shrinkage-free" during the setting reaction[11]; however, their expansion is still possible because they are capable of absorbing water.[55] AH Plus,[53,56,59] Adseal,[56,59] Dia-Proseal,[59] and Easy Seal[53] did not meet the standard (Table 2). These studies showed increases in dimensional changes, which could be explained by water absorption. However, Adseal showed higher values, owing to its property of high hygroscopicity, which distinguishes it from other cement and could contribute to improving the sealing capacity.[59] Another possible explanation for the latter result is the relatively high values of the standard deviation in this study, suggesting measurement inconsistencies. Additionally, the different methodologies used in different studies are prone to errors, as air bubbles may be present in the freshly mixed sealer materials, thus changing their density.[53]

The existence of voids is of clinical relevance because shrinkage of sealers of as low as 1% can result in voids and spaces that are sufficiently large enough for the penetration of bacteria and their harmful products.[69,70] In a study that evaluated the single cone technique in root canals via micro-CT and nano-CT, AH Plus demonstrated a significantly higher void fraction in terms of internal, external, and combined voids compared to Total BC and Sure Seal, which are calcium silicate-based sealers (CSBSs).[69]

Radiopacity

ANSI/ADA No. 57 and ISO 6876 standardizations require a radiopacity greater than 3 mm/Al.[48,49] The sealers AH Plus,[21,51,54–59,62] Acroseal,[11] Adseal,[11,56,59] Dia-Proseal,[59] MM-Seal,[58] and Sealer Plus[21,51] meet the standardizations (Table 2). AH Plus and Sealer Plus have the same radiopacifying agents, namely calcium tungstate, zirconium oxide, and iron oxide,[55,58] while Adseal has bismuth subcarbonate and zirconium oxide, and Acroseal contains only bismuth subcarbonate.[11] It has been reported that there is a deposit of radiopacifying agents at the lower end of the tube, while the upper portion may present a lower content,[11,55] which could be due to the above-mentioned incomplete miscibility between the organic and inorganic components contributing to segregation between both phases.

On the other hand, the radiopacity test shows variations in the behavior of the sealers in relation to the activation protocols of AH Plus and Adseal. As regards sonic activation, the variation in radiopacity may be related to greater or lesser exposure to the inorganic compounds present, which can occur randomly and are due to the hydrodynamic movement caused by the sound waves. Application of the ultrasonic protocol increased the radiopacity of AH Plus and reduced that of Adseal, which may be due to the induced changes in the crystal structures of the radiopacifying agents. The cavitation phenomenon, which induces the implosion of air bubbles and causes a local increase in temperature and pressure conditions, in combination with microflows generated by cavitation oscillations, would cause dispersion effects and agglomerate fragmentation in the inorganic components present in the sealers.[56]

Effects of heat application

Obturation techniques with high temperatures and/or long durations are associated with earlier polymerization, resulting in changes in the chemical structure of epoxy monomers, amine hardeners, and calcium tungstate fillers. These changes are temperature- and time-dependent, and the latter would have a greater impact.[63]

For AH Plus, it has been reported that heat treatment had an adverse effect on physical properties, such as setting time, which was reduced to 12.9 ±0.7 min when the temperature was raised from 37°C to 140°C for 10 min.[71] This reduction may be associated with a change in the setting reaction.[72] The flow rate was raised to 25.6 ±0.7 mm when the temperature was raised from 25°C to 140°C.[71]

In one study, temperatures of 37°C or 100°C for 1 min were used on AH Plus, resulting in a reduction in setting time and an increase in film thickness.[73] This ERBS showed a decrease in its N–H groups when heated at 100°C for 1 min, whereby the reduction of polyamines (dibenzyl diamine, aminoadamantane, and tricyclodecane) affected the polymerization process, with changes in the physical and mechanical properties of the material.[73] However, the overheating of AH Plus was performed using temperatures above those applied in clinical conditions.[72]

Adhesion to dentine

The chemical adhesion of epoxy resins to the tooth structure is produced by covalent bonds between the open epoxy groups and the exposed amino groups in the collagen network of the dentin. This is one of the reasons for the good dislodgment resistance of ERBSs.[74–76] Mechanical bonding is provided by the penetration of the cement into the dentin tubules (tags), and its characteristics depend on the physical properties of the RCCs.[1]

Unlike methacrylate resins, epoxy resins have a lower tag frequency. This may be due to the hydrophilic characteristics of the methacrylate resins as well as their slow chemical reaction, which promotes the reduction of shrinkage stress and allows the sealer to flow more freely, reaching deeper into the dentinal tubules and thus forming a greater number of tags. However, the micromechanical retention of sealers through the penetration of the tags into the tubules is not the most important factor affecting adhesion.[77] The higher bond strength of AH Plus, in contrast to its low tag formation, could be explained by the higher prevalence of cohesive failures for this RCC[16] in contrast to methacrylate resins that presented mixed or adhesive failures with dentin.[77]

Factors that can influence bonding strength

Dentin wettability, the use of antimicrobial irrigants and chelating agents

Adhesion can be affected by the condition and degree of wettability of the dentin,[78] due to the hydrophobic nature of cements.[79] Residual moisture could adversely affect the conversion of the epoxy resin monomer, leading to incomplete polymerization of the resin and decreased bond strength to dentin.[78,79] The use of sodium hypochlorite (NaOCl) may affect the adhesion of ERBSs if it is used as a final irrigant.[80,81] Traces of this strong oxidizing agent or its oxidative by-products, such as hypochlorous acid and hypochlorite ions, would also compromise the bond strength of the sealer to root dentin and its sealing capacity.[80] Another logical reason for this is that oxygen bubbles, which form after the use of NaOCl, impede the penetration of the sealer into the fine openings of the dentin tubules.[80]

