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Especialización en Endodoncia

"Epoxi Resin-Based Root Canal Sealers: An Integrative Literature Review."

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Abstract

Background

Correct obturation of the root canal system is essential for the success of endodontic treatment, which is achieved by means of a core and cement. 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.

Objective

The main aim of this review is to analyze and integrate the available information on the different ERBSs.

Methods

An electronic search was performed in the PubMed and Scopus databases, using as search terms "epoxy resin" AND "root canal treatment", "epoxy resin" AND "endodontics".

Results

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.

Conclusion

A large number of ERBSs were found to be available on the market and AH Plus keeps being the gold standard RCC. However, 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: epoxy resin-based sealer; root canal sealer; root canal treatment; biocompatibility; physicochemical properties; AH Plus.

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1. 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; most techniques use 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 based on 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]. ERBSs can be considered the RCC of choice [6,7] for obturation of the root canal system because they have adequate physicochemical properties [7,8].

The objective of this review is to analyze and integrate the available information on the different ERBSs. The PubMed and Scopus databases were used for this purpose, using the search terms “epoxy resin” AND “root canal treatment”, “epoxy resin” AND “endodontics”. Clinical trials, in vitro studies, literature reviews, and systematic reviews, and only those published in English, were included in this study. 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 excluded because such studies have been considered not useful since reliable and reproducible evaluation methods that are related to clinical outcomes are required [9]. 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.

2. General Characteristics of Epoxy Resins

Epoxy resin was patented by P. Casta, a Swiss chemist from De Trey (Zurich, Switzerland), in 1938 [10]. It is mainly composed of epoxy monomers that when mixed with amine hardeners, such as tricyclodecane, dibenzyldiamine, and aminoadamantane, results in polymerization by means of an addition reaction [11–13].

Epoxy resin-based sealers (ERBSs) were introduced into endodontics by Schroeder in 1950, with the market launch of AH 26 ® (Dentsply, Maillefer) [14]. Due to the release of formaldehyde, which causes cytotoxicity in periapical tissues, this sealer has been modified to what is now marketed as AH Plus ® (Dentsply, Sirona) [15,16]. 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 [17–20]. However, there are other commercially available ERBSs, with different compositions, according to the manufacturer, like Thermaseal Plus, Topseal, AH-26, Acroseal, Adseal, Dia-Proseal, EasySeal, Epoxidin, EZ-Fill Xpress, MM-Seal, Obturys, Obtuseal, Perma Evolution, Radic sealer, Sealer 26, Sealer Plus, Sicura seal, SimpliSeal, 2Seal. Based on our performed search, there is no review that integrates information on the characteristics as well as the physicochemical and biological properties of this type of sealers.

3. Physicochemical Properties

3.1. 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 [21,22]. Available evidence shows that the sealers AH Plus [13,16,30–32,17,23–29], ThermaSeal Plus [23], Acroseal [13], Adseal [13,16,30,33], EasySeal [26] , EZ-Fill Xpress [25], MM-Seal [32], Pherma Evolution [29], Radic sealer [16], Sealer Plus [17,24] and SimpliSeal [25], meet the established requirements. On the other hand, one study evaluated Dia-Proseal and AH Plus [33], falling short in achieving the required values.

The activation of sealer cements with sonic and ultrasonic protocols has evidenced an increase in flow values in 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 [11]. On the other hand, the manufacturer of EZ Fill Xpress recommends that it can be warmed using a heated spatula to improve its fluidity [34]. However, high flow may result in apical extrusion, possibly leading to periapical tissue injury due to RCC cytotoxicity [23] and consequent postoperative pain [35].

3.2. Film Thickness

ANSI/ADA No. 57 and ISO 6876 suggest that this thickness should not exceed 50 µm [21,22]. Resin-based sealers have shown greater adhesion to dentin in thicker layers. The sealers AH Plus [13,25,26], Easy Seal [26], EZ-Fill Xpress [25], SimpliSeal [25] meet standardizations. On the other hand, one study reported values of 85 ± 8 µm for the film thickness of AH Plus [28]. Acrosel and Adseal obtained values higher than 50 µm.

3.3. Water Solubility

The solubility according to ANSI/ADA No. 57 and ISO 6876 must be less than 3% [21,22]. ERBSs have low solubility [13,28], which may be due to the strong crosslinking of these RCCs [28,32]. 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 [36,37]. According to a solubility evaluation of AH Plus and Obturys, values of 0.0% and 0.2% at 24 h, respectively, were obtained [38]. The solubility studies of AH Plus [17,24,26–28,30–33,38], Topseal [39], Acroseal [13,39], Adseal [13,30,33], AH-26 [39], Dia-Proseal [33], EasySeal [26], MM-Seal [32], Obturys [38], Sealer 26 [24], Sealer Plus [17] and 2Seal [39] meet the standardizations.

