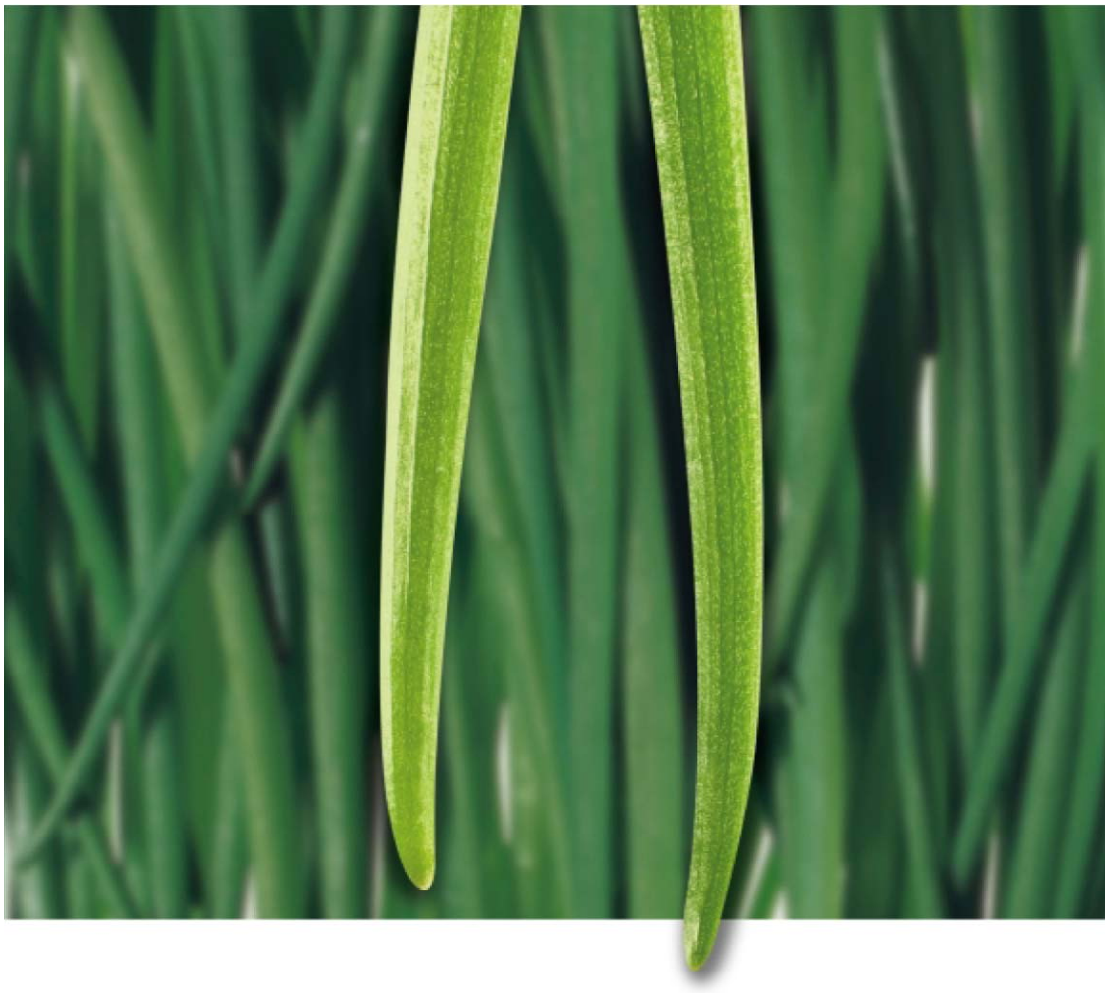
ApexCal®



Scientific Documentation

ivoclar vivadent

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1. Introduction

1.1 Properties of the material

Calcium hydroxide was introduced as a pulp capping material in the 1930s. With time, the clinical indications for this material have grown. Today, calcium hydroxide is used in direct and indirect pulp capping procedures as well as apexification and above all in the temporary disinfection of root canals in endodontic treatment measures.

Calcium hydroxide [$Ca(OH)_2$)] is a white odourless powder with a molecular weight of 74.08. It exhibits a low solubility in water (1.2 g/l) and the saturated aqueous solution has a pH of 12.46 (25 °C). The low solubility of calcium hydroxide is of clinical importance, as it is responsible for the slow release of OH^- ions and the very low resorption of the material. The main effect of calcium oxide is the ionic dissociation of Ca^{2+} and OH^-. The released hydroxyl ions are the most important components of calcium hydroxide, as they are responsible for a significant increase in the pH in the surrounding tissue and therefore stimulate the repair and calcification of dentin. In addition, the high pH value has an antimicrobial effect.