Evidence shows that the final irrigation with EDTA 17%, SmearClear, and QMiX promoted proper smear layer removal, which ensured the adequate bond strength of AH Plus.[82]

Laser

Laser application is another type of treatment of the dentin surface that can influence the bond strength of the RCC.[83] A study on the effect of chemical treatments and the use of lasers on the bond strength revealed that citric acid had a higher average bond strength compared to the Er:YAG laser for RealSeal, AH Plus, and EndoREZ sealers, but not Acroseal.[84] On the contrary, EDTA activation with Nd:YAG (1,064 nm) and diode (980 nm) lasers resulted in better bond strength of the ERBSs at the level of all root canal thirds compared with EDTA alone and EDTA with ultrasonic agitation. The application of these wavelengths, together with EDTA activation, could increase the permeability of the root dentin.[85]

Filling techniques

The highest values of bond strength have been observed using the lateral condensation technique (LCT) and Tagger's hybrid technique (THT).[86] Similar results were obtained in another study wherein the strengths of the bonds to human dentin using AH Plus/gutta-percha (GP), Sealer 26/GP, Epiphany SE/Resilon, and Epiphany SE/GP root canal filling materials, when LCT or THT were used, were evaluated by means of push-out tests. The highest push-out forces were obtained when the canals were obturated using LCT with AH Plus and GP, followed by Sealer 26 and GP.[87] On the other hand, the lowest bond strengths were found with the continuous wave condensation technique, which could be explained by the presence of a thin cement layer, although the micro-CT images showed better results regarding the filling quality.[86]

Considering the need for heat to obtain a positive result in thermoplasticized GP techniques, a systematic review compared these techniques to cold lateral condensation, using micro-CT to evaluate the quality of root canal filling.[88] Although it was evidenced that neither technique could completely obturate the root canal, thermoplasticized techniques did have significantly fewer voids in most studies, which is clinically desirable. It is relevant to point out that six out of the nine included studies used ERBSs.[88]

Retreatment

Once the sealer penetrates the dentin tubules, its removal during retreatment is physically impossible[89]; therefore, no filling material can be completely removed.[90,91] Several studies have evaluated the retreatability of CSBSs compared to AH Plus, showing that the former achieved better results with less RCC residues and shorter retreatment times.[90,91] On the other hand, obturation with BC Sealer and a single GP master cone may result in blockage of the apical foramen and a loss of permeability in some cases, which is not the case for AH Plus obturation. The inability to regain working length and/or permeability may compromise retreatment by preventing adequate cleaning and shaping of the apical canal space, which may harbor bacteria. There is also evidence of retreatability for AH Plus and EndoSequence BC sealer, as they showed similar characteristics during retreatment procedures.[89]

The use of GP solvents like xylene and Endosolv E has been evaluated demonstrating a negative effect on the bond strength of AH Plus to the root canal. These solvents can change the chemical composition of the dentin surface because they are oil-based, making it difficult to remove them completely from the root canal. This waxy film may interfere with the development of resin–dentin bonds.[92]

Biological properties

Biocompatibility (cytotoxicity)

RCCs have demonstrated severe inflammation, but over time, most sealers lose their irritant components and become relatively inert.[22,93] In cases wherein RCCs are extruded, they may be solubilized in periradicular tissue fluids, phagocytized, or become encapsulated by fibrous connective tissue.[66] In a study, only 15% of cases with AH Plus extrusion have shown complete clearance of the material over periods of even 10 years.[66]

The cytotoxicity of an ERBS seems to be directly related to its component epoxy resin and to the type of polymerization promoted by the amines, with the waste products of this reaction being toxic to cells.[4] It has been suggested that ERBSs containing bisphenol A diglycidyl ether can produce cytotoxicity upon release since it is a mutagenic component of these materials.[10,93] These cements could release small amounts of formaldehyde, which could explain their short-term toxicity.[4,22,93] AH Plus also has a greater release of calcitonin gene-related peptide compared to EndoSequence, which indicates a greater potential for causing pain and neurogenic inflammation.[89]

In the case of SimpliSeal, its calcium oxide and calcium phosphate components could contribute to its improved biocompatibility. On the other hand, although Sealer Plus has a similar composition to AH Plus, the addition of $Ca(OH)_2$ in its composition improved its histological results, leading to mild inflammation at 7 days.[22]

As for Sicura Seal, bisphenol A diglycidyl ether is not included in its composition; however, exudates or polymerization and/or degradation products may cause increased cytotoxicity.[93] The cytotoxicity of AH-26 occurs mainly in the first hours after polymerization since this sealer contains hexamethylenetetramine, which decomposes into ammonia and formaldehyde, which have shown significant cytotoxic effects.[10]

Antimicrobial effects

RCCs seem to have some degree of antimicrobial activity due to their composition. This effect is time-dependent, and it is unknown whether it can prevent reinfection of the root canal system in the long term.[94] In this regard, the development of RCCs that have long-term antibacterial properties has been suggested to prevent potential reinfection.[94–96] In recent years, there have been attempts to modify RCCs with antimicrobial nanoparticles, antibiotics, and antiseptics to endow them with such properties, but with minimal or no impact on their physicochemical properties. However, studies used different methodologies to evaluate these effects which precludes the possibility of direct comparisons.[94]

The incorporation of a small percentage of quaternary ammonium polyethylenimine (QPEI) nanoparticles into AH Plus[95,96] and an experimental ERBS[97] have exhibited a strong antibacterial effect on species such as E. faecalis found in dentinal tubules.[95–97] In addition, it has been proven that adequate physical properties are maintained in the experimental cement with added QPEI.[97] The use of quaternary ammonium-based compounds and functionalized nanoparticles seems promising as an approach for conferring bacterial inhibition. Nevertheless, the safety of nanoparticles for human body systems and tissues must first be confirmed before proceeding with their clinical use.[94]

