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Literature Review

Epigallocatechin-3-gallate (EGCG) and tricalcium silicate (C_3S) combination as an antibacterial agent against *Enterococcus faecalis*

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ABSTRACT

***Background*:** *Dental caries affects 57.6% of the Indonesian population, with Enterococcus faecalis found in 80% of deep caries cases. Conventional materials used in vital pulp therapy (VPT), such as calcium hydroxide, have limitations including transient antibacterial action and poor sealing capacity. This prompts the exploration of alternative materials like epigallocatechin-3-gallate (EGCG), a polyphenol from green tea with antimicrobial activity, and tricalcium silicate (C_3S), a bioactive cement known for dentin regeneration potential.* ***Purpose*:** *This review evaluates the synergistic antibacterial potential of EGCG and C_3S combinations against E. faecalis, and assesses their feasibility as an alternative in VPT.* ***Review*:** *EGCG disrupts bacterial membranes, inhibits biofilm formation, and suppresses virulence factors, but lacks remineralization capability. Conversely, C_3S promotes dentin repair and creates an alkaline antibacterial environment, though its efficacy diminishes over time. Their combination compensates for each other's limitations: EGCG enhances antimicrobial potency while C_3S provides long-term alkalinity and regenerative support.* ***Conclusion*:** *The EGCG–C_3S combination exhibits synergistic antibacterial and regenerative effects, offering a promising alternative to current VPT materials.*

Keywords: *Epigallocatechin-3-gallate (EGCG); Tricalcium silicate; Enterococcus faecalis; inhibition zone; good health and well being*

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INTRODUCTION

Dental caries is a chronic disease caused by the interaction between bacteria on the tooth surface, plaque or biofilm, and diet, characterized by the demineralization of hard dental tissues and the breakdown of organic components.[1] In Indonesia, oral health issues have a prevalence of 57.6%[2] with the highest prevalence reported for deep caries at 59.76%, according to data from Universitas Airlangga Dental and Oral Hospital.[3] One of the main bacterial agents responsible for deep caries is *Enterococcus faecalis*, which is detected in 80% of cases and can lead to pulp tissue infections.[4]

Vital Pulp Therapy (VPT) aims to preserve pulp vitality by promoting the formation of reparative dentin through methods such as direct and indirect pulp capping, as well as partial or full pulpotomy.[5] However, the standard material for VPT, calcium hydroxide, has significant limitations, including pulp surface inflammation, necrosis post-capping, poor sealing ability, and high porosity, which increase the risk of reinfection.[6] These shortcomings highlight the need for alternative materials, such as the combination of Epigallocatechin-3-gallate (EGCG) and tricalcium silicate, which show promise as antibacterial agents in vital pulp therapy.

EGCG, a major polyphenolic compound in green tea (*Camellia sinensis L.*), exhibits anti-inflammatory and antimicrobial properties, although its pharmacological effects on pulp cell proliferation and differentiation remain limited.[7,8] *Epigallocatechin-3-gallate* (EGCG) can functions as component in hydrogel scaffolds when combined with collagen and hydroxyapatite (Col-HA-EGCG). EGCG functions as a crosslinking agent, enhancing the structural stability of collagen while exerting anti-inflammatory and antioxidant properties to safeguard tissues from damage, making it an effective material for pulp capping.[9] On the other hand, tricalcium silicate, a base material for mineral-based dental cements, stimulates the proliferation of osteoblasts and osteoclasts, supports tissue regeneration, and exhibits antibacterial activity by creating

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an alkaline environment.[10] However, its antimicrobial efficacy is often temporary, particularly against persistent biofilms in the complex anatomy of root canals, as its effectiveness diminishes over time with reduced alkalinity.[11] Combining EGCG with tricalcium silicate is expected to broaden the antimicrobial spectrum through mechanisms involving bacterial membrane disruption, inhibition of biofilm formation, and suppression of bacterial virulence factors. The objective of this review was to evaluate the effectiveness of EGCG-tricalcium silicate combinations as an antibacterial agent against *Enterococcus faecalis*.

METHODS

The authors investigated English-language literature on the *Epigallocatechin-3-gallate* (EGCG) and tricalcium silicate (C_3S) combination as an antibacterial agent against *Enterococcus faecalis* by using the databases of Science Direct and Google Scholar. Research and literary studies conducted between 2014 and 2024 were included. It was determined that epigallocatechin-3-gallate (EGCG), tricalcium silicate, Enterococcus faecalis, and inhibition zone were the search parameters.