A number of different ready-to-use calcium hydroxide formulations are commercially available. Three different carrier substances are generally used: aqueous, viscous or oil-based formulations. According to Fava & Saunders [1], these formulations show different release kinetics of the OH^- ions. ApexCal is a viscous polyethylene glycol based paste.

1.2 Clinical indication – temporary fillings in endodontic treatment measures

Microorganisms and their products play a fundamental role in the pathogenesis of the pulp and periapical infections. Consequently, one of the main goals of endodontic treatment is to eliminate microorganisms and their products to the best possible extent. This is achieved by mechanical preparation and subsequent disinfection. If a disinfectant temporary filling is required between two treatments, calcium hydroxide is the material of choice [2,3].

The antimicrobial effect of calcium hydroxide is produced by the release of OH^- ions and the subsequent increase in the pH of the surrounding dentin fluid. The pH value plays an important part in the growth, metabolism and cell division of microorganisms. The main area of activity of the pH is the bacterial cell membrane, which is essential for the energy supply of bacteria. A change in the concentration of OH^- ions disturbs the pH gradient at the cell membrane and disrupts the energy supply of the bacteria, causing cells to die. Furthermore, a high pH causes denaturation of cell membrane proteins and extra-cellular toxins. *In vivo* investigations have shown that the pH value of dentin or the dentin fluid considerably increases after the placement of a calcium hydroxide temporary filling. In these studies, the pH of dentin close to the pulp chamber increased from 8.0 to 11.1. In peripheral areas of the dentin the pH value reached 7.4 to 9.6, while the pH of the root cement remained unaffected [4].

Various *in vitro* examinations have shown that calcium hydroxide exhibited a strong bactericidal effect against bacteria that exist in infected root canals. *In vivo* investigations have clearly shown that the application of calcium hydroxide preparations has a positive effect on the reduction of the existing bacteria [5]. In a study conducted by de Souza et al [6], samples were examined for 44 different strains of bacteria before and after the application of calcium hydroxide in a checkerboard analysis. A reduction in the bacteria counts of 41 of the 44 tested strains was observed. However, calcium hydroxide was not capable of completely eliminating the bacteria.

1.3 Clinical indication – pulp capping

Direct pulp capping is indicated when a small part of a clinically healthy pulp (< 1mm^2) is accidentally exposed in non-carious dentin during cavity preparation [2,3].

The application of a highly alkaline calcium hydroxide preparation on the exposed pulp rapidly causes superficial tissue necrosis to a depth of about 2 mm. In addition, the lactic acid produced by osteoclasts is neutralized and alkaline phosphatase, which is involved in the development of hard tissue is induced [3].

The necrotic zone is strictly delimited and superficial, because the bicarbonate buffer of the blood forms a membrane of calcite, which surrounds the calcium hydroxide and protects the pulp tissue from further diffusion of the hydroxide ions. The necrotic pulp tissue which comes in contact with the calcium hydroxide paste shows three layers after about 24 hours: a thin superficial zone of cauterized and compressed tissue, a thicker zone of colliquative necrosis and a zone of varying thickness of coagulation necrosis. Vasomotor dysfunction occurs and changes take place in the blood flow in the underlying pulp tissue. However, these effects are reversible. At a later stage, two additional zones are formed at the pulp periphery: a zone of agranulocytes and a layer of compressed fibrillary elements. This necrotic zone induces the differentiation of fibroblasts towards the pulp and undifferentiated mesenchyme cells to form hard tissue cells. These cells form a collagen fibre network. At the same time, mineralization takes place at the necrotic zone of the pulp periphery. This initial mineralization front influences the subsequent mineralization of collagen, while the necrotic zone disintegrates [2,7].

Originally it was assumed that calcium hydroxide from the calcium hydroxide preparation was involved in the formation of hard tissue. However, experiments with radioactive Ca^{2+} ions have shown that the calcium ions originate exclusively from the pulp tissue [8-10].

