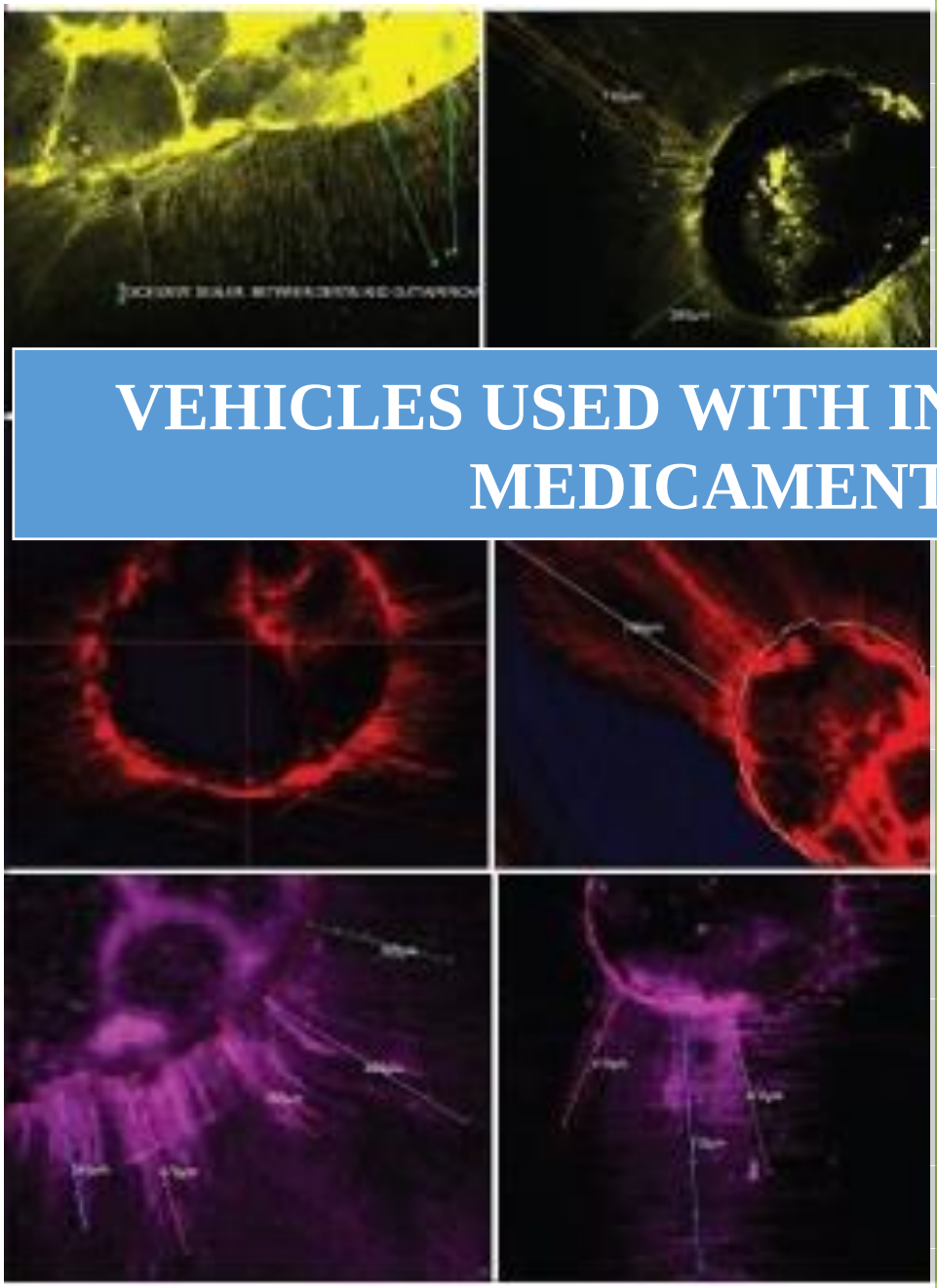

VEHICLES USED WITH INTRACANAL MEDICAMENTS

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Preface

Today's world is full of modern research and rapid advances in dentistry which helps students with a wealth of ever increasing literature. No attempt has been made yet to make a comprehensive text on the subject of transferring the intracanal medicament to the site of infection during Root Canal Treatment. The vehicles used in association with the drugs are important factors to be considered.

Readers will be benefitted while using intracanal medicaments with vehicles mentioned in this monograph. We are thankful to those who have contributed to bring out this monograph with the hope that this venture proves useful to those for whom it is meant.