Bioactivity/Biomineralization

A bioactive material has the ability to create a hydroxyapatite (HA) layer when it is in contact with calcium- and phosphate-rich tissue fluid.[98] The pH level, along with the release of calcium ions, are closely involved in this process.[21] Sealers with calcium oxide or $Ca(OH)_2$ included in their composition have the ability to dissociate into calcium and hydroxyl ions, which could lead to an increase in the local pH and the formation of mineralized tissues.[21] The release of hydroxyl ions, or even the release of calcium ions, depends on the material's area of contact with tissue fluids and its chemical characteristics (hydrophilic or hydrophobic), the presence of calcium-containing substances, the setting time, and the solubility.[21,99]

Based on these biological events, and with the goal of promoting biochemical conditions that accelerate tissue recovery,[100] nanostructured fillers of synthesized bioactive glass (BAG), HA, fluoride substituted hydroxyapatite (FHA),[7] and magnesium hydroxide,[101] among others, have been incorporated into AH Plus. ERBSs such as Acroseal,[11] Sealer Plus,[21] Sealer 26,[11] Dia-Proseal,[59] and Obtuseal[102] have $Ca(OH)_2$ within their composition. However, due to some of the physicochemical properties that each of them possesses, they are not able to release sufficient hydroxyl ions or calcium to promote mineralization. Thus, 1 study analyzed the results of Sealer Plus, in which it was determined that its extremely short setting time in conjunction with its low solubility precludes the release of hydroxyl ions[21]; meanwhile, Acroseal showed the longest setting time, but its calcium release was lower compared to Sealapex due to the presence of its insoluble epoxy base, so it did not demonstrate bioactivity either.[99]

BAG and HA nanostructured fillers represent a promising approach, as they improve the in vitro capacity of ERBSs for apatite formation, while FHA particles do not improve apatite layer formation.[7] As for magnesium hydroxide, it has been found to adequately stimulate bone mineralization, and it has been mentioned that it would be an ideal additive to achieve bioactivity in cements such as AH Plus, as it causes greater osteoblastic differentiation compared to calcium ions.[101]

ERBSs vs. CSBSs

Recently, CSBSs have been introduced in the market as a new class of RCCs.[103] Their biological properties, such as high alkalinity sealing capacity, antibacterial properties, as well as bioactive induction of periapical healing and hard tissue formation,[23] as well as their fine particle structure and ability to set in wet environments,[103] have been highlighted as their main advantages over conventional sealers.[24] Considering these properties, a recent study suggested that GuttaFlow® Bioseal could even represent a promising material for root-end filling as it showed progressive healing, better tissue organization, and a reduction in the inflammatory response.[104]

We are facing a paradigm shift in obturation approaches, in which the objective is no longer only to provide a hermetic seal against bacteria and the reinfection of the root canal but, rather, to establish a more biological concept of obturation, in which CSBSs could become the most important sealers in coming years.[23] However, the number of formulations available on the market, the lack of relevant information on CSBSs in the literature, their high solubility compared to ERBSs,[6] as well as the unavailability of long-term clinical studies[105] prevents the recommendation and positioning of these RCCs as the gold standard in the field of root canal obturation.

Finally, if we consider that bioactivity and biomineralization are the desired properties in an RCC, perhaps the time has come for sound analysis, e.g., a position statement on this issue and a modification of the requirement list of an ideal sealer as originally proposed by Grossman.[5] In fact, some authors have already listed the capacity to be bioactive as an ideal criterion.[9]

Highlights of clinical interest

Shake sealer cements before use.

Discard the initial portion of the dispensing tube, as it may alter the flow, the setting time and radiopacity.

The ultrasonic activation of ERBSs can help to seal anatomical complexities. Take care of sealer extrusion.

ERBS have low solubility, so they are more stable, thus showing fewer spaces and voids, which could affect long-term clinical results.

ERBS can be used in controlled-heat obturation techniques with minimal changes in their chemical structure.

These sealers can be used with LCT and THT, obtaining higher bond strength values and, with the continuous wave condensation technique, show better results in terms of filling quality.

According to present evidence, when using the single cone technique, ERBS may not be a good option, owing to their higher void fraction, as opposed to CSBSs.

The use of ERBS is highly compatible with irrigation protocols that use chelating agents as the final irrigant, prior to root canal drying.

The use of oily solvents should be avoided during retreatment.

Extrusion should be avoided, as it may cause some degree of short-term cytotoxicity.

Conclusions

Despite the large amount of commercially available options for endodontic obturation, the "ideal" material has not yet been identified. This has led to the development of several obturation materials and experimental sealers incorporating nanoparticles and conferring them favorable physicochemical properties, such as increased antibacterial efficacy and bioactivity, which may lead to a concept transformation from a purely preventative cement into a biologically active one.

In general, the ERBSs have good flow properties, film thickness, solubility, dimensional stability, sealing capacity, and radiopacity. They are also able to adhere to dentin while exhibiting low toxicity and some antibacterial effects. However, their main disadvantage is their lack of bioactivity and biomineralization capability. AH Plus sealer, which has been extensively studied, is still considered the gold standard and has become the most important representative of a considerable number of sealer formulations based on epoxy resins, some of which, at present, even lack scientific evidence. The latter emphasizes the need for relevant research on the physicochemical and biological properties of some ERBSs, with the aim of supporting their clinical use with sufficient evidence via prospective and long-term studies. Finally, clinicians and researchers should consider formulation components of the different ERBSs to understand the characteristics and properties of these types of RCCs.

