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RESEARCH ARTICLE

ROLE OF CALCIUM HYDROXIDE IN ENDODONTICS

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ABSTRACT

Calcium Hydroxide is a material which has been used for a variety of purposes since its introduction in dentistry in the early part of the twentieth century. In its pure form, the material has high pH and its dental use is based chiefly on its ability to stimulate mineralization and its antibacterial properties. A range of products have been formulated with different therapeutic actions, the effects of which are partially dependent upon the tissue to which they are applied. The material is reviewed under the following headings:- history, it is physio-chemical properties, mechanism of action, role and uses in endodontics, combination with other agents, methods of placement and removal in root canals and biocompatibility.

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INTRODUCTION

Calcium hydroxide has been used by dentists in the clinical practice for over a century. It is a white odourless powder with the chemical formula $Ca(OH)_2$ and a molecular weight of 74.08. Chemically, it is classified as a strong base in contact with aqueous fluids (its pH is about 12.5 - 12.8).[1] It has low solubility in water (about 1.2 g Lÿ1 at 258C), which decreases as the temperature rises. It has a high pH (about 12.5±12.8) and is insoluble in alcohol. This low solubility is, in turn, a good clinical characteristic because a long period is necessary before it becomes soluble in tissue fluids when in direct contact with vital tissues.[2] In water, $Ca(OH)_2$ has a thyrotrophic behavior, which means it will be very fluid when agitated. When $Ca(0H)_2$ is exposed to carbon dioxide (CO_2) or carbonate ions (COO^-) in biologic tissue, the dissociation of the chemical leads to formation of calcium carbonate ($CaCO_3$) and an overall consumption of Ca^{2+} ions.[3] Calcium hydroxide was introduced in endodontic therapy by Hermann in 1920 as an antibacterial dressing. It was initially used in vital pulp therapy, but it has also been used successfully as a dressing in the treatment of infected teeth.[4] Calcium hydroxide has various applications in endodontics such as antimicrobial agent, intracanal medicament, as pulp capping agent, for apexification, to prevent or resolve external resorption after trauma of tooth, etc. Calcium hydroxide has also been developed as root canal sealers (sealapex, calciobiotic). It also has synergistic effect like anti- endotoxin activity and antifungal activity when used in combination with sodium hypochloride and chlorhexidine.[6] As the delivery of dry $Ca(OH)_2$ powder is difficult, therefore, it should be combined with liquid vehicles. Moreover, the fluid is required for the release of hydroxyl ions.[7] The three main types of vehicles used are water based, viscous vehicle, and oil-based. Examples of water soluble substances are, saline, anesthetic solution, carboxy methylcellulose, methylcellulose and ringer solution.

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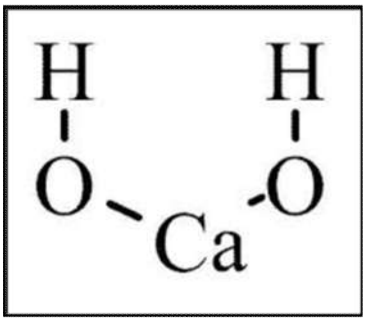

Viscous vehicles used are such as glycerine, polyethylene-glycol and Oil based vehicles such as olive oil, silicone oil camphor, some fatty acids (including oleic, linoleic and isostearic acids) eugenol and metacresylacetate are also used. Dissociation rate of $Ca(OH)_2$ depends upon the vehicle used, faster with the water based and slow with oil based.[8] Depending on its application, the mode of action of $Ca(OH)_2$ may vary. The antimicrobial activity of $Ca(OH)_2$ is related to the release of hydroxyl ions in an aqueous environment. Hydroxyl ions are highly oxidant free radicals that show extreme reactivity with several biomolecules.[9] This reactivity is high and indiscriminate, so this free radical rarely diffuses away from sites of generation. Thus, the lethal effects of hydroxyl ions on bacterial cells are probably due to the mechanism such as damage to the bacterial cytoplasmic membrane, protein denaturation and damage to the DNA.[10]