Sincerely,

Dr. Pradnya Nikhade,
Dean's academics and Professor,
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Publication Partner:
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Table of Content

1 - INTRODUCTION

In simple words, Root canal treatment or endodontic therapy is the treatment in which the pulp inside the tooth is removed, the root canals are cleaned, disinfected and shaped and then filled with an inert and biocompatible material to seal the space**.** This treatment is carried out in cases with pulpal or periapical pathosis, Pulpal inflammation due to traumatic injury or facilitation of restoration (Intentional Endodontic Treatment).

The success of endodontic therapy is dependent on instrumentation, thorough cleaning and shaping of the root canal for elimination of microbial flora from the root canal.[1][i]The Micro-organisms predominantly seen in infected root canals are Eubacterium, Peptococcus, Peptostreptococcus, Prevotella, Porphyromonas and Fusobacterium etc.[2][ii] Amongst these, Enterococcus faecalis, is mainly isolated from failed root canal cases .[3] [iii] This microorganism is a gram-positive facultative anaerobe can deeply invade dentinal tubules , lateral and accessory root canals, isthmi, and apical deltas. It is known to sustain in starvation and extreme pH. [4[iv]] Systemic antibiotics fail to reach the site of infection and eliminate such micro-organisms. Hence, local drug delivery is more advantageous in such cases. [5][v] For the local drug delivery, intra-canal medicament is used which when added with the property of sustained release can aid in better diffusion in the tubules. [6][vi]

An **intra-canal medicament** is a drug, traditionally used in endodontics to disinfect root canals between appointments. [7][vii] These medicaments are nontoxic, non-irritant, stable for different period of time and bactericidal in a limited area. For the Medicament to work, it must be placed deeply and densely into the canal spaces. Some vehicles are used to dispense the intra-canal medicaments. These directly influence the release, action , dissociation of drugs and penetration into dentinal tubules. Propagation of the intra-canal medicament into the canal and its subsequent diffusion into the dentinal tubules and other inaccessible areas depends on the surface tension of the paste applied.

Surface tension by definition is a force existing between the surface molecules, which cause a drop of liquid to spread or to concentrate when placed on a surface. It has been shown that capillary penetration is increased with low surface tension. [8] [viii]Hence, it is advisable to use low surface tension vehicles with the intra-canal medicament for proper penetration into the canal.

The history about medicaments for toothache date back to 1045 AD where. Scribonius wrote of using oils and wine. References of use of clove oil, beech wood creosote as medicaments are noted in middle years. [9] [ix]

Calcium hydroxide introduced in 1920 by Hermann is the preferred material for an intracanal dressing because of

1) Antimicrobial activity, due the presence of hydroxyl ions which inactivate bacterial lipopolysaccharide (LSP), a toxin produced by gram-negative bacteria

2) Capacity to limit root resorption, the high PH of 12.5 leads to the alkalinisation of resorption areas on the root surface

3) Promotion of repair of periapical and surrounding tissues. [10,11,12][xxixii]

But Calcium hydroxide is known to have poor handling properties which makes its uniform distribution throughout the canal difficult. So, a viscous vehicle can be used and mixed with the powdered calcium hydroxide to form a paste which may remain within the root canal for the interval of 2–4 months .[13][xiii]

According to some authors these pastes should have the following characteristics:

1) Improve physicochemical properties such as radio-opacity, flow and consistency.
   Iodoform or bismuth carbonate can be added to improve the radio-opacity of the paste [14][xiv]
2) Slowly or rapidly Soluble or resorbed within vital tissues depending on the necessity.
3) Easy to prepare and use.
4) Should be used as a temporary dressing. [15][xv]

In 1952, Yacometti et al stated that a paste of penicillin, calcium hydroxide and distilled water can be used as a pulp capping material. [16][xvi]

The Dissociation of calcium and hydroxyl ions and the availability of hydroxyl ions determines the effectiveness of Calcium hydroxide. [17][xvii]. Different vehicles will permit different degrees of hydroxyl ions to release from calcium hydroxide paste. [18][xviii]

According to Fava (1991), the ideal vehicle should:

1. Allow a gradual and slow Ca2+ and OH- ionic release.
2. Allow slow diffusion in the tissues with low solubility in tissue fluids.

3. Have no adverse effect on the induction of hard tissue deposition.[10]

Chemically, the available vehicles can be classified into 3 categories-

1. **Hydrosoluble vehicles** – Example- Saline solution, Ringer's solution, Distilled water, Dental anaesthetics with or without a vasoconstrictor, aqueous suspension of methylcellulose or carboxymethylcellulose and anionic detergent solution

2. **Viscous vehicles**- Example- Polyethylene glycol, Glycerine, Propylene Glycol.