Ethics approval and consent to participate

Not applicable.

Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

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References

1. Chandra SS, Shankar P, Indira R. Depth of penetration of four resin sealers into radicular dentinal tubules: A confocal microscopic study. *J Endod*. 2012;38(10):1412–1416. doi:10.1016/j.joen.2012.05.017
2. Tyagi S, Tyagi P, Mishra P. Evolution of root canal sealers: An insight story. *European J Gen Dent*. 2013;2(3):199–218. doi:10.4103/2278-9626.115976
3. Diaconu OA, Dascalu IT, Amarascu M, et al. Long term results regarding the clinical applicability of two root canal sealers. *Mater Plast*. 2017;54(2):308–311. doi:10.37358/mp.17.2.4840
4. Khan MT, Moeen F, Safi SZ, Said F, Mansoor A, Khan AS. The structural, physical, and in vitro biological performance of freshly mixed and set endodontic sealers. *Eur Endod J*. 2021;6(1):98–109. doi:10.14744/EEJ.2020.36349
5. Suresh Chandra B, Gopikrishna V, eds. *Grossman's Endodontic Practice*. 13th ed. Mumbai, India: Wolters Kluwer Health (India); 2014.
6. Silva EJ, Cardoso ML, Rodrigues JP, De-Deus G, Da Silva Fidalgo TK. Solubility of bioceramic- and epoxy resin-based root canal sealers: A systematic review and meta-analysis. *Aust Dent J*. 2021;47(3):690–702. doi:10.1111/aej.12487
7. Jerri Al-Bakhsh BA, Shafiei F, Hashemian A, Shekofteh K, Bolhari B, Behroozibakhsh M. In-vitro bioactivity evaluation and physical properties of an epoxy-based dental sealer reinforced with synthesized fluorine-substituted hydroxyapatite, hydroxyapatite and bioactive glass nanofillers. *Bioact Mater*. 2019;4:322–333. doi:10.1016/j.bioactmat.2019.10.004
8. De Miranda Candeiro GT, Lavor AB, De Freitas Lima IT, et al. Penetration of bioceramic and epoxy-resin endodontic cements into lateral canals. *Braz Oral Res*. 2019;33:e049. doi:10.1590/1807-3107BOR-2019.VOL33.0049
9. Komabayashi T, Colmenar D, Cvach N, Bhat A, Primus C, Imai Y. Comprehensive review of current endodontic sealers. *Dent Mater J*. 2020;39(5):703–720. doi:10.4012/dmj.2019-288
10. Ashraf H, Najafi F, Heidari S, Yadegary Z, Zadsirjan S. Cytotoxicity of two experimental epoxy resin-based sealers. *Iran Endod J*. 2018;13(2):257–262. doi:10.22037/iej.v13i2.19530
11. Marciano MA, Guimaraes BM, Ordinola-Zapata R, et al. Physical properties and interfacial adaptation of three epoxy resin-based sealers. *J Endod*. 2011;37(10):1417–1421. doi:10.1016/j.joen.2011.06.023
12. Tiwari S, Murthy CS, Usha HL, Shivekshith AK, Kumar NN, Vijayalakshmi L. A comparative evaluation of antimicrobial efficacy and flow characteristics of two epoxy resin-based sealers – AH plus and Perma Evolution: An in vitro study. *J Conserv Dent*. 2018;21(6):676–680. doi:10.4103/JCD.JCD_305_18
13. Pane ES, Palamara JE, Messer HH. Behavior of resin-based endodontic sealer cements in thin and thick films. *Dent Mater*. 2012;28(9):e150–e159. doi:10.1016/j.dental.2012.04.012
14. Rahimi M, Jainaen A, Parashos P, Messer HH. Bonding of resin-based sealers to root dentin. *J Endod*. 2009;35(1):121–124. doi:10.1016/j.joen.2008.10.009
15. Baldi JV., Bernardes RA, Duarte MAH, et al. Variability of physicochemical properties of an epoxy resin sealer taken from different parts of the same tube. *Int Endod J*. 2012;45(10):915–920. doi:10.1111/j.1365-2591.2012.02049.x
16. Do Prado M, De Assis DF, Gomes BP, Simão RA. Adhesion of resin-based sealers to dentine: An atomic force microscopy study. *Int Endod J*. 2014;47(11):1052–1057. doi:10.1111/iej.12247
17. Editorial Board of the *Journal of Endodontics*. Wanted: A base of evidence. *J Endod*. 2007;33(12):1401–1402. doi:10.1016/j.joen.2007.09.004
18. Hopia H, Latvala E, Liimatainen L. Reviewing the methodology of an integrative review. *Scand J Caring Sci*. 2016;30(4):662–669. doi:10.1111/SCS.12327
19. Khandelwal D, Ballal NV. Recent advances in root canal sealers. *Int J Clin Dent*. 2016;9(3):183–194
20. Lee JK, Kwak SW, Ha JH, Lee WC, Kim HC. Physicochemical properties of epoxy resin-based and bioceramic-based root canal sealers. *Bioinorg Chem Appl*. 2017;2017:2582849. doi:10.1155/2017/2582849
