

Assesment Of Antibacterial Activities Of Contemporary Endodontic Sealers

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ABSTRACT

Endodontic therapy's main goal is to remove bacteria from the root canal. Although they all contribute to a reduction in the quantity of bacteria in the canal, intra-canal medications, irrigation, and instrumentation cannot eradicate all microorganisms from the root canal. Therefore, it would be advantageous to use a high-quality root canal filling material with antibacterial qualities to help reduce the amount of remaining germs.

In this regard the goal of this review article is to summarize the results of in vitro investigations of root canal sealers' antibacterial efficacy against *Enterococcus faecalis*, *Staphylococcus aureus*, *Candida albicans*, also evaluation and comparison of solubility and pH of these root canal sealers in vitro. Root canal sealer selected for this review are Bioceramic based (Endosequence BC Sealer, or Smartpaste bio), Resin based (AH Plus), Zinc oxide-eugenol based (Tubliseal) Calcium hydroxide based (Sealapex), and Mineral trioxide aggregate (MTA Fillapex).

Keywords: Antimicrobial activity, root canal sealers, *E. faecalis*, *Candida albicans*, *Staphylococcus aureus*,

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I. Introduction

Eliminating germs from the root canal system and avoiding reinfection are the primary goals of root canal therapy. However, even after comprehensive chemo- mechanical debridement, germs can still be detected in the root canal system because of the complicated root canal morphology.(1)

Despite the fact that there are numerous factors that could contribute to root canal failure, it has been determined that the most significant one is the persistence of microorganisms in the root canal system even after treatment. These microorganisms have the following characteristics that allow them to resist disinfection measures: the capacity to form biofilms, the ability to settle in spaces unreachable to root canal instrumentation techniques, synergism, the capacity to express survival genes, and the capacity to activate alternative metabolic pathways.(2)

After root-canal therapy failed, only a few, mostly Gram-positive bacteria species were present in the microbial flora in the canals. However, the most often isolated microbes were facultative anaerobes, particularly *E. faecalis*.(3)

Periapical disease and chronic failure of an endodontically treated tooth may be caused by *E. faecalis* cells' capacity to penetrate dentinal tubules and remain alive there. In the presence of human serum, *E. faecalis* cells continue to be alive and keep their capacity to colonize dentinal tubules and adhere to collagen. This process might explain why *E. faecalis* cells in radicular dentinal tubules perform pathologically in teeth with unsuccessful endodontic treatment.(4)

Complete elimination of *Enterococcus faecalis* is difficult because it has survival and virulence factors as following:

- Suffers extended periods of nutritional deficiency
- Bonds to the dentin and invades the dentinal tubule with ease.
- Changes the host's response
- Inhibit the action of lymphocytes
- Possesses lytic enzymes, cytolysin, aggregation substance, pheromones, and lipoteichoic acid
- Use serum as a nutritional supply
- Resists in tr canal medicaments

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- Competes with other cells
- Forms a biofilm(5)

Bacteria in intracanal biofilms form methods to protect themselves from antibacterial drugs, increasing to 1,000 -1,500 times more durable in comparison bacterial species that are in planktonic form.(6)

The most typical yeast found in infected root canals is *Candida albicans*. *C.albicans* may attach to and enter dentine thanks to a range of virulence factors, additionally *C.albicans* can resist challenging ecological circumstances, such as excessive alkalinity, the capacity of *C. albicans* to co-operate with dentine may be significant for its capacity to survive in the ecologically demanding medium of the necrotic or treated root canal.(7)

The pathogenic potential of this fungus has been linked to a number of factors and activities. The virulence factor of this fungus is thought to include the production of hydrolytic enzyme, molecules that cause adhesion and attack host cells, yeast-to-hypha mutation, biofilm formation, and phenotypic switching.(8)

In particular, root canal sealers that shown increased antibacterial activity after manipulation seem to be extremely important, understanding that even after chemo-mechanical preparation and intracanal dressing, microorganisms can still be found in the ramification of the root canal system. Due to their antibacterial properties, sealers can work against these microorganisms, lowering their numbers and increasing the chances that a root canal treatment will be successful.(9)

Antimicrobial components in root canal sealers may become a critical component in limiting the regrowth of leftover germs and controlling bacterial re-entry into the root canal system. (10)

Regarding the root canal sealers selected for this review special importance will be given to bioceramics sealers, because they are considered to be an advantageous technology in endodontics.(11)

In scientific literature, the word "bioceramic" is being used more frequently. It serves as a definition for a class of materials used as endodontic sealer in clinical practice in the area of endodontics that are mostly based on calcium silicate cements. (12)

There are two significant advantages to using bioceramic materials as root canal sealers.