3. **Oily vehicles**- Camphorated parachlorophenol, Metacresylacetate, Olive oil, silicone oil, oleic acid, linoleic acid and isostearic acid. [10]

The effectiveness of vehicles depends on chemical properties like dissociation and diffusion. [19] [xix]An aqueous vehicle induces ionic dissociation at a higher speed than viscous vehicles. These vehicles have higher solubility rate, causing it to be rapidly resorbed by macrophages. Hence, in such cases the canal must be redressed several times until the desired effect is achieved. [13] Whereas the high molecular weight of viscous vehicles reduces the rate of dispersion and helps in maintaining the paste for longer intervals in the canal, thus reducing the number of appointments. [20] [xx]In clinical situations such as inhibiting inflammatory root resorption, healing of large periapical lesions, this prolonged release of medication proves beneficial. [21][xxi]

The lowest solubility and diffusion of the paste within the tissues is said to be via the Oily Vehicles (Lopes et al. 1996). [22][xxii]

Leonardo et al. (1982) stated that a paste prepared with hydrosoluble non-viscous vehicle lack radio-opacity and has high solubility in the tissues.

Hence, Leonardo et al. (1982) recommended the addition of other substances to the paste:

1) To improve flow and consistency of the material
2) To improve radio-opacity;
3) To make clinical use easier
4) Not to alter the excellent biological properties of the medicament.[15]

The various low surface tension vehicles are-

1) Water
2) Saline
3) Glycerine
4) Chlorhexidine
5) Propylene glycol
6) Camphorated paramonochlorophenol
7) Corticosteroid + Antibiotics
8) Local Anaesthetic solution
9) Detergent (Sodium Lauryl Sulfate)
10) Chitosan
11) Polyethylene glycol
12) Ringer Lactate
13) Others

2-WATER

Sterile water, distilled water, sterile distilled water, bi-distilled water and sterile bi-distilled water are the different types of water used to make intra-canal medicament pastes. [10]

a) Sterile water-

The paste made up of medicament and sterile water has been indicated for-

i. Direct pulp capping (Sommer et al. 1975)[23][xxiii]
ii. Pulpotomy and apexogenesis (Sommer et al. 1975)[23]
iii. Apexification procedures (Erdogan 1997)[24][xxiv]
iv. Apical plug before gutta-percha filling in non-vital teeth with an open apex (Michanowicz & Michanowicz 1967) [25][xxv]
v. Internal resorption with perforation of the dentinal wall (Barclay 1993).[26][xxvi]

b) Distilled water-

Crabb et al. was the first to use the paste in treating periapical lesion in 1965, according to him, "the locally destructive action of calcium hydroxide with its high pH, acting as a chemical cautery, might affect breakdown of the epithelium."[27][xxvii]

Clinically, it has been used for-

i. Induction of hard tissue deposition in apexification procedures (Saad 1981)[28][xxviii]
ii. Pulpotomy of permanent teeth (Acosta & Heredia 1986)[29][xxix]
iii. Temporary dressing after vital pulp extirpation (Leonardo 1973) [30][xxx]
iv. In non-vital teeth with associated chronic periapical disease (Crabb 1965)[27]
v. In internal resorption (Souza Neto et al. 1991)[31][xxxi]
vi. In perforations (Bogaerts 1997)[32][xxxii]
vii. To arrest external cervical resorption after bleaching of pulpless teeth (Santos 1996).[33][xxxiii]

One of the commonest vehicles used in delivering intra-canal medications is distilled water. Distilled water as a vehicle provides an alkaline pH but only for a short duration of time. [34] [xxxiv].Distilled water alone had a surface tension of 70.5 dynes/ cm, which decreased to 66.5 dynes/cm when used as a vehicle for calcium hydroxide powder. The formation of carbonates possibly due to rapid carbonation of calcium hydroxide from the atmospheric carbon dioxide or tissue decomposition may be said to delay resolution of infection. These carbonates do not possess any therapeutic value.[35,36][xxxvxxxvi]

Disadvantages of using distilled water as a vehicle-

1) High degree of solubility when the paste of medicament comes in direct contact with tissue and tissue fluid. This leads to rapid solubilization and resorption by tissue macrophages. The high degree of solubility is due to high viscosity and surface tension.[10]
2) Possesses no antimicrobial activity.[34]

c) Sterile distilled water-

Paste of Sterile distilled water and intra-medicaments was evaluated-

i. Human direct pulp capping by Patterson & Van Huysen in 1954.
ii. Apexification procedures by Wechsler et al. in 1978. [10]

d) Bidistilled water-

Bi-distilled water was first used a carrier by Albou. [37][xxxvii]

It was recommended for-

i. Apexogenesis procedures.
ii. Apexification procedures. [38][xxxviii]

3- SALINE

Normal Saline is a sterile solution used for fluid and electrolyte replenishment.

Saline is prepared by dissolving 9 g of sodium chloride in water to make 1000 mL, according to the United States Pharmacopeia (1989).

It contains no antimicrobial agents. The pH is 5.0 (4.5 to 7.0).