21. Vertuan GC, Hungaro Duarte MA, De Moraes IG, et al. Evaluation of physicochemical properties of a new root canal sealer. *J Endod*. 2018;44(3):501–505. doi:10.1016/j.joen.2017.09.017
22. Angelo Cintra LT, Benetti F, De Azevedo Queiroz ÍO, et al. Evaluation of the cytotoxicity and biocompatibility of new resin epoxy-based endodontic sealer containing calcium hydroxide. *J Endod*. 2017;43(12):2088–2092. doi:10.1016/j.joen.2017.07.016
23. Donnermeyer D, Bürklein S, Dammaschke T, Schäfer E. Endodontic sealers based on calcium silicates: A systematic review. *Odontology*. 2019;107(4):421–436. doi:10.1007/S10266-018-0400-3
24. Silva Almeida LH, Moraes RR, Morgental RD, Pappen FG. Are premixed calcium silicate-based endodontic sealers comparable to conventional materials? A systematic review of in vitro studies. *J Endod*. 2017;43(4):527–535. doi:10.1016/j.joen.2016.11.019
25. Licari JJ, Swanson DW. Chemistry, formulation, and properties of adhesives. In: Licari JJ, Swanson DW. *Adhesives Technology for Electronic Applications. Materials, Processing, Reliability*. Norwich, NY: William Andrew/Elsevier; 2011:75–141.
26. Ali MS, Kano B. Endodontic materials: From old materials to recent advances. In: Khurshid Z, Najeeb S, Zafar M, Sefat F, eds. *Advanced Dental Biomaterials*. Sawston, UK: Woodhead Publishing/Elsevier; 2019:255–299.
27. Chung SH, Park YS. Local drug delivery in endodontics: A literature review. *J Drug Deliv Sci Technol*. 2017;39:334–340. doi:10.1016/j.jddst.2017.04.018
28. Gantrade Corporation. PTMEG di-p-aminobenzoate curing agent for epoxy resins. Published March 9, 2018. https://www.gantrade.com/blog/ptmeg-di-p-aminobenzoate-curing-agent-for-epoxy-resins. Accessed September 2, 2021.
29. Xu X, Zhang X, Abbas S, et al. Methenamine in dairy products by isotope dilution gas chromatography coupled with triple quadrupole mass spectrometry: Method validation and occurrence. *Food Control*. 2015;57:89–95. doi:10.1016/j.foodcont.2015.03.048
30. Kahl J, Easton J, Johnson G, Zuk J, Wilson S, Galinkin J. Formocresol blood levels in children receiving dental treatment under general anesthesia. *Pediatr Dent*. 2008;30(5):393–399. PMID:18942598.
31. Checkoway H, Boffetta P, Mundt DJ, Mundt KA. Critical review and synthesis of the epidemiologic evidence on formaldehyde exposure and risk of leukemia and other lymphohematopoietic malignancies. *Cancer Causes Control*. 2012;23(11):1747–1766. doi:10.1007/s10552-012-0055-2
32. Chruściel JJ, Leśniak E. Modification of epoxy resins with functional silanes, polysiloxanes, silsesquioxanes, silica and silicates. *Prog Polym Sci*. 2015;41:67–121. doi:10.1016/j.progpolymsci.2014.08.001
33. Rølla G, Ellingsen JE, Gaare D. Polydimethylsiloxane as a tooth surface-bound carrier of triclosan: A new concept in chemical plaque inhibition. *Adv Dent Res*. 1994;8(2):272–277. doi:10.1177/08959374940080022101
34. Zhang D, Wang C, Wang Q, Wang T. High thermal stability and wear resistance of porous thermosetting heterocyclic polyimide impregnated with silicone oil. *Tribol Int*. 2019;140:105728. doi:10.1016/j.triboint.2019.04.012
35. Pinkerton KE, Southhard RJ. Silica, crystalline. *Encyclopedia of Toxicology*. 2005:14–16. doi:10.1016/B0-12-369400-0/00877-2
36. Lechner CC, Becker CFW. Silaffins in silica biomineralization and biomimetic silica precipitation. *Mar Drugs*. 2015;13(8):5297–5333. doi:10.3390/md13085297
37. Markowska-Szczupak A, Ulfig K, Morawski AW. The application of titanium dioxide for deactivation of bioparticulates: An overview. *Catal Today*. 2011;169(1):249–257. doi:10.1016/j.cattod.2010.11.055
38. Scalarone D, Lazzari M, Chiantore O. Ageing behaviour and pyrolytic characterisation of diterpenic resins used as art materials: Colophony and Venice turpentine. *J Anal Appl Pyrolysis*. 2002;64(2):345–361. doi:10.1016/S0165-2370(02)00046-3
39. Kugler S, Ossowicz P, Malarczyk-Matusiak K, Wierzbicka E. Advances in rosin-based chemicals: The latest recipes, applications and future trends. *Molecules*. 2019;24(9):1651. doi:10.3390/molecules24091651

