Calcium Hydroxide–Based Root Canal Sealers: A Review

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Abstract

The aim of this review was to consider laboratory experiments and clinical studies of calcium hydroxide–based root canal sealers. An extensive search of the endodontic literature was made to identify publications related to calcium hydroxide–based root canal sealers. The articles were assessed for the outcome of laboratory and clinical studies on their biological properties and physical characteristics. Comparative studies with other sealers were also considered. Several studies were evaluated covering different properties of calcium hydroxide–based sealers including physical properties, biocompatibility, leakage, adhesion, solubility, antibacterial properties, and periapical healing effect. Calcium hydroxide–based root canal sealers have a variety of physical and biological properties. Comparative studies reveal their mild cytotoxicity, but their antibacterial effects are variable. Further research is required to establish the tissue healing properties of calcium hydroxide in root canal sealers. *(J Endod 2009;■:1–6)*

Key Words

Calcium hydroxide, root canal sealer

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Dentists have been using calcium-based chemicals in clinical practice for over a century. Calcium hydroxide was introduced to endodontics by Herman in 1920 for its pulp-repairing ability (1). In endodontics, it is mainly used for pulp-capping procedures, as an intracanal medicament, in some apexification techniques, and as a component of several root canal sealers.

It is well understood that when filling root canals with a solid core material, some form of cement is required for a fluid tight seal that fills the minor gaps between the core material and the dentinal wall of the canal to prevent leakage (2). According to Ørstavik, sealers play an important role in sealing the root canal system with entombment of remaining microorganisms and filling of inaccessible areas of prepared canals (3). Sealer selection may influence the outcome of endodontic treatment (4). The properties of an ideal root canal sealer were outlined by Grossman (5) (Table 1).

The first clinical use of calcium hydroxide as a root canal–filling material was probably by Rhoner in 1940 (6). It took another 20 years for calcium hydroxide to become popular for apexification, the sealing of perforations, and management of resorption (7). A "miracle' material" Biocalex (Laboratoire SPAD, Dijon, France), developed by French researchers, was believed to make radical changes to endodontic instrumentation methods (8). The calcium hydroxide containing a pulp-capping agent, Dycal (Dentsply-Caulk, Milford, DE), also became popular as a sealer among some clinicians in late 1970s (9). Shortly afterward, root canal sealers based on calcium hydroxide became available. Because calcium hydroxide–containing sealers have been in use over a quarter of a century and remain popular, a literature review on these materials focusing on their physical and biological properties is timely.

The two most important reasons for using calcium hydroxide as a root-filling material are stimulation of the periapical tissues in order to maintain health or promote healing and secondly for its antimicrobial effects. The exact mechanisms are unknown, but the following mechanisms of actions have been proposed:

1. Calcium hydroxide is antibacterial depending on the availability of free hydroxyl ions (10, 11). It has a very high pH (hydroxyl group) that encourages repair and active calcification. There is an initial degenerative response in the immediate vicinity followed rapidly by a mineralization and ossification response (12).
2. The alkaline pH of calcium hydroxide neutralizes lactic acid from osteoclasts and prevents dissolution of mineralized components of teeth. This pH also activates alkaline phosphatase that plays an important role in hard tissue formation (13).
3. Calcium hydroxide denatures proteins found in the root canal and makes them less toxic.
4. Calcium hydroxide activates the calcium-dependent adenosine triphosphatase reaction associated with hard tissue formation (13, 14).
5. Calcium hydroxide diffuses through dentinal tubules and may communicate with the periodontal ligament space to arrest external root resorption and accelerate healing (12, 15).

Leakage

The rationale for the addition of calcium hydroxide to root canal sealers is from observations of bases and liners containing the material and their antibacterial and tissue repair abilities. This is exerted via the leaching of calcium and hydroxyl ions to surrounding tissues (16-19). The role of root canal sealers is to fill gaps; therefore, solubility, leakage, and adhesion are prime concerns. Accordingly, sealers should be insoluble and not disintegrate in fluids. Even though calcium hydroxide has low solubility and diffusibility, unless calcium and hydroxyl ions dissociate out of the sealer

TABLE 1. The Ideal Root Canal Sealer

Grossman (1982) listed 11 requirements and characteristics for root canal sealers:
1. It should be tacky when mixed to provide good adhesion between it and the canal wall when set.
2. It should make a hermetic seal.
3. It should be radiopaque so that it can be visualized on the radiograph.
4. The particles of powder should be very fine so that they can mix easily with liquid.
5. It should not shrink upon setting.
6. It should not discolour tooth structure.
7. It should be bacteriostatic or at least not encourage bacterial growth.
8. It should set slowly.
9. It should be insoluble in tissue fluids.
10. It should be well tolerated by the periapical tissue.
11. It should be soluble in common solvents if it is necessary to remove the root canal filling.