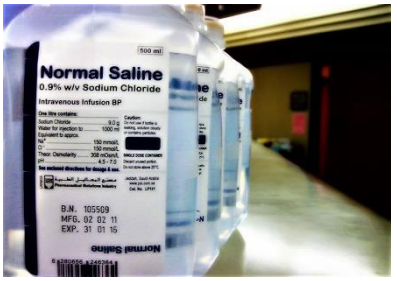

Fig-1 Saline

In hospitals, Saline can be used for treating dehydration, for wound cleaning and irrigation.

Clinically, it was evaluated in-

i. Human non-vital immature teeth (Yates 1988),[39] [xxxix]
ii. Perforations (Bogaerts 1997)[40][xl]
iii. Internal resorption at the site of an intra-alveolar root fracture (Cvek 1974)[41][xli]
iv. External inflammatory root resorption (Rabie et al. 1988)[42][xlii]
v. Antibacterial dressing in infected teeth (Barbosa et al. 1995)[43][xliii]
vi. Endodontic retreatment after endodontic and surgical failures (West & Lieb 1985) [44][xliv]

Normal saline solution is usually used as a vehicle because of

1. Constant pH of 7
2. Easy availability.

It has composition similar to that of protein-free plasma found clinically in the periapical area. [45][xlv]

4- GLYCERINE

In 1811, the term Glycerine was introduced by French chemist, Michel-Eugene Chevreul

It is applied to commercial products containing more than 95% glycerol

Glycerol is clear, colourless, viscous sweet tasting liquid of alcohol family of organic compounds.

Its molecular weight is 92.02

Fig-2 Glycerine

Advantages of using Glycerol-

1) Soluble in water-Facilitate easy removal
2) Non-toxic and non-irritant (Olson & Hoover 1975)[46] [xlvi]
3) Lubricant (Walton & Torabinejad 1989)[47][xlvii]
4) Hygroscopic Nature

Steiner et al.in 1968 reported first the use of glycerine as a vehicle with calcium hydroxide along with CMCP and Barium Sulphate for treating apexification.[48][xlviii]

The use of such pastes has been advocated by C Ë aliskan et al over the years for-

- Acute abcesses or chronic periapical lesion
- Chronic abcesses with extraoral fistulae
- Internal resorption with or without root perforation
- Repair a fractured root

According to Antony et al. in 1997, Glycerine is said to show anti-microbial activity only at 100% concentration. Other studies demonstrated bactericidal activity at 30% and 25% concentration but at a longer incubation time, i.e. after 48 h and 7 days, which is contrary to the findings of the present study. [49][xlix]

5 -CHLORHEXIDINE

Chlorhexidine is a cationic bisbiguanide. It contains two chlorophenyle rings and two bigunide groups connected by a central hexamethylene chain. It is most stable in the form of salts. It is basic in nature. [50][l]

Fig3.Chlorhexidine

Advantages of using Chlorhexidine as a carrier are-

1) Biocompatibility
2) Substantivity, which is with prolonged gradual release at therapeutic levels the ability of chlorhexidine to adsorb to dental tissues and mucous membranes. [51,52][lilii]
3) According to Heling et al.16 (1992) chlorhexidine is effective against gram-positive and gram-negative, aerobic and facultative anaerobic microorganisms, yeasts and viruses .Hence, it is chosen as a vehicle with medicaments.[53][liii]
4) Anti-candidal agent- As Ferguson et al, showed that chlorhexidine diffuses through the root canal, and possibly into the dentinal tubules. [54][liv]

The antimicrobial action of Chlorhexidine –

- Chlorhexidine is a positively charged hydrophobic and lipophilic molecule.
- The interaction of the positive charge of the molecule and the negatively charged phosphate groups of phospholipids and lipopolysaccharides on the microbial cell walls.
- This alters the cells' osmotic equilibrium.
- This leads to increased permeability of the cell wall, which allows the CHX molecule to penetrate into the bacterial cell.[55][lv]

According to Jenkins, et al, This attributes to a bacteriostatic effect occurs at low concentrations. Furthur, the precipitation or coagulation of cytoplasmic contents leads to the Bactericidal effect at high concentrations. [56][lvi]

Chlorhexidine alone had a surface tension of 39.8 dynes/ cm. With the addition of calcium hydroxide the surface tension was reduced to 36.4 dynes/cm. The decrease in surface tension was due to the fact that commercially

available chlorhexidine formulations contain a surfactant. A surfactant has hydrophilic (polar or ionic) and hydrophobic (hydrocarbon or urocarbon) parts in the same molecule. Because the hydrophilic parts of the molecule do not bond to one another very well, it is easier to stretch the surface of the water. The reduction in surface tension is due to ability to adsorb the liquid-gas interface. [57].[lvii]When associated with calcium hydroxide, 2% chlorhexidine and calcium hydroxide paste showed