40. Tao P, Li J, Li J, Shang S, Song Z. Enhanced performance of rosin-based epoxy composites mixed with carbon nanotubes and cork powders from oriental oak bark. *Ind Crops Prod*. 2020;158:113051. doi:10.1016/J.INDCROP.2020.113051
41. Bell RF, Moreira VM, Kalso EA, Yli-Kauhaluoma J. Liquorice for pain? *Ther Adv Psychopharmacol*. 2021;11:20451253211024873. doi:10.1177/20451253211024873
42. Danso R, Hoedebecke B, Whang K, et al. Development of an oxirane/acrylate interpenetrating polymer network (IPN) resin system. *Dent Mater*. 2018;34(10):1459–1465. doi:10.1016/J.DENTAL.2018.06.013
43. Elfakhri F, Alkahtani R, Li C, Khaliq J. Influence of filler characteristics on the performance of dental composites: A comprehensive review. *Ceram Int*. 2022;48(19):27280–27294. doi:10.1016/J.CERAMINT.2022.06.314
44. Lopes CM, Barata P, Oliveira R. Stimuli-responsive nanosystems for drug-targeted delivery. In: Grumezescu AM, ed. *Drug Targeting and Stimuli Sensitive Drug Delivery Systems*. Norwich, NY: William Andrew/Elsevier; 2018:155-209. doi:10.1016/B978-0-12-813689-8.00005-7
45. National Library of Medicine/National Center for Biotechnology Information (NLM/NCBI). PubChem Compound Summary for CID 6880 (2-Hydroxyethyl salicylate). https://pubchem.ncbi.nlm.nih.gov/substance/87569417. Accessed August 30, 2022.
46. Vitti RP, Prati C, Sinhoreti MAC, et al. Chemical-physical properties of experimental root canal sealers based on butyl ethylene glycol disalicylate and MTA. *Dent Mater*. 2013;29(12):1287–1294. doi:10.1016/J.DENTAL.2013.10.002
47. Fetters LJ, Lohse DJ, Richter D, Witten TA, Zirkel A. Connection between polymer molecular weight, density, chain dimensions, and melt viscoelastic properties. *Macromolecules*. 1994;27(17):4639–4647. doi:10.1021/ma00095a001
48. American National Standards Institute/American Dental Association ANSI/ADA. Endodontic Sealing Materials ANSI/ADA Standard No. 57- 2000 (R2012). Published 2012. https://webstore.ansi.org/Standards/ADA/ANSIADA572000R2012?source=preview. Accessed September 12, 2021.
49. International Organization for Standardization (ISO). ISO 6876:2012. Dentistry – Root canal sealing materials. https://www.iso.org/standard/45117.html. Accessed September 13, 2021.
50. Zhou HM, Shen Y, Zheng W, Li L, Zheng YF, Haapasalo M. Physical properties of 5 root canal sealers. *J Endod*. 2013;39(10):1281–1286. doi:10.1016/j.joen.2013.06.012
51. Tanomaru-Filho M, Prado MC, Esteves Torres FF, Viapiana R, Pivoto-João MMB, Guerreiro-Tanomaru JM. Physicochemical properties and bioactive potential of a new epoxy resin-based root canal sealer. *Braz Dent J*. 2019;30(6):563–568. doi:10.1590/0103-6440201802861
52. Christensen GJ. Should you change your endodontic sealer? *Clin Rep*. 2017;10(3). https://www.surgicalserenitysolutions.com/wp-content/uploads/2017/03/CF-News-March-17.pdf. Accessed August 31, 2021.
53. Sonntag D, Ritter A, Burkhart A, Fischer J, Mondrzyk A, Ritter H. Experimental amine-epoxide sealer: A physicochemical study in comparison with AH Plus and EasySeal. *Int Endod J*. 2015;48(8):747–756. doi:10.1111/iej.12372
54. Mendes AT, Da Silva PB, Só BB, et al. Evaluation of physicochemical properties of new calcium silicate-based sealer. *Braz Dent J*. 2018;29(6):536–540. doi:10.1590/0103-6440201802088
55. Viapiana R, Flumignan DL, Guerreiro-Tanomaru JM, Camilleri J, Tanomaru-Filho M. Physicochemical and mechanical properties of zirconium oxide and niobium oxide modified Portland cement-based experimental endodontic sealers. *Int Endod J*. 2014;47(5):437–448. doi:10.1111/iej.12167
56. Lopes FC, Zangirolami C, Mazzi-Chaves JF, et al. Effect of sonic and ultrasonic activation on physicochemical properties of root canal sealers. *J Appl Oral Sci*. 2019;27:e20180556. doi:10.1590/1678-7757-2018-0556
57. Zordan-Bronzel CL, Esteves Torres FF, Tanomaru-Filho M, Chávez-Andrade GM, Bosso-Martelo R, Guerreiro-Tanomaru JM. Evaluation of physicochemical properties of a new calcium silicate-based sealer, Bio-C Sealer. *J Endod*. 2019;45(10):1248–1252. doi:10.1016/j.joen.2019.07.006