First of all,in biological settings bioceramics are chemically stable, shrink-resistant, non-toxic and extremely biocompatible. In the field of endodontics, it is essential to note that bioceramics are not going produce an inflammatory reaction ,if an overfill occurs during a root restoration or the obturation procedure. The material's ability to produce hydroxyapatite and make a connection between dentin and the filling components is another advantage.(13)

Based on existing research, the primary antibacterial characteristics of root canal sealers are attributed to their alkalinity. Bacteria are those which may produce acids like lactic acid and lower the pH of their surroundings, allowing them to exist. Sealer's alkalinity can help to minimize this favorable environment, preventing bacterial growth. Sealer's antibacterial action is directly proportional to its pH. (14)

There are multiple microscopic and macroscopic contacts between the root canal system, the periodontal ligament, and the surrounding bone in addition to the apical foramen, dentinal tubules, supplementary foramina, and lateral canals are examples of these structures.(15) As a result, tissue fluid can easily access the root canal system, causing the sealer material to degrade. (16)

The integrity of the sealer, not the core material, is what determines the root canal's long-term bacteria-proof seal. (17,18)

II. Aim of review

The purpose of this paper is to do a review of the literature on the bioceramic materials and their unique properties in endodontic treatments compared to conventional sealers like: zinc oxide-eugenol based , calcium hydroxide based,rezine based and mineral trioxide aggregate based materials against most present endo-microbes: *Enterococcus faecalis*, *Staphylococcus aureus* and *Candida albicans*.

III. Materials and methods

We searched the international databases (PubMed) and (Google Scholar) to find papers published in the last 20 years.

The search strategy is done in conjunction with specific search terms related to antimicrobial activities of different root canal sealers in different bacterial species.

In the framework of this review we have selected studies applying the following inclusion criteria: articles published in English between 2000 and 2021 in scientific journals, original articles, in vitro studies, review articles, and systematic reviews.

IV. Discussion

In the framework of the discussion we have included the studies conducted within the period 2000 -2021.

Based on the literature, bioceramic cements have acceptable working qualities, are simple to handle, and have great antibacterial action and an alkaline pH. They showed biocompatibility, acceptable cytotoxicity, the capacity to stimulate osteoblastic development of periodontal ligament cells and dentin remineralization, and the capacity to release calcium ions that facilitate adaption and marginal sealing.

They can also be employed in humid environments and are easily removed in the event of reintervention. They have good dentin adhesion, which increases root fracture resistance, and they do not produce coronary discolouration. All of these characteristics indicate that bioceramic cements are suitable for usage. (19)

EndoSequence BC (Brasseler, Savannah, USA)—also referred to as iRoot SP (Innovative Bioceramix, Vancouver, Canada)—is a brand-new bioceramic root canal sealer that was introduced in 2009. EndoSequence BC is an insoluble, aluminum-free, radiopaque material, according to its maker. It is made up of zirconium oxide, calcium hydroxide, calcium hydroxide, and calcium silicate. EndoSequence BC needs water to set and solidify, in contrast to other bioceramic root canal sealants.(20)

Switzerland produced Totalfill BC Sealer, a substance with the same composition.(21)

We compared the antibacterial performance of these three sealers since they have the same component.

Author **G. T. D. M. Candeiro** in his study concluded that Endosequence BC Sealer showed alkaline pH in all experimental times, with maximum ph value in 168 hours in comparison with AH Plus which demonstrated slightly neutral pH also Endosequence BC Sealer demonstrated a considerably higher release of Ca²⁺ than AH Plus.(22)

Through a modified direct contact test, **Zhang et al.** evaluated the antibacterial activity of iRoot SP sealer against *Enterococcus faecalis* in vitro and discovered that it had a high pH value (11.5) even after setting but that its antibacterial effect was greatly diminished after seven days,

hydrophilicity and active calcium hydroxide diffusion were reported as two additional mechanisms related to the antibacterial activity of iRoot SP by the researchers, however, a low contact angle, indicating a sealer's hydrophilic surface properties, may make it easier for the sealer to penetrate the complex details of the root canal system and hence improve its in vivo antibacterial efficiency. (23)