1. High surface tension value (58.00 dynes/cm)
2. pH values equal to 10.2.[58][lviii]
3. Generation of excessive reactive oxygen species, which may potentially kill various root canal pathogens .[59][lix]

The chlorhexidine formulations used in various studies include Chlorhexidine gel, combination of Chlorhexidine along with calcium hydroxide and Chlorhexidine alone. According to Almyroudi et al (2005), 1% Chlorhexidine gel working slightly better than the other preparations in eliminating E. faecalis from the dentinal tubules.[60] [lx] Studies were conducted by Gomes et al. in 2003 on bovine dentine and Schafer and Bossmann in 2005 on human dentine. They concluded that the order of efficiency of the intracanal medicament against E.Faecalis was 2% Chlorhexidine gel followed by Chlorhexidine and then Calcium Hydroxide used alone. [61,[lxi]62[lxii]]

Similarly, the reduced antibacterial activity of Calcium Hydroxide and Chlorhexidine association was reported in a study by Athanassiadis et al in 2007.

The optimal antimicrobial activity of chlorhexidine is achieved at a pH range of 5.5–7.0. Therefore, alkalinizing the pH by adding Calcium Hydroxide to Chlorhexidine will lead to precipitation of the Chlorhexidine molecule. This may be the probable reason for decreased effectiveness against bacteria.[55] According to a agar diffusion study by Haenni et al in 2003, in a mixture of Calcium Hydroxide powder with Chlorhexidine (0.5 percent), Chlorhexidine showed reduced antibacterial action. However, Calcium Hydroxide did not lose its antibacterial properties. The reason is said to be the deprotonation of Chlorhexidine at a pH greater than 10. The altered charge of the molecule, reduces its solubility and alters its interaction with bacterial surfaces. [63][lxiii]

6 –PROPYLENE GYLCOL

Propylene glycol is a colourless liquid with a mildly acrid smell and somewhat sweet taste. Propylene glycol (1,2-propanediol), a dihydric alcohol. Its chemical formula is CH3CH(OH)CH2OH .It has a molecular weight of 76.09 according to United States Pharmacopeia 1989.

Figure 4- Propylene Glycol

In a study by Seidenfeld & Hanzlik in 1932, they the used propylene glycol as a vehicle and pharmaceutical solvent for Preparations in medicine

It has been reported to be less toxic than ethylene glycol. [64] [lxiv]

The first report using a Ca (OH) 2 paste containing propylene glycol as vehicle was by Saiijo in 1957.

He also added antibacterial agents and asbestos powder.[65] [lxv]

Later on, Laws 1962 employed Propylene Glycol as a vehicle .Paste is made up of of 10 g of calcium hydroxide powder with 7.5 mL of propylene glycol [45]

Simon et al. in 1995 recommended PG as the best vehicle in Calcium Hydroxide preparations. As it is possible to control the level of pH rise and Ca2+ release that can be sustained for a long period when PG is mixed with calcium hydroxide. [36]

Advantages of using Propylene Glycol as a vehicle for intra canal medicament-

1) According to Fava and Saunders in 1999, Propylene glycol is hygroscopic in nature that means it allow absorption of water, which results in a sustained release of intra-canal medicaments for prolonged periods.[10]
2) Viscous consistency due to high molecular weight which improves the handling qualities of the paste.[36]

3) Less cytotoxic than other commonly used vehicles for intra-canal medicaments

4) Antibacterial properties when used in concentrations up to 20%

These properties might be due to the slow diffusion of calcium and hydroxyl ions as compared to the paste prepared with distilled water.[10,66,67,68,69][lxvilxviilxviiilxix]

When Calcium Hydroxide is mixed with propylene glycol – It Exhibits dual effect

- None tissue irritating effect
- Being alcoholic in nature, it remains in paste form for a longer time.[7, 66,70,71,72][lxxlxxilxxii]

The paste can be used for-

- Post vital pulpectomy dressing (Saiijo 1957) [73][lxxiii]
- Non-surgical treatment of large periapical lesions (Hussey & Kennedy 1990).[74][lxxiv]

In a Study done by Paul in 1997, the paste of the Calcium Hydroxide and propylene glycol exerted significant antibacterial action and was considered better than tissue irritating phenolic compound like camphorated p-monochlorophenol. [75] [lxxv]

Kollöffel et al. in 1996, stated acceptable daily intake as prescribed by the World Health Organization, is 25 mg kg–1 body weight .[76] [lxxvi] Glover & Reed (1996) reported adverse effects associated with propylene glycol following excessive ingestion of a propylene glycol-containing product. [77] [lxxvii]But based on chronic toxicity data according to Ruddick 1972, no deleterious effects are produced with use of propylene glycol in small amounts. [78][lxxviii]

7-CAMPHORATED PARAMONOCHLOROPHENOL

It was introduced by Walkhoff in 1891.