58. De Camargo RV, Silva-Sousa YTC, Ferreira da Rosa RP, et al. Evaluation of the physicochemical properties of silicone- and epoxy resin-based root canal sealers. *Braz Oral Res*. 2017;31:e72. doi:10.1590/1807-3107BOR-2017.vol31.0072
59. Song YS, Choi Y, Lim MJ, et al. In vitro evaluation of a newly produced resin-based endodontic sealer. *Restor Dent Endod*. 2016;41(3):189–195. doi:10.5395/rde.2016.41.3.189
60. Elyassi Y, Moinzadeh AT, Kleverlaan CJ. Characterization of leachates from 6 root canal sealers. *J Endod*. 2019;45(5):623–627. doi:10.1016/j.joen.2019.01.011
61. Azadi N, Fallahdoost A, Mehrvarzfar P, Rakhshan H, Rakhshan V. A four-week solubility assessment of AH-26 and four new root canal sealers. *Dent Res J (Isfahan)*. 2012;9(1):31–35. doi:10.4103/1735-3327.92924
62. Viapiana R, Guerreiro-Tanomaru JM, Hungaro-Duarte MA, Tanomaru-Filho M, Camilleri J. Chemical characterization and bioactivity of epoxy resin and Portland cement-based sealers with niobium and zirconium oxide radiopacifiers. *Dent Mater*. 2014;30(9):1005–1020. doi:10.1016/j.dental.2014.05.007
63. Atmeh AR, AlShwaimi E. The effect of heating time and temperature on epoxy resin and calcium silicate-based endodontic sealers. *J Endod*. 2017;43(12):2112–2118. doi:10.1016/j.joen.2017.08.008
64. Essential Dental Systems. http://edsdental.com/inst/ezfill/exfillexpress_inst.pdf. Accessed August 31, 2021.
65. Ates AA, Dumani A, Yoldas O, Unal I. Post-obturation pain following the use of carrier-based system with AH Plus or iRoot SP sealers: A randomized controlled clinical trial. *Clin Oral Investig*. 2019;23(7):3053–3061. doi:10.1007/s00784-018-2721-6
66. Ricucci D, Rôças IN, Alves FRF, Loghin S, Siqueira JF. Apically extruded sealers: Fate and influence on treatment outcome. *J Endod*. 2016;42(2):243–249. doi:10.1016/j.joen.2015.11.020
67. Siqueira JF Jr., Rôças IN. *Treatment of Endodontic Infections*. Chicago, IL: Quintessence Publishing; 2011:403.
68. Versiani MA, Abi Rached-Junior FJ, Kishen A, Pécora JD, Silva-Sousa YT, De Sousa-Neto MD. Zinc oxide nanoparticles enhance physicochemical characteristics of Grossman sealer. *J Endod*. 2016;42(12):1804–1810. doi:10.1016/j.joen.2016.08.023
69. Huang Y, Celikten B, De Faria Vasconcelos K, et al. Micro-CT and nano-CT analysis of filling quality of three different endodontic sealers. *Dentomaxillofac Radiol*. 2017;46(8):20170223. doi:10.1259/dmfr.20170223
70. Milanovic I, Milovanovic P, Antonijevic D, Dzeletovic B, Djuric M, Miletic V. Immediate and long-term porosity of calcium silicate-based sealers. *J Endod*. 2020;46(4):515–523. doi:10.1016/j.joen.2020.01.007
71. Qu W, Bai W, Liang YH, Gao XJ. Influence of warm vertical compaction technique on physical properties of root canal sealers. *J Endod*. 2016;42(12):1829–1833. doi:10.1016/j.joen.2016.08.014
72. Donnermeyer D, Urban K, Bürklein S, Schäfer E. Physico-chemical investigation of endodontic sealers exposed to simulated intracanal heat application: Epoxy resins and zinc oxide–eugenols. *Int Endod J*. 2020;53(5):690–697. doi:10.1111/iej.13267
73. Camilleri J. Sealers and warm gutta-percha obturation techniques. *J Endod*. 2015;41(1):72–78. doi:10.1016/j.joen.2014.06.007
74. Bowen RL. Use of epoxy resins in restorative materials. *J Dent Res*. 1956;35(3):360–369. doi:10.1177/00220345560350030501
75. Leal Silva EJ, Canabarro A, Canabarro Andrade MR, et al. Dislodgment resistance of bioceramic and epoxy sealers: A systematic review and meta-analysis. *J Evid Based Dent Pract*. 2019;19(3):221–235. doi:10.1016/j.jebdp.2019.04.004
76. Vilanova WV, Carvalho-Junior JR, Alfredo E, Sousa-Neto MD, Silva-Sousa YT. Effect of intracanal irrigants on the bond strength of epoxy resin-based and methacrylate resin-based sealers to root canal walls. *Int Endod J*. 2012;45(1):42–48. doi:10.1111/j.1365-2591.2011.01945.x
77. Haragushiku GA, Teixeira CS, Furuse AY, Silva Sousa YT, De Sousa Neto MD, Silva RG. Analysis of the interface and bond strength of resin-based endodontic cements to root dentin. *Microsc Res Tech*. 2012;75(5):655–661. doi:10.1002/jemt.21107
78. Nagas E, Uyanik MO, Eymirli A, et al. Dentin moisture conditions affect the adhesion of root canal sealers. *J Endod*. 2012;38(2):240–244. doi:10.1016/j.joen.2011.09.027