Criterion 10 may be expanded by stating that an ideal sealer should not provoke an immune response in periradicular tissue and it should be neither mutagenic nor carcinogenic.

(20), it will not promote the expected healing effects on surrounding tissues. This raises serious questions regarding the long-term sealing ability of the calcium hydroxide sealers and their therapeutic effects.

Many experiments have been conducted to compare the leakage around different sealers, the majority of which involve *in vitro* dye penetration and bacterial leakage tests. When compared with zinc oxide eugenol (ZOE), AH 26 (Dentsply-Maillefer, Tulsa, OK), and Ketac-Endo (ESPE AG, Seefeld, Germany) sealers in dye leakage studies, Sealapex (SybronEndo, Orange, CA), CRCS (Coltene/Whaledent/Hygienic; Cuyahoga Falls, OH), and Apexit (Vivadent, Germany) showed no significant difference in leakage at 30 days to 32 weeks (21-25). A German experimental calcium hydroxide sealer showed acceptable sealing ability at 1 week (26). Apexit was reported to have better sealing properties than Sealapex at 48 hours and Ketac-Endo at 3 weeks (27). In a contrary report, Apexit had poor performance in a 1-year experiment against Diaket (ESPE AG, Seefeld, Germany), AH 26, AH Plus (Dentsply-Maillefer, Tulsa, OK), and Ketac-Endo (28). Sealer 26 (a modification of AH 26 with the addition of calcium hydroxide, Dentsply-Brazil, RJ, Brazil) showed less leakage in a dye penetration study compared with Grossman's sealer (29). A recent *Enterococcus faecalis* bacterial leakage study with Sealapex showed 85% penetration at 30 days and 100% at 60 days. Although not statistically different to results with AH 26, AH Plus, and Ketac-Endo, Sealapex exhibited slower bacterial penetration than AH 26 (30). These studies arrive at dissimilar conclusions with regard to leakage around root canal sealers. Ingle et al (31) attribute these variations to the use of a variety of dyes, experimental methods and different experimental durations. Some might also be targeted toward market-driven product promotion.

Leakage of sealers is mainly related to their solubility and their adhesion to dentin and gutta-percha. In an animal study, Sealapex in tissue contact dissolved and was partially replaced by ingrowths of connective tissue. Large quantities of sealer particles were noticed in cells and tissues at some distance from the sample (32). This was supported in a study by Soares et al (33) who reported the presence of disintegrated Sealapex sealer particles in macrophage cytoplasm away from the root-filling material in the periapical regions of dog teeth. Subcutaneously implanted radioactive Vitapex (NEO Dental, Tokyo, Japan) in rats was identified in distant blood capillaries, bones, and the digestive tract and was partially phagocytized by macrophages at 2 weeks (34). A study investigating the solubility of Apexit noted its very high solubility compared with AH Plus and Tubliseal (SybronEndo, Orange, CA) (35).

Sealapex, CRCS, and Apexit performed poorly in dentin adhesion experiments irrespective of the presence of smear layer or methods of smear layer removal (1, 36-38). Sealers showed adhesion failure within the cement layer rather than at the dentin or gutta-percha interface (39, 40). At least for Sealapex, this was possibly because of its setting qualities. Sealer 26 showed better adhesiveness to dentin surfaces after the removal of the smear layer with EDTA (1) or using an Er:YAG laser (38).

All sealers leak (21) so the important clinical question is do calcium hydroxide sealers show a minimum or clinically acceptable leakage? Based on current information in the literature, it can be concluded that in terms of leakage, calcium hydroxide–based sealers are not superior to other groups of sealers. However, most studies conducted so far are laboratory-based experiments or animal studies. Extrapolation of such results to clinical situations may not be appropriate.

The Effect of Calcium Hydroxide on Periapical Tissue Healing

Ideal periapical healing after root canal treatment features bone regeneration, resumption of an intact periodontal ligament space, and the deposition of cementum around the root apex.