When $Ca(OH)_2$ is used for direct pulp-capping, it is in direct contact with connective tissues and gives rise to a zone of necrosis because of high pH thus altering the physicochemical state of inter-cellular substance which, through rupture of glycoproteins determines protein denaturation. Thus, formation of mineralized tissue following contact between $Ca(OH)_2$ and connective tissue has been observed from the 7^{th} to the 10^{th} day following application.[11] Calcium hydroxide when used for apexification or perforation repair it induces formation of calcified barrier due to its property of mineralization. The elevated pH of calcium hydroxide activates alkaline phosphatase, the best pH for the activation of this enzyme.[12]

Alkaline phosphatase is a hydrolytic enzyme that acts by means of the liberation of inorganic phosphate from the esters of phosphate. It is believed to be intimately related to the process of mineralization.[13] This enzyme can separate the phosphoric esters, freeing phosphate ions which, once free, react with calcium ions from the blood stream to form a precipitate, calcium phosphate, in the organic matrix. This precipitate is the molecular unit of hydroxyapatite.[13] Thus, what makes calcium hydroxide so special in dentistry is probably that, it is one of those few materials which have both an antibacterial property and an august property of inducing a hard tissue barrier, an elixir of life for the dying teeth. Calcium hydroxide has an upper hand over the rest of the materials as it is easy to manipulate and has low cost as compared to that of the currently available materials.[14] The purpose of this review article is to critically analyze all the data related to calcium hydroxide in endodontics in the light of present research and to present it in a scientific manner.

History: Since the introduction to dentistry of calcium hydroxide by Hermann (1920, 1930), this medicament has been indicated to promote healing in many clinical situations. However, the initial reference to its use has been attributed to Nygren (1838) for the treatment of the `fistula dentalis', whilst Codman (1851) was the first to attempt to preserve the involved dental pulp.[15] According to Cvek (1989) calcium hydroxide became more widely known in the 1930s through the pioneering work of Hermann (1936) and the introduction of this material in the Unite d States.[16]

Physio-Chemical Properties: Limestone is a natural rock mainly composed of calcium carbonate ($CaCO_3$) which forms when the calcium carbonate solution existing in mountain and sea water becomes crystallized.[17]
The combustion of limestone between 900 and 1200^0C causes the following chemical reaction:

$$CaCO_3 \rightarrow CaO + CO_2$$

The calcium oxide (CaO) formed is called `quicklime' and has a strong corrosive ability. When calcium oxide contacts water, the following reaction occurs:

$$CaO + H_2O \rightarrow Ca(OH)_2$$

So to define Calcium hydroxide, it is a strong alkali with the pH of 12.5 - 12.8, which can be formed by the reaction of calcium oxide with water and the process is known as slaking. Synonyms of calcium hydroxide are calcium hydrate, caustic lime, hydrated lime and slake lime. It is a white odorless powder with the formula $Ca(OH)_2$, and a molecular weight of 74.08, the percentage of hydroxyl ions in calcium hydroxide is 45.98% while that of calcium ion is 54.11%.[18]

Mechanism Of Action

Anti-Microbial Action Of Calcium Hydroxide

Antibacterial activity: Antimicrobial provoke two types of effects on bacteria. They either inhibit growth or reproduction or they lead to its death. These actions are exercised essentially by interfering in the synthesis of the cell wall, altering the permeability of the cytoplasmic membrane and interfering in protein synthesis.[19] $Ca(OH)_2$ exert their mechanism of action in the cytoplasmic membrane because that is where enzymatic systems of bacteria are located and they involve themselves in the last stage of the formation of cellular wall. Cellular wall acts as an osmotic barrier to ionized substances and are freely permeable to sodium ions and amino acids (selective permeability). Cellular wall also participates in the biosynthesis of lipids and are responsible for the conveyance of electron, formed by double phospholipoproteic layer.[20] The enzymatic systems of the cytoplasmic membrane take on primordial functions for the bacteria, such as metabolism and cellular growth and division.[21]

Anti-fungal activity: Fungi constitute a small proportion of the oral microbiota and are largely restricted to *Candida albicans*. The incidence of C. albicans in the oral cavity has been reported to be 30- 45% in healthy adults and 95% in patients infected with human immunodeficiency virus.[22] It seems that the combinations of $Ca(OH)_2$ with camphorated paramonochloro-phenol or CHX have the potential to be used as effective intracanal medicaments for cases in which fungal infection is suspected.