Composition- 33±37% parachlorophenol and 63±67% camphor (United States Pharmacopeia 1989). Molecular Formula-C_6H_5OCl

Molecular weight 128.56

Camphor ($C_{10}H_{16}O$, molecular weight 152.54)

Fig.5- Camphorated p-monochlorophenol (CMCP)

Camphorated p-monochlorophenol (CMCP) is a phenolic compound used as a disinfectant due to the liberation of the chlorine in the presence of phenol (Breillat & Laurichesse 1986) and vehicle in root canal treatment. [79][lxxix]

Camphor is considered as an oily vehicle as it is an essential oil with low solubility in water.

It is used in-

- Apexification (Kleier & Barr 1991).[80][lxxx]
- Perforation defects after internal resorption (Frank & Weine 1973)[81][lxxxi]
- Treatment of external root resorption (Montgomery 1984) [82][lxxxii]
- Intracanal dressing in cases of non-vital teeth with associated large periapical lesions (Souza et al. 1989).[83][lxxxiii]

When mixed with calcium hydroxide dual effect was noticed-

- High Ph which is toxic for the bacteria
- Activation of hydrolytic enzyme alkaline phosphatase leading to tissue mineralization.[7,70,71]

According to Frank et al in 1966, extended antibacterial spectrum of Calcium Hydroxide, mainly against some facultative or anaerobic bacteria was proposed when mixed with camphorated p-monochlorophenol. [84] [lxxxiv]In contradiction, in a Study by Georgopoulo et al in 1993, Calcium Hydroxide has a better antimicrobial effect than Camphorated p-monochlorophenol on anaerobic bacteria.[85][lxxxv] Calcium hydroxide and camphorated

monochlorophenol paste has a tendency to become sticky and set fast. Surface tension of Camphorated paramonochlorophenol plus calcium hydroxide is 37.50 dynes/cm.[86][lxxxvi] Leonardo et al. (1993), Barbosa et al. (1997) , Siqueira & Uzeda (1997) and Estrela (2001) have reported greater effectiveness when calcium hydroxide is associated with Camphorated p-monochlorophenol.[87,88,89] [lxxxviilxxxviiilxxxix]Anthony, Gordon and del Rio (1982) reported that when calcium hydroxide is mixed with camphorated parachlorophenol or metacresylacetate, the products formed could cause a reduction in pH over an extended period of time.[90][xc]

Major disadvantage of using camphorated p-monochlorophenol is its toxicity. In 1996, Saekont evaluated phenol, camphorated phenol and camphorate monochlorophenol. They confirmed that these are irritant to the periapical tissue. [91][xci] Chang et al in 1999 found that camphorated p-monochlorophenol is cytotoxic to the periodontal ligament cell. The toxic nature is due to inhibition of cell viability and proliferation. [92] [xcii]Similar findings were seen in a study by Claudia et al in 2011, which were that this association kills microorganisms in 15 seconds.[93] [xciii]Esberard et al, in 1996 indicated that calcium hydroxide in Camphorated p-monochlorophenol vehicle diffuses more rapidly than calcium hydroxide in an aqueous vehicle in cervical and middle of teeth.[94][xciv]

In studies dated from 1994 by Spangberg et al to 2014 by Ganesh et al, it is stated that amongst all the vehicles used in Endodontics, camphorated monochlorophenol (CMCP) an effective antimicrobial agent but is irritant to the tissue. Hence, the use of CMCP as vehicle should be avoided. [34,95][xcv]

8- CORTICOSTERIODS AND ANTIBIOTICS

Various combinations are available in market which can be used along with intracanal medicament. Otosporin is one of the drug used in various studies. It is composed of

1. Neomycin (5 mg) -

Neomycin is an aminoglycoside.The mechanism of action is inhibition of bacterial protein synthesis through irreversible binding to the 30 S ribosomal subunit of susceptible bacteria. Neomycin is active against Gram-positive and Gram-negative, as well as acid-fast bacilli. Neomycin is a strong bactericidal. It does not readily allow resistance against micro-organisms.

2. Polymixin B sulphate (10 000 IU) -

In 1947, Polymyxins, a group of cationic polypeptide antibiotics were discovered. They are available as Polymyxins A-E but only polymyxin B and polymyxin E (colistin) are used in clinical practice. The cationic polypeptides of polymyxin B interact with anionic lipopolysaccharide (LPS) molecules in the outer membrane of gram-negative bacteria. This further leads to an increase in the permeability of the cell membrane, leakage of cell contents, and ultimately cell death of the bacteria. I.V. administration of Polymyxin B may lead to nephrotoxicity and neurotoxicity.