Calcium hydroxide is effective in the formation of calcific bridges when applied to exposed pulpal tissue (16). When calcium hydroxide comes in contact with water, it releases calcium ions during ionic dissociation. The quantity of free calcium ions determines its potential to induce mineralized tissue (41). Free calcium ions are reported to be required for cell migration, differentiation, and mineralization (19, 42). Torneck and co-workers (14) noted the importance of free calcium ions for the activation of calcium dependent ATPase. In laboratory-based experiments, CRCS showed very little initial release of calcium ions, while Sealapex demonstrated a higher dissociation of calcium but the sample disintegrated in 2 hours (41, 43). A recent study has suggested higher diffusion of calcium ions through root dentin after pretreatment with sodium hypochlorite and citric acid (44).

Animal experiments to evaluate effects of calcium hydroxide–based sealers on direct contact with the living tissue have shown favorable outcomes. Subcutaneous implants of calcium hydroxide in rats showed formation of a calcified, bonelike tissue (45). Similarly, injection of Sealapex, Hypocal, and CRCS into the subdermal tissue of guinea pigs showed varying degrees of calcification in 80-day specimens (46). In an experimental study on dog and monkey teeth, Sealapex was found to encourage apical closure by cementum deposition compared with Kerr Root Canal Sealer (SybronEndo/Kerr) when the root filling was 1 mm short of radiographic apex (47). Vitapex introduced into the mandibular canal of dogs caused heterotopic calcification and ossification within the area of penetration (48). Others found no significant differences in periapical tissue responses between Sealapex, CRCS, and a ZOE-based sealer in dog teeth (33). A study to compare the effects of CRCS, Sealapex, and AH 26 on monkey teeth revealed mild to severe inflammatory lesions at the apical foramina of the roots filled with core and sealers AH 26 or CRCS at 8 to 14 months, but most teeth with Sealapex showed no inflammatory cells at the apex except macrophages with sealer particles (49).

Early in 1921, Grove (50) wrote concerning nature's contribution to periapical healing through secondary cementum formation after root filling, provided there is no or minimal chemical injury to the apical tissue. Unfavorable periapical responses have been observed in teeth with root canals filled beyond the apical "stops," even with the use of calcium hydroxide–containing sealers (33, 47). A clinical study following the effects of different sealers on the outcome of root canal treatment concluded that sealers had a minor role in periapical healing.

Calcium hydroxide–based sealers had a statistically insignificant association to the rapid healing of apical periodontitis (51). Recently, Sealapex has been recommended as a root-filling material for primary teeth. In prospective clinical studies, Sealapex and Vitapex showed high success rates for pulpectomies (52, 53).

The Antimicrobial Effect

The incorporation of antibacterial components in root canal sealers may be an important factor in preventing the regrowth of residual bacteria and controlling bacterial re-entry into the root canal system. The antibacterial effect of calcium hydroxide is based on its ability to release hydroxyl ions and to raise pH (10, 11). The pH of calcium hydroxide paste has been shown to be as high as 12.5 when used for intracanal medicament purposes (11). In an experimental study, the pH of distilled water in contact with Sealapex reached 11.5 during 30 days, most of which was gained in the first 1 hour, followed by CRCS (10.5), Apexit (10.5), and Sealer 26 (9.5) (41). In another experiment, the maximum pH of Sealapex and CRCS in a 1-week study did not exceed 9.1 and 7.8, respectively (54). Further research on Sealapex showed a slow and gradual rise in pH (not exceeding 9.57) in bidistilled water in the first hour, after which the sample disintegrated in solution, whereas CRCS did not cross the 7.65 mark (43). Ehrman et al (55) found similar values (9.14 and 8.6, respectively) for the same products. Apexit was unsuccessful in the *in vitro* elimination of *Candida albicans* and *Staphylococcus aureus* because of insufficient elevation of pH (56).

Several studies have investigated the relative antimicrobial effects of calcium hydroxide–containing sealers and their duration of activity using different bacterial species and different test methods. The methods used to show short- and long-term antibacterial activity of sealers are the agar diffusion inhibitory test (ADT) (57), dentin tubule penetration (58, 59), and the direct contact test (60, 61).

The ADT for sealers shows that the largest zone of inhibition is with Roth's sealer (Roth Drug Co, Chicago, IL) followed by Ketac-Endo, Tubliseal, Apexit, and Sealapex on the anaerobic bacteria *Capnocytophaga ochracea, Porphyromonas gingivalis*, and *Peptostreptococcus micros* at 48 hours (62). Several other studies using a similar test method depicted Sealapex, Dycal, and Apexit as only mildly antibacterial against many anaerobic and aerobic bacteria found in root canal systems (57, 63-66). Sealapex was not quite as effective in the elimination of *Enterococcus faecalis* (67). Experiments have reported the ineffectiveness of calcium hydroxide sealers against *Candida* (56, 57, 68).