Anti-Endotoxin Activity: Endotoxin, a component of the cell wall of Gram-negative bacteria, plays a fundamental role in the genesis and maintenance of periapical lesions because of the induction of inflammation and bone resorption. $Ca(OH)_2$ inactivates endotoxin in vitro and in vivo and appears currently the only clinically effective medicament for inactivation of endotoxin.[23] In a laboratory study, Safavi and Nichols evaluated the effect of $Ca(OH)_2$ on bacterial LPS and concluded that it hydrolysed the highly toxic lipid A molecule that is responsible for the damaging effects of endotoxin.[24]

Anti-inflammatory action of calcium hydroxide: Endogenous inflammatory mediators like interleukin-1α and tumour necrosis factor-α play a decisive role in regulation of inflammation and the consequential tissue destruction. A recent in vitro study concluded that $Ca(OH)_2$ causes denaturation of such pro-inflammatory cytokines. The resultant significant reduction in their levels may be a potential mechanism by which $Ca(OH)_2$ exerts its immunomodulatory effect.[25]

Tissue Necrosis By Calcium Hydroxide: When $Ca(OH)_2$ is placed against pulp, the high pH of the material causes irritation and produces a superficial burn at the area of exposure. This zone of coagulation necrosis has been suggested to be vital for formation of tertiary dentine.[26]

Calcium Hydroxide Induced Osseous Mineralization: Heithersay (1975) suggested that calcium ions may reduce the permeability of new capillaries, so that less intercellular serum is produced thus, increasing the concentration of calcium ions at the mineralization site. The presence of a high calcium concentration may also increase the activity of calcium dependent pyrophosphatase which represents an important part of the mineralization process. Once mineralization has been initiated, it can continue unabated if the normal self limiting enzymes (pyrophosphates) fail to operate.[27] The reduced capillary permeability following the increase in the number of calcium ions could reduce serum flow within the dental pulp and consequently the concentration of the inhibitory pyrophosphate ion would be reduced. This would coincide with an increase in levels of calcium-dependent pyrophosphatase as promulgated by Heithersay (1975), and would result in uncontrolled mineralization of the pulp tissue.[28]

Dentinogenesis By Calcium Hydroxide: $Ca(OH)_2$ was initially introduced primarily for dentinogenic activity, the seal was expected to be provided by overlying restoration. Bacterial contamination occurred which lead to imperfections in dentine bridges, the so-called tunnel defects, which may provide passage for bacteria from the exposure site of pulp. In the case of a high pH material such as pulpdent a necrotic zone is formed adjacent to the material, and the dentine bridge then forms between this layer and the underlying vital pulp. The necrotic tissue eventually degenerates and disappears, leaving a void between the capping material and the bridge.[29]

In the case of a material of lower pH, such as Dycal, the necrotic zone is similarly formed but is resorbed prior to the formation of the dentine bridge, which then comes to be formed directly against the capping material. Dentine bridges formed by the high pH materials are histologically identical to those produced by lower pH materials, but are easier to distinguish on a radiograph because of the space between the bridge and the calcium hydroxide.[30]

Uses Of Calcium Hydroxide: Calcium hydroxide has various uses in endodontics such as antimicrobial agent, intracanal medicament, as pulp capping agents for apexification, to prevent or resolve external resorption after trauma of tooth etc. Calcium hydroxide has also been developed as root canal sealers (sealapex, calciobiotic). It also has synergistic effect like anti- endotoxin activity and antifungal activity when used in combination with sodium hypochloride and chlorhexidine.