79. Fahmy SH, El Gendy AAH, El Ashry SH. Dentin wettability enhancement for three irrigating solutions and their effect on push out bond strength of gutta percha/AH Plus. *J Clin Exp Dent*. 2015;7(2):237–279. doi:10.4317/jced.51865
80. Kumar PS, Meganathan A, Shriram S, Sampath V, Sekar M. Effect of proanthocyanidin and bamboo salt on the push-out bond strength of an epoxy resin sealer to sodium hypochlorite-treated root dentin: An in vitro study. *J Conserv Dent*. 2019;22(2):144–148. doi:10.4103/JCD.JCD_377_18
81. Prado M, Simão RA, Gomes BP. Effect of different irrigation protocols on resin sealer bond strength to dentin. *J Endod*. 2013;39(5):689–692. doi:10.1016/j.joen.2012.12.009
82. Aranda-Garcia AJ, Kuga MC, Vitorino KR, et al. Effect of the root canal final rinse protocols on the debris and smear layer removal and on the push-out strength of an epoxy-based sealer. *Microsc Res Tech*. 2013;76(5):533–537. doi:10.1002/jemt.22196
83. De Almeida Franceschini K, Silva-Sousa YTC, Lopes FC, Pereira RD, Palma-Dibb RG, De Sousa-Neto MD. Bond strength of epoxy resin-based root canal sealer to human root dentin irradiated with Er,Cr:YSGG laser. *Lasers Surg Med*. 2016;48(10):985–994. doi:10.1002/lsm.22496
84. Akisue E, Araki AT, Costa Michelotto AL, Moura-Netto C, Gavini G. Effect of chemical and Er:YAG laser treatment on bond strength of root canal resin-based sealers. *Lasers Med Sci*. 2013;28(1):253–258. doi:10.1007/s10103-012-1138-8
85. De Macedo HS, Furtado Messias DC, Rached-Júnior FJ, De Oliveira LT, Silva-Sousa YTC, Raucci-Neto W. 1064-nm Nd:YAG and 980-nm diode laser EDTA agitation on the retention of an epoxy-based sealer to root dentin. *Braz Dent J*. 2016;27(4):424–429. doi:10.1590/0103-6440201601006
86. Nhata J, Machado R, Vansan LP, et al. Micro-computed tomography and bond strength analysis of different root canal filling techniques. *Indian J Dent Res*. 2014;25(6):698–701. doi:10.4103/0970-9290.152164
87. Carneiro SM, Sousa-Neto MD, Rached FA Jr., Miranda CE, Silva SR, Silva-Sousa YT. Push-out strength of root fillings with or without thermomechanical compaction. *Int Endod J*. 2012;45(9):821–828. doi:10.1111/j.1365-2591.2012.02039.x
88. Bhandi S, Mashyakhy M, Abumelha AS, et al. Complete obturation – cold lateral condensation vs. thermoplastic techniques: A systematic review of micro-CT studies. *Materials (Basel)*. 2021;14(14):4013. doi:10.3390/MA14144013
89. Kim H, Kim E, Lee SJ, Shin SJ. Comparisons of the retreatment efficacy of calcium silicate and epoxy resin-based sealers and residual sealer in dentinal tubules. *J Endod*. 2015;41(12):2025–2030. doi:10.1016/j.joen.2015.08.030
90. Donnermeyer D, Bunne C, Schäfer E, Dammaschke T. Retreatability of three calcium silicate-containing sealers and one epoxy resin-based root canal sealer with four different root canal instruments. *Clin Oral Investig*. 2018;22(2):811–817. doi:10.1007/s00784-017-2156-5
91. Neelakantan P, Grotra D, Sharma S. Retreatability of 2 mineral trioxide aggregate-based root canal sealers: A cone-beam computed tomography analysis. *J Endod*. 2013;39(7):893–896. doi:10.1016/j.joen.2013.04.022
92. Nasim I, Neelakantan P, Subbarao CV. Effect of gutta-percha solvents on the bond strength of two resin-based sealers to root canal dentin. *Acta Odontol Scand*. 2014;72(5):376–379. doi:10.3109/00016357.2013.841987
93. Troiano G, Perrone D, Dioguardi M, Buonavoglia A, Ardito F, Lo Muzio L. In vitro evaluation of the cytotoxic activity of three epoxy resin-based endodontic sealers. *Dent Mater J*. 2018;37(3):374–378. doi:10.4012/dmj.2017-148
94. Brezhnev A, Neelakantan P, Tanaka R, Brezhnev S, Fokas G, Matinlinna JP. Antibacterial additives in epoxy resin-based root canal sealers: A focused review. *Dent J (Basel)*. 2019;7(3):72. doi:10.3390/dj7030072
95. Abramovitz I, Wisblech D, Zaltsman N, Weiss EI, Beyth N. Intratubular antibacterial effect of polyethyleneimine nanoparticles: An ex vivo study in human teeth. *J Nanomater*. 2015;2015:ID 980529. doi:10.1155/2015/980529
96. Shvero DK, Zaltsman N, Weiss EI, Polak D, Hazan R, Beyth N. Lethal bacterial trap: Cationic surface for endodontic sealing. *J Biomed Mater Res A*. 2016;104(2):427–434. doi:10.1002/jbm.a.35576
97. Beyth N, Shvero DK, Zaltsman N, et al. Rapid kill – novel endodontic sealer and *Enterococcus faecalis*. *PLoS One*. 2013;8(11):e78586. doi:10.1371/journal.pone.0078586
98. Talabani RM, Garib BT, Masaeli R, Zandsalimi K, Ketabat F. Biomineralization of three calcium silicate-based cements after implantation in rat subcutaneous tissue. *Restor Dent Endod*. 2021;46(1):e1. doi:10.5395/RDE.2021.46.E1
99. Eldeniz AU, Erdemir A, Kurtoglu F, Esener T. Evaluation of pH and calcium ion release of Acroseal sealer in comparison with Apexit and Sealapex sealers. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;103(3):e86–e91. doi:10.1016/j.tripleo.2006.10.018
100. De Oliveira RL, Oliveira Filho RS, De Carvalho Gomes H, De Franco MF, Silva Enokihara MM, Hungaro Duarte MA. Influence of calcium hydroxide addition to AH Plus sealer on its biocompatibility. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2010;109(1):e50–e54. doi:10.1016/j.tripleo.2009.08.026
101. Sun X, Sun A, Jia X, et al. In vitro bioactivity of AH plus with the addition of nano-magnesium hydroxide. *Ann Transl Med*. 2020;8(6):313–313. doi:10.21037/ATM.2020.02.133
102. Simsek N, Akinci L, Gecor O, Alan H, Ahmetoglu F, Taslidere E. Biocompatibility of a new epoxy resin-based root canal sealer in subcutaneous tissue of rat. *Eur J Dent*. 2015;9(1):31–35. doi:10.4103/1305-7456.149635
103. Reszka P, Nowicka A, Dura W, Marek E, Lipsk M. SEM and EDS study of TotalFill BC Sealer and GuttaFlow Bioseal root canal sealers. *Dent Med Probl*. 2019;56(2):167–172. doi:10.17219/dmp/105561
104. Rady D, Abdel Rahman MH, El-Mallah S, Khalil MM. Biocompatibility assessment of different root-end filling materials implanted subcutaneously in rats: An in vivo study. *Dent Med Probl*. 2021;58(4):525–532. doi:10.17219/dmp/132240
105. Sfeir G, Zogheib C, Patel S, Giraud T, Nagendrababu V, Bukiet F. Calcium silicate-based root canal sealers: A narrative review and clinical perspectives. *Materials (Basel)*. 2021;14(14):3965. doi:10.3390/MA14143965