2. Technical data

2.1 Composition

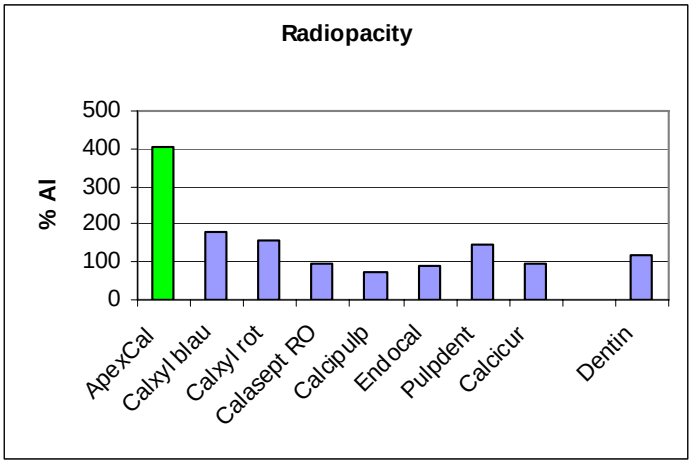
	weight percent
Calcium hydroxide	29.0
Bismuth carbonate	22.0
Excipients (polyethylene glycol, glycerine, water)	49.0

2.2 pH value

The pH value of the paste at room temperature is above 12.4 and therefore corresponds to the theoretical value of a saturated $Ca(OH)_2$ solution (pH = 12.46).

2.3 Radiopacity

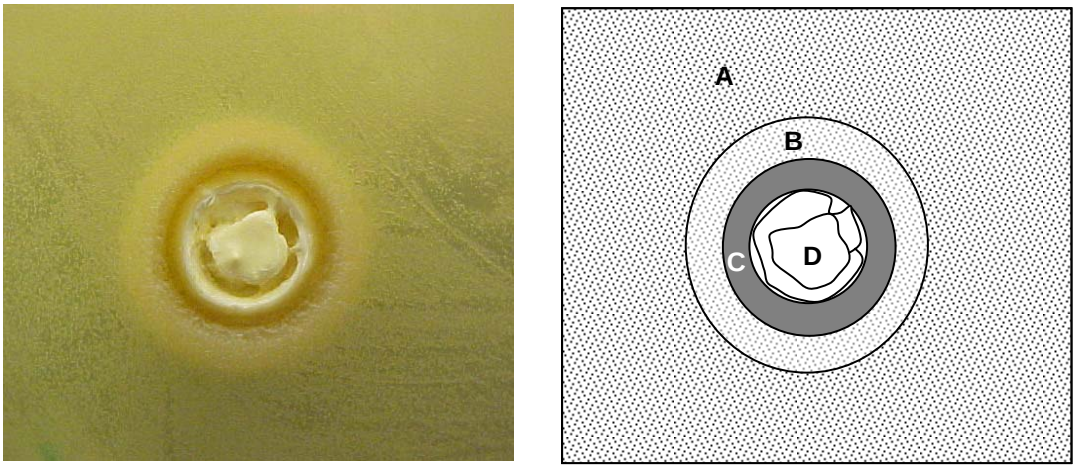
The radiopacity of ApexCal complies with ISO 6876 [Ivoclar Vivadent, R&D] and is about four times higher than that of dentin [11].



3. *In vitro* and clinical investigations

3.1 In vitro investigations on the antimicrobial effect

The antimicrobial effect of ApexCal was examined in comparison to that of Calxyl, Calcipulp and calcium hydroxide using agar diffusion tests. This investigation did not establish any difference in the materials tested. As expected, the antimicrobial effect was limited to a narrow area of approx 0.5 to 1 mm in the immediate vicinity of the samples.



Agar diffusion test of ApexCal: An inhibition zone (C) is visible adjacent to the ApexCal sample (D). The whitish aureole (B) is an artefact caused by the diffusion of the material along the Petri dish. A: Bacteria lawn (*Lactobacillus*) [13].

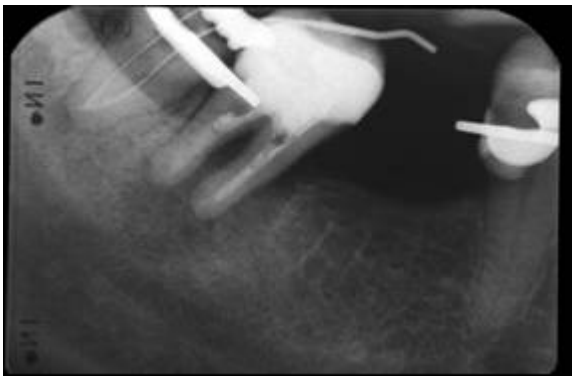
	Inhibition zone [mm]				
	ApexCal	Calxyl	Calcipulp	$Ca(OH)_2$	Ref
Staphylococcus aureus	0.5 – 1	0.5 – 1	n.d.	0.5 – 1	12
Escherichia coli	0.5 – 1	0.5 – 1	n.d.	0.5 – 1	12
Enterococcus faecalis	0.5 – 1	0.5 – 1	n.d.	0.5 – 1	12
Lactobacillus acidophillus	0.5 – 1	n.d.	0.5 – 1	0.5 – 1	13
Streptoccocus gordonii	0.5 – 1	n.d.	0.5 – 1	0.5 – 1	13