Pulp-Capping Agent: Calcium hydroxide is generally accepted as the material of choice for pulp capping. Histologically there is a complete dentinal bridging with healthy radicular pulp under calcium hydroxide dressings. When calcium hydroxide is applied directly to pulp tissue there is necrosis of adjacent pulp tissue and an inflammation of contiguous tissue. Dentinal bridge formation occurs at the junction of necrotic tissue and vital inflamed tissue. Beneath the region of necrosis, cells of underlying pulp tissue differentiate into odontoblasts and elaborate dentin matrix.[31] Three main calcium hydroxide products are: Pulpadent, Dycal, Hydrex (MPC). Pulpadent paste is considered to be most capable of stimulating early bridge formation. Hydrex has also been considered as fast and capable of forming a bridge. Commercially available compounds of calcium hydroxide in a modified form are known to be less alkaline and thus, less caustic on the pulp. The action of calcium hydroxide to form a dentin bridge appears to be a result of the low grade irritation in the underlying pulp tissue after application.[32]

Calcium Hydroxide As An Intracanal Medicament: Calcium hydroxide cannot be categorized as a conventional antiseptic, but it kills bacteria in root canal space. It is a slowly working antiseptic. Direct contact experiments in vitro require a 24 hour contact period for complete kill of *enterococci*. Calcium hydroxide not only kills bacteria, but it also reduces the effect of the remaining cell wall material lipo-polysaccharide.[33]

Calcium Hydroxide As An Endodontic Sealer: To be therapeutically effective calcium hydroxide must be dissociated into Ca^{2+} and OH^-. Therefore to be effective, an endodontic sealer based on calcium hydroxide must dissolve and the solid consequently lose content. Thus one major concern is that the calcium hydroxide content dissolve, leaving obturation voids. This would ruin the function of the sealer, because it would disintegrate in the tissue. Recently introduced several calcium hydroxide sealers are sealapex and apexkit. Calcium hydroxide-based root canal sealers have a variety of physical and biological properties.[34]

Calcium Hydroxide In Apexification: $Ca(OH)_2$ is used as a temporary canal filling material and has a bactericidal effect. Although apexification had been attempted in the past, the technique was given impetus by the description of three cases by Frank in 1966 who cleaned and irrigated canals and then sealed them with a paste of camphorated chlorophenol and $Ca(OH)_2$.[35]

Calcium Hydroxide In Horizontal Root Fractures: The use of $Ca(OH)_2$ in teeth with horizontal root fractures was first recommended by Cvek (1974). He proposed that the canal at the level of the fracture line was comparable to the apical formation of an immature tooth. Thus, he assumed that the repair would be similar to the apexification procedure employed for a tooth with an open apex (Cvek 1974). The benefits of root canal treatment with $Ca(OH)_2$ occur probably because of its antibacterial effect and its ability to promote the formation of a hard-tissue barrier at the apical opening of the coronal fragment. There by facilitating filling with Guttapercha.[36]

Calcium Hydroxide Used In Perforations: Root or furcation perforations can cause failure of root canal treatment, leading to tooth loss. $Ca(OH)_2$ has many benefits in this treatment modality including, easy manipulation, rapid resorption when extruded into the periodontium, promotion of the reorganization of periodontal tissues and induction of mineralized material.[37]

Calcium Hydroxide In Root Resorption: Calcium hydroxide has an active influence on the local environment around a resorptive area by reducing osteoclastic activity and stimulating repair.[38] This is directly related to the alkaline pH of $Ca(OH)_2$ which permeates through the dentine. Hard-tissue resorption with its enzymatic activity, takes place in an acidic pH $Ca(OH)_2$creates an alkaline environment in which the reaction is reversed and hard-tissue deposition can take place. The phenomenon of pH change towards the periphery is increased, especially where resorption has exposed dentine.[38]