3.4. Setting Time

This time should not exceed more than the 10% of that indicated by the manufacturer [22]; however, a sufficiently long time is required to allow the placement and adjustment of the sealing material, which provides a clinical advantage [40]. On the other hand, a slow setting time may cause tissue irritation and affect solubility, leading to seal failure [27], and is therefore considered a critical clinical issue [31]. 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 [28,41]. 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 ratio [41].

One study evaluated how sonic and ultrasonic activation influence 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 to 2 °C. The ultrasonic devices may possibly generate radicals in the organic portion (catalysts) due to the increase in temperature and pressure, generating a slow polymerization reaction [30]. 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, which may be related to the different percentages and types of polymerizing agents present in the compositions of these sealers [13,30].

3.5. Dimensional Change after Setting

ANSI/ADA No. 57 standardizations recommend that this value should range from −1% (linear shrinkage) to +0.1% (expansion) [21]. ERBSs are considered “shrinkage-free” during the setting reaction [13], however their expansion is still possible because they are capable of absorbing water [28]. AH Plus [26,30,33], Adseal [30,33], Dia-Proseal [33] and Easy Seal [26] did not meet the standard. These studies showed increases in dimensional change, which could be explained by water absorption. However, Adseal showed higher values, maybe owing to its property of high hygroscopicity, which distinguishes it from other cements and could contribute to improving the sealing capacity [33].

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 [42,43]. 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) [42].

3.6. Radiopacity

ANSI/ADA No. 57 and ISO 6876 standardizations require a radiopacity greater than 3 mm/Al [21,22]. The sealers AH Plus [17,24,27,28,30–33,44], Acroseal [13], Adseal [13,30,33], Dia-Proseal [33], MM-Seal [32], Sealer Plus[17,24] meet the standardizations. AH Plus and Sealer Plus have the same radiopacifying agents, namely calcium tungstate, zirconium oxide, and iron oxide [28,32], while Adseal has bismuth subcarbonate and zirconium oxide and Acroseal contains only bismuth subcarbonate [13]. 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 [13,28].

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 [30].

4. Effects of Heat Application

Obturation techniques with high temperatures and/or long duration 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 [11].
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 to 140 °C for 10 min [45]; this reduction may be associated with a change in the setting reaction [46]. The flow rate was raised to 25.6 ± 0.7 mm when the temperature was raised from 25 to 140 °C [45].
In one study, temperatures of 37 or 100 °C for 1 min were used on AH Plus, resulting in a reduction in setting time and an increase in film thickness [47].

5. 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 [12,48,49]. 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 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 [50]. 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 [51] in contrast to methacrylate resins that presented mixed or adhesive failures with dentin [50].

5.1. Factors That Can Influence Bonding Strength

5.1.1. Dentin Wettability, Use of Antimicrobial Irrigants, and Chelating Agents

Adhesion can be affected by the condition and degree of wettability of the dentin [52], due to the hydrophobic nature of these cements [53]. 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 [52,53]. The use of sodium hypochlorite (NaOCl) may affect the adhesion of ERBSs if it is used as a final irrigant [54,55]. Traces of this strong oxidizing agent or its oxidative byproducts, such as hypochlorous acid and hypochlorite ions, would also compromise the bond strength of the sealer to root dentin and its sealing capacity [54]. 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 [54].
Evidence shows that final irrigation with EDTA 17%, SmearClear, and QMiX promoted proper smear layer removal, which ensured the adequate bond strength of AH Plus [56].

5.1.2. Laser

Laser application is another type of treatment for the dentin surface that can influence the bond strength of the RCC [57]. A study on the effect of chemical treatment and the use of laser on the bond strength revealed that citric acid had a higher average bond strength compared to Er:YAG laser for RealSeal, AH Plus, and EndoREZ sealers, but not Acroseal [58]. On the contrary, EDTA activation with Nd:YAG (1064 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 or EDTA with ultrasonic agitation. The application of these wavelengths together with EDTA activation could increase the permeability of root dentin [59].

5.1.3. Filling Techniques

The highest values of bond strength have been observed using the lateral condensation technique (LCT) and Tagger's hybrid technique (THT)[60]. Similar results were obtained in another study wherein the strengths of the bonds to human dentin of 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 with LCT with AH Plus and GP, followed by Sealer 26 and GP [61]. On the other hand, the lowest bond strengths were found in 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 [60].

6. Retreatment

Once the sealer penetrates the dentinal tubules, its removal during retreatment is physically impossible [62]; therefore, no filling material can be completely removed [63,64]. 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 [63,64]. On the other hand, obturation with BC Sealer and a single gutta-percha 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 in retreatment procedures [62].