3.2 Clinical investigations

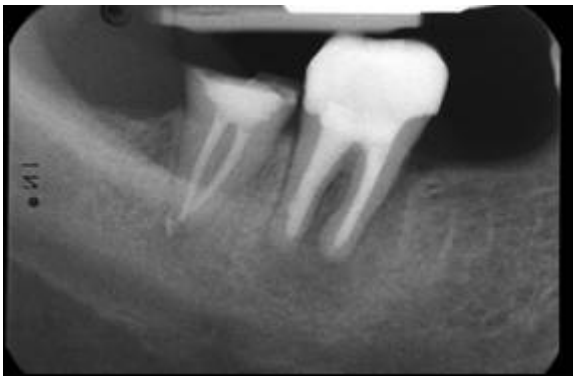
The effectiveness and safety of ApexCal as a temporary endodontic filling was examined in a clinical study (Dr A Peschke, Ivoclar Vivadent, R&D Clinic). In this investigation 20 teeth with periapical lesions were treated. The teeth were instrumented with rotating NiTi-instruments (ProFile, Maillefer), cleaned with NaOCl, medicated with ApexCal and obtruated using the lateral condensation technique.

The periapical index (PAI) [14] was established (4.3± 0.8) before the treatment began. After the dressing had been *in situ* for an average period of 1.8 month, an improvement of the periapical situation was observed radiographically in 90 % of the cases. At the time when the root canal filling was placed the PAI score had improved to 3.9 ± 0.9. In all the cases, the canals were dry and odour-free after the placement of ApexCal.

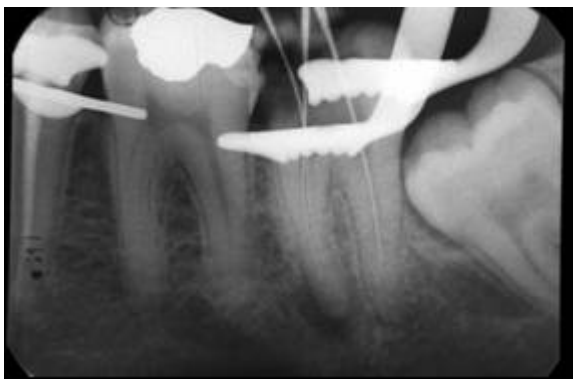
Compared to other commercially available preparations, ApexCal showed a very homogenous and constant consistency over time. Because of its excellent stability, ApexCal is easy to pick up with lentulo spirals, yet easy to spin into the canals.



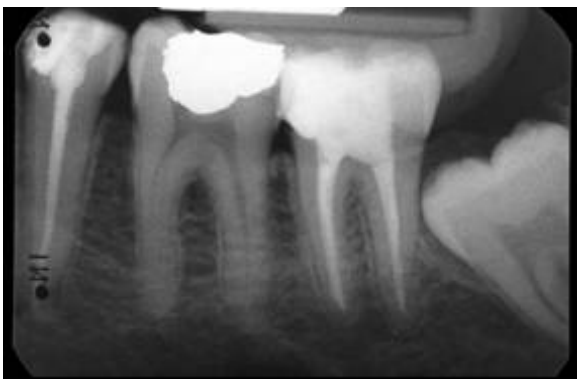
Radiography of tooth 48. Tooth 47 is already instrumented and filled with ApexCal as disinfecting dressing. Both teeth are revisions of insufficient root canal fillings with prominent apical periodontitis.



Radiography of teeth 47 and 48 after obtruating with the definitive root canal filling: After 2 month with ApexCal in situ, a significant decrease in apical translucency was observed.



Tooth 37 at the beginning of the endodontic treatment: A marked apical translucency could be observed.



Situation of tooth 37 directly after placing the definite root canal filling. A complete apical healing could be achieved by placing ApexCal for several month.

4. Biocompatibility

4.1 Exposition

ApexCal contains calcium hydroxide and bismuth carbonate in a mixture of water, glycerine, polyethylene glycol and auxiliary materials. In general, the material is completely surrounded by tooth structure. If it is used as directed, it will not come in contact with soft tissue or bodily fluids. Contact with periapical tissue may occur in the event of accidental overfilling. Accidental contact with the oral mucous membrane or non-oral tissue may occur during the treatment. However, the material can be removed very easily by the dentists if superficial contamination should occur.