Combination Of Calcium Hydroxide With Other Agents

Synergism between $Ca(OH)_2$ and sodium hypochlorite – Wadachi *et al*. in 1998 evaluated the tissue-dissolving ability of NaOCl and $Ca(OH)_2$ in a bovine tooth model and reported that the amount of debris was reduced remarkably in teeth treated with NaOCl for >30 s or $Ca(OH)_2$ for 7 days. However, the combination of $Ca(OH)_2$ and NaOCl was more effective than the separate treatments. In summary, the pretreatment of root canals with $Ca(OH_{)2}$ enhances the tissue-dissolving capability of sodium hypochlorite and this may confer an advantage to multiple-visit root canal treatment where NaOCI would be used following a period of $Ca(OH)_2$ medication.[39]

$Ca(OH)_2$ and Chlorhexidine: Chlorhexidine is a cationic biguanide whose optimal antimicrobial activity is achieved within a pH range of 5.5-7.0. Therefore, it is likely that alkalinizing the pH by adding $Ca(OH)_2$ to CHX will lead to precipitation of CHX molecules, thereby decreasing its effectiveness.[39] It has been demonstrated that the alkalinity of $Ca(OH)_2$ when mixed with CHX remained unchanged.[58] Therefore, the usefulness of mixing $Ca(OH)_2$ with CHX still remains unclear and controversial. When used as an intracanal medicament. CHX was more effective than $Ca(OH)_2$ in eliminating E. faecalis from inside dentinal tubules.[40] In summary, although the usefulness of mixing $Ca(0H)_2$ with CHX remains unclear and controversial, it seems that by mixing $Ca(OH)_2$ with CHX the antimicrobial activity of $Ca(OH)_2$, is increased. In other words, the descending order of the antimicrobial activity of $Ca(OH)_{2,}$ CHX and their combination is as follows: CHX, Ca(OH),/CHX and $Ca(OH)_2$.[41]

Calcium hydroxide used with Corticosteroids: A very popular formulation is a paste composed of a mixture of calcium hydroxide and Ledermix. This anti-inflammatory and antibiotic compound has triamcinolone acetonide and demethylchlorotetracycline calcium and was chemically evaluated for its ionic diffusion by Abbott *et al*. (1989) and clinically evaluated in direct pulp capping, pulpotomy, routine intracanal dressing and apexification procedures[114] and in the treatment of large periapical lesions.

Calcium hydroxide used with Antibiotics: The use of calcium hydroxide and antibiotic pastes has been suggested and these have been tested in laboratory studies, but still the research is going on.[42]

Setting Reactions Of Calcium Hydroxide Containing Materials

There are two basic setting mechanisms: The two-paste system, which is based on the reaction between calcium and zinc ions and a salicylate chelating agent, and is accelerated by the presence of water.[43]

- The single-paste system, which utilizes the polymerization of a dimethacrylate by means of light, and is represented by Prisma VLC Dycal. A potential disadvantage of the dimethacrylates stems, when used as a base beneath composite restorations, is their adherence to the composite material and subsequent withdrawal from the base of the cavity during polymerization.[44]

Methods Of Placement Of Calcium Hydroxide And Effects Of Vehicles: Powder form of calcium hydroxide is mixed with suitable vehicles and can be placed in the canal with the help of lentil spiral, hand pluggers, finger pluggers ultrasonic tips, paper points coated with calcium hydroxide. Calcium hydroxide based sealers can be placed by coating the master cone and placing the sealer in the canal, placing the sealer in the canal with lentulospiral. Sealer can also be placed by using the final file used at the correct working length and turning the file counter clockwise. Injecting the sealer with special syringes.

Effect of vehicles- Vehicles mixed with $Ca(OH)_2$ powder play an important role in the overall dissociation process because they determine the velocity of ionic dissociation causing the paste to be solubilized and resorbed at various rates by the periapical tissues and from within the root canal.