There has been debate in the literature regarding the use of the ADT as a method to determine the short-term antibacterial activity of calcium hydroxide sealers. The method relies on the solubility and physical properties of the antimicrobial component of the sealer. This works well for water-soluble materials (60, 67), but calcium hydroxide has low water solubility and diffusibility. In contrast, set ZOE when exposed to aqueous media releases free eugenol by the hydrolysis of zinc eugenolate, and even at low concentration this can inhibit cell respiration and division (69, 70). This factor could account for the relatively high antibacterial effect of ZOE compared with calcium hydroxide in short duration experiments using ADT.

Dentinal tubule penetration tests have shown Sealapex and Apexit to be less effective in killing bacteria than resin and eugenol-based sealers (58, 59). Direct contact tests of sealers and microorganisms concluded Sealapex and Apexit to be mildly effective antimicrobial agents over short duration (60, 61).

Laboratory experiments to measure radicular dentin pH have suggested an inadequate rise in pH in dentinal tubules for effective results (71, 72). The limited antibacterial activity of calcium hydroxide sealer might be attributed to a lack of sufficient pH elevation, limited solubility, and diffusibility of calcium hydroxide into dentinal tubules and possibly buffering ions present in the tubules (58).

Biocompatibility

Root canal sealers and filling materials may be exposed to the periradicular tissue at the apical and lateral foraminae so superior tissue tolerance to sealer is required to minimize local and systemic side effects. The cytotoxicity of sealers has been measured *in vitro* by cell culture or *in vivo* in animal studies. Several studies have compared the cytotoxic effects of calcium hydroxide–containing root canal sealers with the other types.

Cell culture tests using either human periodontal ligament cells or monolayer or multilayer mouse cells have shown Sealapex and Apexit to be less toxic compared with ZOE and resin-based sealers (73-77). Meryon and Brook (78) found Sealapex to be moderately cytotoxic compared with Kloroperka and Diaket on a monolayer fibroblast cell culture with dentinal chips.

Cytotoxic studies of sealers by means of subcutaneous or intraosseous implantation present similar results. Sealapex planted in rat subcutaneous connective tissue gives rise to a foreign body reaction with granulomatous tissue, the reaction increasing gradually to 30 days and still in progress at 90 days. In contrast, tissues in contact with CRCS had an initial severe inflammatory reaction that resolved at the end of a 90-day observation period (79). However, in a similar study on guinea pigs, Sealapex at 6, 15, and 80 days yielded milder inflammatory reactions compared with CRCS, Grossman's sealer, and Hypocal, indicating a tendency toward repair (46). Comparable results for CRCS were obtained in a study of intraosseous implants in dogs (32). CRCS possibly has a severe inflammatory reaction in the initial stage because of the presence of eugenol in its liquid. Unlike traditional ZOE sealers, the free eugenol content of set CRCS is lowered but may still be enough to result in an inflammatory reaction (46). A recent histologic investigation into the biocompatibility of Sealapex, Apexit, and Sealer 26 in rat subcutaneous tissue revealed that all three materials induced severe to mild inflammatory reactions at 48 hours to 60 days. When compared against each other, tissues surrounding Sealapex displayed a progressive reduction in the numbers of inflammatory cells over the period of 60 days, and tissue surrounding Apexit showed more aggressive reactions compared to Sealapex. Tissues adjacent to Sealer 26 continued to show high numbers of neutrophils (initial stages) and macrophages (later stages) compared with Apexit and Sealapex (80). In a scanning x-ray microanalysis of root canal sealers, it was found that a calcium-containing sealer exhibited less toxicity than one containing lead or magnesium (eg, N2 apical and RC-2B) (81).

Neurotoxic investigations on rat nerves have concluded reversible blockage of nerve conduction in the short-term (up to 5 minutes) after contact with Sealapex and CRCS. With Sealapex, the reversal was quicker than CRCS, N2, SPAD, and Endomethasone (Septodont, Saint-Maur des Fosses, France). Unfortunately, permanent damage to neural tissues occurred within 30 minutes of contact with Sealapex and CRCS (82, 83).