In a biofilm created of 8-week-old *Enterococcus faecalis* adhering to surfaces, **Bukhari and Karabucak** compared the antibacterial efficacy of bioceramic cement to AH Plus using a model of dentin infection. In comparison to the AH Plus cement, they found that the EndoSequence BC Sealer has strong antibacterial efficacy in the presence of dentin for up to 2 weeks in an 8 week old *E. faecalis* biofilm.(24)

The purpose of the study done by the author **Gurpreet Singh** was to evaluate the antibacterial properties of some endodontic sealers against *E. faecalis*, he concluded that the bioceramic root canal sealer (Endosequence) has superior antibacterial activity compared to the other two most used types of sealers zinc oxide-eugenol and resin -based sealers, however it is comparable to that of both MTAs. (25)

In his investigation, author **Yakup Ustun** tested the antibacterial effectiveness of four different sealers AH Plus, EndoRez, mineral trioxide aggregate (MTA) Fillapex, iRoot SP against *Enterococcus faecalis* in vitro by time kill assay method. He demonstrated that only fresh I Root SP and AH Plus had maintained bactericidal activity against *E. faecalis*.. Both sealers had retained their bacteriostatic qualities at the first, seventh, and thirty days.(26)

In this work, **Zhejun Wang et al.** used a unique dentin infection model to assess the antimicrobial effects of AH Plus, Endosequence BC sealer (BC sealer), and pulp canal sealer EWT (PCEWT) root canal sealers on *Enterococcus faecalis* biofilms in dentinal tubules. He came to the conclusion that the three endodontic root canal sealants exhibited antibacterial qualities against *E. faecalis* in the dentinal tubules. Comparing BC sealer and AH Plus to PCEWT, they demonstrated stronger antibacterial properties.(27)

Author **Duddi Narendra Nirupama** and co-authors by using a direct contact test, assessed the antimicrobial efficacy of four endodontic sealers, including AH Plus, Tubliseal EWT, EndoRez, and iRoot SP, against three distinct bacteria, including *E. faecalis*, *C. albicans*, and *S. aureus*. *E. faecalis* growth was inhibited by iRoot SP only in the first 8 hours, whereas *S. aureus* growth was inhibited only in the first 7 hours.(28)

Agar diffusion test (ADT) and a direct contact test were both used by author **G. T. M. Candeiro** to evaluate and compare the antibacterial activity of Endosequence BC sealer and AH Plus sealer on an *Enterococcus faecalis* strain. After 24 hours of direct contact, BC sealer showed better antibacterial activity. In the agar diffusion test (ADT), the AH Plus sealer's inhibitory diameter was substantially larger than that of the EndoSequence BC sealer (29).

The antimicrobial effectiveness of newly developed EndoSequence BC sealer was compared to that of commonly applied zinc oxide-eugenol-based (Zical) and epoxy resin-based sealer (MM-Seal) against *Candida albicans*, *Lactobacillus*, *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* by author **Singh G** which concluded that in comparison to the other two sealers, EndoSequence BC sealer demonstrated antibacterial activity against all microbes and was found to be the preferable choice. To avoid recurrent infection

of complicated root canals, endodontic sealers' antimicrobial characteristics are necessary. In this regard, EndoSequence BC sealer has been shown to be superior. (30)

Author **Vasileios Kapralos** examined into the antibacterial properties of four endodontic sealers against bacteria which were planktonic or found in biofilms, which are often seen as a result of recurrent and secondary endodontic infections. The antibacterial qualities of RoekoSeal, Gutttaflow 2, TotalFill BC sealer, and AH Plus were evaluated against planktonic-grown and 24-hour-old biofilms of *Enterococcus faecalis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Streptococcus mutans*. Comparing TotalFill BC sealer to AH Plus, it showed a greater antibacterial effect on planktonic microorganisms up to 7 days after setting, but weaker antibacterial action against biofilms of *S. aureus* and *E. faecalis*.(31)

Alsubait et al. assessed the antibacterial efficacy of BioRoot RCS against *Enterococcus faecalis* biofilms in dentinal tubules using confocal laser scanning microscopy, comparing it to that of Totalfill BC and AH Plus sealers. He demonstrated that in comparison to BioRoot RCS, Totalfill BC demonstrated a considerably greater proportion of dead bacteria after 7 days when compared to days 1 and 30. Compared to the control group and BioRoot RCt, Totalfill BC eliminated a considerable more bacteria.(32)