The use of gutta-percha 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 [65].

7. Biological Properties

7.1. Biocompatibility (Cytotoxicity)

RCCs have demonstrated severe inflammation, but over time, most sealers lose their irritant components and become relatively inert [18,66]. In cases wherein RCCs are extruded, they may be solubilized in periradicular tissue fluids, phagocytized, or become encapsulated by fibrous connective tissue [36]. In a study, only 15% of cases with AH Plus extrusion have shown complete clearance of the material over periods of even 10 years [36].

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 [15,66]; these cements could release small amounts of formaldehyde, which could explain their short-term toxicity [4,18,66]. AH Plus also causes the greater release of calcitonin gene-related peptide compared to EndoSequence, which indicates a greater potential for causing pain and neurogenic inflammation [62].

In the case of SimpliSeal, its calcium oxide and calcium phosphate components could contribute to improving its 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 [18].

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 [66]. 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 [15].

7.2. Antimicrobial Effect

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 [67]. In this regard, the development of RCCs that have long-term antibacterial properties has been suggested to prevent potential reinfection [67–69]. 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 use different methodologies to evaluate these effects, which precludes the possibility of direct comparisons [67].

The incorporation of a small percentage of quaternary ammonium polyethylenimine (QPEI) nanoparticles into AH Plus [68,69] and an experimental ERBS [70] has evidenced a strong antibacterial effect on species such as *E. faecalis* found in dentinal tubules [68–70]. In addition, it has been proven that adequate physical properties are maintained in the experimental cement with added QPEI [70]. 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 [67].

7.3. Bioactivity/Biomineralization

A bioactive material has the ability to create a hydroxyapatite layer when it is in contact with calcium- and phosphate-rich tissue fluid [71]; pH level, along with the release of calcium ions, are closely involved in this process [17].

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 local pH and the formation of mineralized tissue [17]. 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 [17,72].

Based on these biological events, and with the goal of promoting biochemical conditions that accelerate tissue recovery [73], nanostructured fillers of synthesized bioactive glass (BAG), hydroxyapatite (HA), fluoride substituted hydroxyapatite (FHA) [7], and magnesium hydroxide [74], among others, have been incorporated into AH

Plus. ERBSs such as Acroseal [13], Sealer Plus [17], Sealer 26 [13], Dia-Proseal [33] and Obtuseal [75] have $Ca(OH)_2$ within their composition. However, due to some of the physicochemical properties that each of them possess, they are not able to release sufficient hydroxyl ions or calcium for promoting mineralization. Thus, one 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 [17]; meanwhile, Acroseal showed the longest setting time, but its calcium release was lower compared to Sealapex, due to the presence of the insoluble epoxy base, so it did not demonstrate bioactivity either [72]. 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 is even mentioned that it would be the ideal additive to achieve bioactivity in cements such as AH Plus, as it causes the greater differentiation of osteoblasts compared to calcium ions [74].

7.4. ERBSs vs. CSBSs

Recently, CSBSs have been introduced in the market as a new class of RCCs. Their biological properties, such as sealing capacity, antibacterial properties, as well as bioactive induction of periapical healing and hard tissue formation [19], have been highlighted as their main advantages over conventional sealers [20].

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 [19]. However, the number of formulations available on the market, the lack of relevant information on CSBSs in the literature, as well as the unavailability of long-term clinical studies [76], prevent 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 a sound analysis, e.g., a position statement, on this issue, and to modify the list of requirements 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 [10].

8. Highlights of clinical interest

- Discard the initial portion of the dispensing tube as it may alter flow, setting time, and radiopacity.
- 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 would imply long-term clinical results.
- ERBS can be used in controlled-heat obturation techniques, with minimal changes on their chemical structure.
- These sealers can be used with LCT and THT, obtaining higher bond strength values and, with the continuous wave condensation technique, showing 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.

9. 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 preventive 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.

Abbreviations: RCCs, root canal cements; ERBSs, epoxy resin-based sealers; Ca(OH)2, calcium hydroxide; DGEBA, diglycidyl ether of bisphenol A; TEA, triethanolamine; ANSI/ADA, American National Standards Institute/American Dental Association; ISO, International Organization for Standardization; micro-CT, micro-computed tomography; CSBSs, calcium silicate-based sealers; NaOCl, sodium hypochlorite; LCT, lateral condensation technique; THT, Tagger’s hybrid technique; GP, gutta-percha; QPEI, quaternary ammonium polyethylenimine; BAG, bioactive glass; HA, hydroxyapatite; FHA, fluoride substituted hydroxyapatite.

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