There are considerable variations in these outcomes, mainly because of the assessment of different stages of sealers (freshly mixed or set), the use of different techniques (cell culture systems or animals), and evaluations for different durations of effect.

Physical Properties

Flow

An acceptable flow within the working time is important for any root canal sealer in order to reach and seal the apical foramen and lateral dentinal wall irregularities. Flow depends on particle size, shear rate, temperature, and time from mixing. It can be measured with either a rheometer or from the diameter of the film of sealer between two glass plates under load (3). Pitt Ford et al (84) reported significant differences in flow between Apexit and Tubliseal EWT, the former being superior in a rheometer test and the latter with the traditional method. In another study, the flow of Apexit was comparable to AH Plus and Tubliseal EWT (35).

Setting Time

Dycal has a very short setting time, and in its use as a root canal sealer users recommended first introducing the catalyst paste into the canal with a lentulospiral followed by a gutta-percha cone coated with the base paste (9). In contrast, Biocalex takes days to set (8). The setting reactions of calcium hydroxide–containing sealers are complex. Even though the sealer surface becomes hard, the inner mass may remain soft for an extended period (3). Apexit was reported to have a setting time of under 2 hours at 100% relative humidity (35). CRCS sets within 3 days in both dry and humid environments. Sealapex sets in 2 to 3 weeks in 100% relative humidity and does not set in a dry environment (31, 85, 86).

Dimensional Stability

Biocalex in the presence of moisture in the canal expands by up to 280%. This has the potential to create severe postoperative pain and vertical root fractures. Apexit also has exhibited high water sorption but along with its equally high solubility gives rise to minor overall dimensional change (35). CRCS was quite stable with volumetric changes in water for 21 days. Sealapex displayed significant sorption in a 100% humid atmosphere with volumetric expansion (86).

Staining of Teeth

Studies on tooth staining conclude that all root canal sealers can stain dentin (87, 88). Limited data are available on the staining ability of calcium hydroxide–containing root canal sealers, but two studies concluded moderate to minimal discoloration of coronal dentin with Sealapex (89, 90).

Radiopacity

Radiopacity is generally achieved by the addition of various metal salts. Comprehensive studies found difficulties in the assessment of the quality of root canal fillings on radiographs because of the large variance in radiopacifiers (91). The type and the thickness of sealers influence the radiopacity of root fillings (92). According to ISO 6876/2001 standards, the recommended radiopacity of the root canal sealer should be at least that of a 3-mm thick aluminium wedge. Radiographs of samples of Sealapex showed large voids in their structure, and they were less radiopaque than CRCS for 3 weeks, after which the voids disappeared and there was an increase in radiopacity for Sealapex (86). An experiment to compare the radiopacity of various root canal sealers showed Sealapex to be least radiopaque, equivalent to 2 mm of aluminium, whereas Sealer 26 was equivalent to 4 mm of aluminium and AH Plus to 16 mm of aluminium (93). In contrast, a recent study using similar methods and materials established the radiopacity of Sealapex and Sealer 26 to be equivalent to 6 mm of aluminium and statistically different to a glass-ionomer material Activ GP sealer (Brasseler, Savannah, GA) (2 mm of aluminium). The difference in the value of radiopacity for Sealapex was explained by the addition of bismuth trioxide in the recent formulation (94).

Other Calcium-Based Root Canal Sealers

Calcium phosphate cements have shown good results in several laboratory trials (95, 96). Further work is necessary to establish the long-term suitability of these sealers in clinical situations. Mineral trioxide aggregate (MTA) is a relatively new and important endodontic material that includes calcium-based minerals among of its key ingredients. After hardening, it contains calcium oxide that could react with tissue fluids to form calcium hydroxide. Although MTA is not formulated for use as a sealer around a core material, it is increasingly used particularly to manage cases with open apices. MTA has been thoroughly tested for its solubility (97), physical properties (98), and its biocompatibility and effects on the periapical tissues (99, 100). Many of its properties support its use alone as a root canal–filling/sealing material, although its placement in canals may be challenging.

Conclusion

This review of calcium hydroxide–based root canal sealers shows that these materials do not fulfil all the criteria described by Grossman (5). Most studies are laboratory based or in animal models, which may differ from the clinical situation. The antibacterial effects of calcium hydroxide in sealers are variable. Cytotoxicity appears to be milder than for other groups of sealers. Solubility is a concern, but leakage cannot be linked directly to solubility, with studies reporting the potential for the formation of calcific repair tissues in the vicinity of the materials.

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