Using an experimental calcium silicate-based endodontic material, the author **Zordan-Bronzel et al** assessed its cytocompatibility, bioactive potential, antimicrobial, and antibiofilm capabilities compared to TotalFill BC Sealer and AH sealer. Using the DCT, TotalFill BC Sealer considerably decreased the amount of *E. faecalis* in comparison to the control group. Using the MDCT test, TotalFill BC demonstrated considerably greater efficacy against *E. faecalis* as compared to AH Plus and the control group.(33)

Author **Colombo et al** in his study evaluated the antimicrobial properties of bioceramic-based root canal sealers, calcium hydroxide-based, MTA-based and epoxy resin-based root canal sealers, against standard strain of *Enterococcus faecalis* by using DCT and ADT. Whith DCT TotalFill BC eradicated all bacteria, whereas whith ADT eradicated no bacteria.(34)

Author **Poggio et al** tested the antimicrobial activity of different root canal sealers against *Enterococcus faecalis*. Except for TotalFill BC Sealer, all other sealers examined showed antibacterial activity when tested with ADT; however, when tested with DCT, TotalFill BC Sealer eradicated all germs during all time periods.(35)

A consistent conclusion regarding the comparative effectiveness of Endosequence BC Sealer, iRoot SP, and Totalfill BC Sealer in terms of their antimicrobial effect could not be drawn for this group of studies due to the high degree of heterogeneity among the studies—using different comparators, different research methods, and different bacterial species.

Author **Rethi G** compared the antimicrobial activity of four different endodontic sealers, including Tubli-Seal EWT (zinc oxide eugenol sealer), RoekoSeal (polydimethyl siloxane-based sealer), EndoRez (urethane dimethacrylate resin-based sealer), and Sealapex (calcium hydroxide-based sealer), on *Enterococcus faecalis* based on the direct contact test at time intervals of 20 minutes, 1 day and 7 day, who concluded that Zinc oxide Eugenol based sealer (Tubli-Seal EWT) was the most effective effective against *Enterococcus faecalis*.(36)

Author Lavanya **Anumula**, evaluated the antibacterial activity of four endodontic sealers on *Enterococcus faecalis* by a direct contact test he concluded that the sealers examined in his investigation demonstrated various inhibiting effects across the time period studied, Zinc oxide eugenol sealer was the most effective and also showed total suppression of bacterial growth for the duration of incubation. In order to stop the proliferation of leftover bacteria and manage bacterial reentry into the root canal space, root canal sealers may need to have antimicrobial components.(37)

Using the agar diffusion test, **Saha et al.** evaluated the antimicrobial activity of three root canal sealers Endomethasone, AH 26, and Apexit against seven bacterial strains (aerobes, facultative, and obligate anaerobes) known to be common isolates in necrotic pulps and endodontic lesions at different time intervals. They came to the conclusion that Zinc oxide eugenol-based sealers produced the largest inhibitory zones followed by epoxy resin based sealer and least by calcium hydroxide based root canal.(38)

Using the agar diffusion method, author **Alexandra Mussolino de QUEIROZ** in his study assessed the antibacterial activity of four root canal filling materials for primary teeth against five bacterial strains that are frequently found in endodontic infections he concluded that the ZOE had the strongest antibacterial efficacy against the test pathogens.(39)

While regarding the calcium hydroxide based materials in comparison to zinc oxide-eugenol-based (Tubliseal), resin-based (AH Plus), and mineral trioxide aggregate, author **Swati Dalmia** in his study concluded that Sealapex had the strongest antibacterial efficacy against *E. faecalis*.(40) Author **GC Rezende**, and co-authors in their study compared the antimicrobial activity of Acroseal, Sealapex and AH Plus in an in vitro biofilm model of *E. faecalis* which concluded that in all time periods, Sealapex shown greater antibacterial action against *E. faecalis*. (41)

Author **Sipert CR**, determined the antimicrobial activity of Fill Canal, Sealapex, Mineral Trioxide Aggregate(MTA), Portland cement and EndoRez on different species of microorganisms in vitro, In his study he concluded that Sealapex showed inhibitory activity against all tested facultative strains.(42) According to

Zhang et al Sealapex had the most effective antimicrobial effect against *E. faecalis* after 7 days mixing eliminating all *E. faecalis* cells at 20 and 60 minutes.(23)

The Sealapex endodontic sealer's antimicrobial properties, as well as those of other calcium hydroxide-based , depend on ionization, which releases hydroxyl ions and raises pH, so making the environment unsuitable for the development of microorganisms .(43)

Epoxy resin-based sealers contain antibacterial properties due to either the release of formaldehyde during polymerization or bisphenol A diglycidyl ether.(30)