REVIEW

This review article aims to explore the potential of combining Epigallocatechin-3-gallate (EGCG) and Tricalcium Silicate (C_3S) as antibacterial agents in endodontic therapy. EGCG, a major polyphenolic compound in green tea, exhibits antimicrobial mechanisms such as biofilm inhibition, bacterial cell membrane disruption, and inhibition of lipid synthesis, making it effective against *Enterococcus faecalis*. Meanwhile, C_3S is renowned for its ability to stimulate reparative dentin formation and create an alkaline environment that inhibits bacterial growth. The combination of these two materials is expected to overcome their individual limitations, such as the temporary antibacterial effect of C_3S and the limited remineralization capability of EGCG, resulting in a synergistic effect in vital pulp therapy.

DISCUSSION

Epigallocatechin-3-gallate (EGCG)

Tea plant products (*Camellia sinensis* L.) with antibacterial activity are catechin polyphenols, which also contribute to the immune system. Catechins found in green tea include *epigallocatechin gallate* (EGCG), *epigallocatechin* (EGC), *epicatechin gallate* (ECG), *epicatechin* (EC), and *gallocatechin* (GC).[12] In green tea, EGCG and EGC are the most abundant catechins, accounting for approximately 59% and 19% of the total *catechin* content, respectively. EGCG is a polyphenol derivative responsible for its biological activities, with a molecular formula of $C_{22}H_{18}O_{11}$.[13] Numerous studies have shown that EGCG is active against various pathogenic microorganisms, including many Gram-positive and Gram-negative bacteria, certain viruses, fungi, and prions.[14] However, EGCG does not exhibit strong pharmacological effects on proliferation and differentiation to support the remineralization process. EGCG does not directly enhance the proliferation of human dental pulp cells (hDPCs) and only slightly increases alkaline phosphatase (ALP) activity as an early marker of odontogenic differentiation, but this increase is not significant enough to indicate strong differentiation.[8]

Tricalcium Silicate

Tricalcium silicate is a base material in mineral microparticle cement that can enhance the physicochemical and chemical properties of pulp therapy materials. It has the capability to replace lost dentin structure by stimulating reparative dentin growth, facilitating restoration in secondary caries, and serving as a material for vital pulp therapy.[15] Tricalcium silicate releases calcium ions, which promote the proliferation and differentiation of osteoblasts and osteoclasts, regulate osteogenesis by supporting new angiogenesis in damaged bone, stimulate growth factor release, increase bone density, inhibit osteoporosis, and enhance cell proliferation and bone mineralization.[9] Additionally, tricalcium silicate exhibits antibacterial effects by producing calcium hydroxide, which dissociates into calcium and hydroxide ions. The hydroxide ions create an alkaline environment that contributes to antibacterial and anti-inflammatory activities.[16] However, these antimicrobial effects are often limited in duration and clinical effectiveness, particularly against persistent biofilms in the complex anatomy of root canals, and they diminish as the alkalinity decreases.[10]

Antibacterial Activities

EGCG (*Epigallocatechin-3-Gallate*) exhibits antimicrobial effects through various mechanisms, including bacterial cell membrane disruption, inhibition of lipid synthesis, and enzyme activity suppression. It disrupts bacterial membranes by binding to the lipid bilayer, compromising membrane integrity. This prevents bacteria from adhering to host cells, forming biofilms, and releasing toxins. Additionally, EGCG inhibits lipid synthesis, crucial for bacterial phospholipid structures and energy, by inactivating enzymes such as FaBG and FabI. EGCG also interferes with bacterial enzymatic functions, targeting DNA gyrase involved in DNA replication and dihydrofolate reductase essential for folate synthesis. Furthermore, EGCG generates hydrogen peroxide through autooxidation, which damages glycan chains and peptide bonds, reducing the stability of bacterial cell walls.[17]

Tricalcium silicate (TCS) exhibits antibacterial effects against *Enterococcus faecalis* through chemical processes, including the release of calcium hydroxide and modulation of pH. TCS produces calcium silicate hydrate (C-S-H) gel and calcium hydroxide $Ca(OH_2)$, which elevate environmental pH. This high-pH environment inhibits bacterial survival, as it disrupts the growth of bacteria

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like *Enterococcus faecalis*. The release of calcium ions (Ca^{2+}) further supports antibacterial activity by affecting the physiological mechanisms of microorganisms and promoting mineralization, aiding in the repair of damaged dentin tissue. Direct contact between hydrated TCS and bacteria creates a significant inhibition zone, enhancing its antibacterial effects. Additionally, the C-S-H gel formed during hydration fosters a bioactive environment that supports tissue healing and prevents further microbial colonization.[18]

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