4.2 Toxicological data

4.2.1 Acute toxicity and cytotoxicity

If administered orally [ORL-RAT], all the primary substances exhibit LD50 > 5,000 mg/kg [15]. The cytotoxicity of ApexCal has been evaluated in an XTT test [16]. No indication of cytotoxicity was recorded in this test. Examinations of comparable calcium hydroxide preparations for pulp capping applications showed a very high biocompatibility [17-19].

4.2.2 Genotoxicity

The available data on the primary materials do not give an indication of any genotoxic effect [15,20]. The genotoxic potential of ApexCal has been examined *in vitro* in an AMES test. This test did not reveal any genotoxic potential of the material [21].

4.2.3 Irritation

ApexCal has a pH of > 12.4 % and therefore causes irritation. The product must have this high pH value if it is to fulfill its designated purpose.

4.2.4 Sensitization

The available data on the primary materials do not show any indication of a sensitizing effect [15].

4.3 Conclusion

The information available to date indicates that ApexCal does not represent a heightened toxicological risk for the patient or user if it is used as directed.

5. References

1 Fava LR, Saunders WP: Calcium hydroxide pastes: classification and clinical indications. Int Endod J. 1999 Aug;32(4):257-82.

2 Kockapan C: Curriculum Endodontie. Quintessenz Verlags-GmbH, Berlin 2003

3 Carrotte P: Endodontics: Part 9. Calcium hydroxide, root resorption, endo-perio lesions. Br Dent J. 2004 Dec 25;197(12):735-43.

4 Tronstad L, Andreasen JO, Hasselgren G, Kristerson L, Riis I: pH changes in dental tissues after root canal filling with calcium hydroxide. J Endod. 1980 Jan;7(1):17-21.

5 Sjogren U, Figdor D, Spangberg L, Sundqvist G: The antimicrobial effect of calcium hydroxide as a short-term intracanal dressing. Int Endod J. 1991 May;24(3):119-25.

6 de Souza CA, Teles RP, Souto R, Chaves MA, Colombo AP. Endodontic therapy associated with calcium hydroxide as an intracanal dressing: microbiologic evaluation by the checkerboard DNA-DNA hybridization technique. J Endod. 2005 Feb;31(2):79-83.

7 Cohen S, Burns R: Pathways of the pulp. 3rd. edition. C.V. Mosby Company, St. Louis Missouri 1984

8 Attala MN, Noujaim AA: Role of calcium hydroxide in the formation of reparative dentin. J Can Dent Assoc 1969 35:267

9 Pisanti S, Sciaky I: Origin of calcium in the repair wall after pulp exposure in dog. J Dent Res. 1964 43:641

10 Sciaky I, Pisanti S: Localization of calcium placed on amputated pulp in dog's teeth. J Dent Res 1960 39:1128

11 Hein CM, Noack MJ, Roulet JF: Die Röntgenopazität von Kompositmaterialien und Zahnhartsubstanzen. DZZ 1989, 44:536-539

12 BioChem: Prüfung der antimikrobiellen Wirksamkeit einer Paste aus Canciumhydroxid. 2002, Study report

13 Ivoclar Vivadent AG, Department of Biotechnology. 2003, Test report

14 Orstavik D, Kerekes K, Eriksen HM: The periapical index: a scoring system for radiographic assessment of apical periodontitis. Endod Dent Traumatol. 1986 Feb;2(1):20-34.

15 RTECS Datenbank

16 RCC: Cytotoxicity assay in vitro: Evaluation of materials for medical devices (XTT-test). 2004, Study report.

17 Cavalcanti BN, Rode SM, Marques MM: Cytotoxicity of substances leached or dissolved from pulp capping materials. Int Endod J. 2005 Aug;38(8):505-9.

18 Murray PE, Kitasako Y, Tagami J, Windsor LJ, Smith AJ: Hierarchy of variables correlated to odontoblast-like cell numbers following pulp capping.J Dent. 2002 Sep-Nov;30(7-8):297-304.

19 Medina VO 3rd, Shinkai K, Shirono M, Tanaka N, Katoh Y: Histopathologic study on pulp response to single-bottle and self-etching adhesive systems. Oper Dent. 2002 Jul-Aug;27(4):330-42.

20 IARC Monographs Database on Carcinogenic Risks to Humans, The International Agency for Research on Cancer (IARC)

21 RCC: Salmonella typhimurium reverse mutation assay. 2004, Study report

Ivoclar Vivadent AG
Research and Development
Scientific Service
Bendererstrasse 2
FL - 9494 Schaan
Liechtenstein

Content: Dr. Sandro Sbicego
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