3. Hydrocortisone (10 mg)

Adrenocorticoids are released by the adrenal glands and can be classified as glucocorticoids or mineralocorticoids.Cortisone, hydrocortisone and corticosterone are examples of glucocorticoids. Cortisone was isolated in the late 1930s but was synthesized in 1948.These are released in fright and flight situations and affect the cell metabolism .Glucocorticoids are anti-inflammatory. These are indicated in conditions such as skin and mucosal inflammations, asthma and rheumatoid arthritis.

According to Holland et al in 1971, Otosporin and calcium hydroxide mixture is said to maintain the integrity of the pulp stump in vital pulpectomy in dog teeth.

According to Fava (1992), favourable results seen with regard to postoperative pain after pulpectomies in humans. [10]

In a study by Estrella (2001), the Otosporin® paste consists of hydrocortisone, neomycin and polyxin B. It was found to be effective against all microorganisms except Candida albicans up to 1 min but by 48 hr Candida albicans was killed.[89]

9- LOCAL ANAESTHETIC SOLUTION

Drugs that have little or no irritating effects when injected into tissues and that will temporarily interrupt conduction when absorbed into the nerve are called as Local Anaesthetics.

Local anesthetics produce a local reversible block of nerve conduction. These is no permanent damage. They can block the nerve impulse at various sites along the neural pathways.

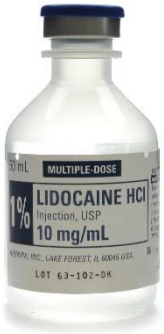

Fig-6 Lidocaine

Classification-

I)Ester Group-

A) Benzoic acid esters

1.Cocaine

2.Benzocaine

B) Para- aminobenzoic acid esters

1.Procaine

2.Tetracaine

3.Propoxycaine

4.2-Chloroprocaine

11)Non-ester Group-

1. Bupivacaine

2.Etidocaine

3.Lidocaine

4.Mepivacaine

5.Prilocaine .[96][xcvi]

Advantages of Anaesthetic solutions with or without a vasoconstrictor-

1) Availability
2) Sterility
3) Ease of handling. [10]

According to Özcelik, et al.17 (2000), anaesthetic solution was the most favourable vehicle with the lowest surface tension values (44.00 to 51.00 dynes/ cm) amongst. glycerine, Ringer's solution, anaesthetic solution and saline, alone and the calcium hydroxide combinations.[97] [xcvii]The chemical reaction may occur between the anaesthetic and calcium hydroxide due to the acid pH of local anaesthetics and the alkaline pH of calcium hydroxide.

However, Anthony, Gordon and del Rio (1982) and Stamos, Haasch and Gerstein (1985) demonstrated high level alkaline pH of calcium hydroxide–local anaesthetic (with lidocaine or mepivacaine) mixtures.[90,98][xcviii] The antimicrobial action of calcium hydroxide is determined by the liberation of hydroxyl ions in high pH for appropriate amount of time.

Disadvantages-

1) Lack of radio-opacity
2) Lack of Antibacterial properties

Hence, For Radio-opacity addition of barium sulphate to calcium hydroxide powder in 1:4 Ratio by (Dumsha & Gutmann 1985). Or 1:8 Ratio by Marais (1996) [10]

For the antibacterial property of the paste, addition of one drop of camphorated parachlorophenol in cases of –

- Dressing in infected nonvital cases, Teplitsky (1986)[99][xcix]
- Human apexification by Webber et al. (1981) (1984) [100,101][cci]
- Pulp capping material by Armstrong & Hoffman (1962)[102][cii]

10 – DETERGENTS

The penetration of antimicrobial solutions into irregularities of the root canal system (RCS) and into the depth of dentinal tubules depend on wettability. Wettability depends on surface tension.

Surface tension is defined as defined as the force between molecules tending to reduce the surface area of a liquid.

Detergents decrease the surface tension between two surfaces and facilitate substance penetration.

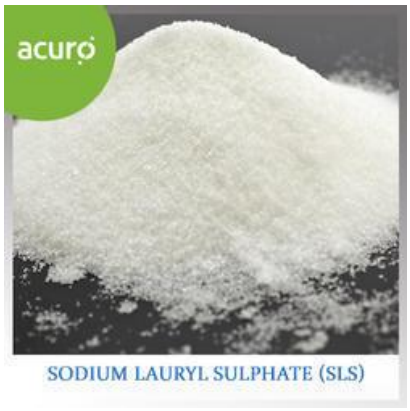

Figure 7- Sodium Lauryl Sulfate

Sodium Lauryl Sulfate has the chemical formula $C_{12}H_{25}NaO_4S$ or CH_3-$(CH2)_{11}$-O-SO_3-Na+. SLS is an anionic surfactant. It has a negatively charged sulfonate group as its "hydrophilic" end and a saturated 12-40 carbon chain for its "lipophilic" end. SLS has a faint odor of fatty substances at room temperature, it occurs as white or cream-colored crystals, flakes, or powder.[103][ciii]