There are three main types of vehicles:

- Water-soluble substances such as water, saline. anaesthetic solutions. Carboxymethyl cellulose, methylcellulose and Ringers solution.
- Viscous vehicles such as glycerine, polyethylene glycol (PlC) and propylene glycol.
- Oil-based vehicles such as olive oil, silicone oil, camphor (the oil of camphorated parachloro-phenol), some fatty acids (including oleic, linoleic, and isostearic acids), eugenol and metacresylacetate.[45]

In summary, the vehicle to which calcium hydroxide is added affects the physical and chemical properties of the compound and therefore its clinical applications. Compared with water-soluble agents, viscous and oily vehicles prolong the action of the calcium hydroxide but can have associated negative side effects.

Removal Of Calcium Hydroxide From Canals: It seems that complete removal of $Ca(OH)_2$ paste from the root canal walls is not achievable using routine techniques. However, the type of vehicle used, use of patency filing and combining EDTA and NaOCl with hand instrumentation improves the efficacy of $Ca(OH)_2$ paste removal. Furthermore, it seems that ultrasonic methods are more efficient in removing $Ca(OH)_2$ remnants than passive irrigants.

Biocompatibility: Briseno and Willershausen in 1992 assessed the cytotoxicity of four different calcium hydroxide-based root canal sealers (Sealapex), Apexit (Ivoclar Vivadent), CRCS (Coltene Whaledent, Altstatten, switzerland) and Endoflas FS (Sanlor, Miami, FL, USA) on human gingival fibroblast (HGF) and concluded that the biocompatibility of calcium hydroxide based sealers were within an acceptable range compared to other root canal sealers.[46] Early reports on the outcome of $Ca(OH)_2$ extruded into the periapical region concluded it was well tolerated and was resorbed . However, the periapical response to $Ca(OH)_2$ based on results from other reports seems to be equivocal.[47] In summary, it seems that $Ca(OH)_2$is well tolerated by bone and dental pulp tissues. However, its effect on the periodontal tissue is controversial.

Conclusion

Initially calcium hydroxide was introduced as a pulp capping material by Herman in 1920 but, now it has various application in endodontics and pedodontics such as antimicrobial, antifungal, as an intracanal medicament for apexification, to prevent or resolve external root resorption after trauma of tooth etc. Calcium hydroxide is classified as a strong base with a high pH (approximately 12.5–12.8). Its main properties come from the ionic dissociation of $Ca^{2+}$and OH ions and their effect on vital tissues. At least 7-day application of a $Ca(OH)_2$ medicament is needed to reduce canal bacteria to a level that gives a negative culture. Calcium hydroxide compounds are the agents of choice since they not only are bactericidal but directly stimulate the formation of reparative dentin. $Ca(OH)_2$ has been the material of choice to create a calcified barrier in non-vital open-apex teeth. It has been successfully used to manage perforations, horizontal root fracture and root resorption. Calcium hydroxide inactivates endotoxin and appears currently the only clinically effective medicament for inactivation of endotoxin. Thus even though calcium hydroxide has limited use in the primary teeth, it has innumerable applications in permanent teeth.

$Ca(OH)_2$ when in direct contact with connective tissue gives rise to a zone of necrosis, altering the physicochemical state of inter-cellular substance which, through rupture of glycoproteins, determines protein denaturation. The formation of mineralized tissue following contact between $Ca(OH)_2$ and connective tissue has been observed from the 7^{th} to the 10^{th} day following application. Dissociation rate of $Ca(OH)_2$ depends upon the vehicle used, faster with the water based and slow with oil based. Mainly three main types of vehicles used are water based, viscous vehicle and oil –based. Many newer materials are now available in market, which claim to be superior to calcium hydroxide, but when compared to the prices of newer materials calcium hydroxide is more cost effective. Although some preparations of calcium hydroxide are still expensive but a simple calcium hydroxide powder and sterile water can serve many purposes and works out to be reasonable and affordable to many patients. Last but not the least, one must also consider the ease in manipulation and time factor associated with calcium hydroxide preparation. Hence calcium hydroxide has become one of the most widely accepted material in dentistry.

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