Author **Yoshiyuki Yasuda et al** in his work compared the antimicrobial activities of six endodontic sealers against *Staphylococcus aureus*, *Enterococcus faecalis*, *Candida albicans*, *Streptococcus mutans*,*Streptococcus sanguinis* ,among the sealers AH plus exhibited the highest antimicrobial activity.(44)

Author **Erhan Özcan and co-authors** in their study evaluated the antifungal activity of several root canal sealers (iRoot SP, MTA Fillapex and GuttaFlow) against *Candida albicans* and compare them to that of AH Plus they concluded that freshly mixed AH Plus presented the highest antifungal activity and showed complete inhibition of fungal growth.(45)

Nirupama et al. tested the antimicrobial efficacy of four endodontic biomaterials against *E. faecalis*, *Candida albicans*, and *Staphylococcus aureus* by direct contact test, and concluded that AH plus had the best antimicrobial activity against *C. albicans* and *S. aureus*, *E.faecalis*.(46)

According to **Pizzo et al.** only freshly prepared AH Plus had antibacterial action in DCT; samples that were older than 24 hours or 7 days did not have any impact against *E. faecalis*. (47)

Hui Zhang's research also showed that settled samples of AH Plus lacked antimicrobial activity whereas only fresh AH Plus had a strong antibacterial efficacy.(23)

MTA -Fillapex (Angelus, Londrina, Brazil), which was presented to the market in 2010, was the first sealer based on MTA. Silica, a matrix made of salicylate resin, and MTA (40%) compose the majority of this sealer.(48)

Duarte et al. confirmed the mechanism of increase in pH and formation of calcium and hydroxide ions in MTA, which is responsible for the antibacterial effect of MTA.(49)

Using two different techniques, author **Hasheminia et al** examined the antibacterial efficacy of five various sealers against *Enterococcus faecalis*. MTA Fillapex demonstrated a significantly greater antibacterial activity than all other sealers in the direct test.(50)

Using a dentin infection model, author **Tianfeng Du** examined the combination antibacterial effects of sodium hypochlorite (NaOCl) and root canal sealers on *Enterococcus faecalis* biofilms. He concluded that the highest level of efficiency was demonstrated by the mixture of NaOCl and MTA Fillapex , which killed 83% of the bacteria in dentin.(51)

Author **Faria-Junior et al** assessed the pH and solubility of AH Plus, Sealer 26, Epiphany SE, Sealapex, Activ GP, MTA Fillapex , and an experimental MTA-based Sealer as well as their antibiofilm efficacy against *Enterococcus faecalis*.In the three periods examined, a comparison of the different materials showed that MTA Fillapex was linked to a higher reduction in *E. faecalis* than the other materials, as compared to the control group also MTA Fillapex had the highest pH in all three periods.The Author conclude that the high solubility and pH may be related to the antibacterial activity of this material.(52)

By using an agar diffusion test, author **Gholamhoseini Z et al** assessed Endoseal-MTA, MTA-fillapex, and SureSeal's antibacterial effects on *Enterococcus faecalis* and *Staphylococcus aureus*. The MTA-Fillapex sealer demonstrated an antibacterial activity against *E. faecalis*, while two other sealers did not.(53)

Using White MTA and Endofill as benchmarks for comparison, **Morgental et al.** investigated the pH and bactericidal activity of Endo CPM Sealer and MTA Fillapex using two different techniques. He came to the conclusion that MTA Fillapex and Endofill had an antibacterial effect against *E. faecalis* prior to setting, despite the high pH of the MTA-based materials.However, none of the sealers continued to have an antibacterial effect after setting. (54)

The antifungal efficacy of two different sealers, AH-26 and MTA Fillapex, against three strains of *Candida*, 24, 48, 72, and 7 days after mixing, is investigated by authors **Jafari et al**, which concluded that with direct method MTA Fillapex sealer had the strongest antifungal activity against *C. albicans* and the lowest antifungal activity against *C. krusei*.(55)

V. Conclusion

The effectiveness of bioceramic-based root canal sealers is promising, however the studies were so highly heterogeneous using various comparators, various research methods, and various bacterial species, and it was not possible to draw a consistent conclusion. The research has shown that bioceramic sealers may have varying degrees of antimicrobial activity.

It is impossible to determine their relative efficacy or suggest using one of them based on the facts provided.

More study, especially in vivo research, is required to clarify the clinical implications associated with the use of these sealers.

Refereces

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