Calcium hydroxide in association with anionic detergent showed low surface tension (31.60 dynes/cm).[58] According to C.Estrelal (2001),the paste with $Ca(OH)_2$ + SLS did not show a stronger antimicrobial action in comparison with the one containing saline solution, due to the low superficial tension of the detergent. E. faecalis, P. aeruginosa and B. subtilis showed sensitivity after long exposure periods. Which were resistant to the paste containing 1% chlorhexidine after 1 min. [89]

11- CHITOSAN

Chitosan is a natural and biodegradable polymer derived from the exoskeleton of crustaceans (such as crabs). [104][civ].Chitin is a natural polysaccharide. It is composed of β (1→4) linked N-acetyl glucosamine units. The partial deacetylation of chitin forms Chitosan, which contains copolymers of glucosamine and N-acetyl glucosamine. [105][cv]

Fig 8- Chitosan

Mechanism of Action-The cationically charged amino group of chitosan may combine with anionic components such as N-acetyl muramic acid, sialic acid, and neuramic acid on the cell surface .This will impair the exchanges with medium, chelate the transition metal ions, and inhibit enzymes. This suppresses the growth of bacteria .The possibility of potential additive or synergistic effect when used with intracanal medications like TAP and CH on the viability of C. albicans and E. faecalis. Makes chitosan a good carrier. [106][cvi]

Advantages of using chitosan as a vehicle-

1. Antimicrobial properties.
2. Antifungal properties.[107][cvii]

Senel et al. in 2000 used chitosan as an oral mucosal delivery agent.It was combined with chlorhexidine. The results concluded that the highest antifungal activity against Candida Albicans was obtained with 2% chitosan gel containing 0.1% Chlorhexidine. Also, prolonged release of Chlorhexidine was noted. [108][cviii]

3. Biodegradable and nontoxic properties.[106]
4. The ability to retain high amounts of water and form gels in acidic aqueous environments -which could be the reason for used in slow-release formulations.[109][cix]

This sustained release of medication minimizes side-effects and prolongs the efficacy of the drug. In early stage, a stagnant gel layer controls the diffusion. In due course of time, the network of the gel starts to disintegrate and thus diffusion is facilitated. Drug release rate is regulated, which aids in reducing the frequency of administration, thus assuring better patient compliance. It has been suggested persistence of formulations at sites of drug action or

absorption could be prolonged through use of chitosan. It has also been suggested that chitosan increases drug bioavailability and might be valuable for delivery of drugs to specific regions such as stomach, buccal mucosa.[110][cx] According to Kristl et al in 1993, the drug release when chitosan gel was used as a vehicle was slow and sustained.[111][cxi]

5. The property of insolubility of Chitosan is said to increase intracanal medicament stability. [106,112,113][cxiicxiii]

6. Chitosan increases drug bioavailability which might be valuable for delivery of drugs to specific regions such as stomach, buccal mucosa. [110]

In 2013, Silva et al., investigated the efficacy of smear layer removal using Chitosan. They concluded that 15% EDTA and 0.2% chitosan were associated with the greatest effect on root dentine demineralization when compared with 10% citric acid and 1% acetic acid.[114][cxiv]

12- POLYETHYLENE GLYCOL

It is a colourless water soluble and hygroscopic polymer. It is miscible with water in all proportions.[115] [cxv] Polyethylene glycol is referred to as "Macrogol". It is abbreviated as PEG 400 , PEG 1000 etc. This number denotes its molecular weight. Higher the number, higher is its viscosity. [116] [cxvi]In Mid 1970's ,the components such as polyethylene glycol (PEG) 400 and colophony resin (a thickening agent) were added to alter the viscosity to improve the clinical handling of the calcium hydroxide paste(calen). [10]

Fig.9- Polyethylene glycol

Takushige et al., (2004) was first to use the combination of propylene glycol with Macrogol dentistry in vivo.[117][cxvii] PEG 400 can be used as a vehicle with calcium hydroxide, antibiotics and corticosteroids or calcium hydroxide and ibuprofen.[115]

Advantages of using Polyethylene Glycol-

1) Synergism in bactericidal activity-

   This phenomenon was seen in a study by Carreira et al. (2007)

   It was observed in Ciprofloxacin–PEG 1000 association, Metronidazole–PEG 1000 association, and Ciprofloxacin–Metronidazole–PEG 1000 combination.

   The bactericidal activity might possibly be due to hydrophilic property of PEG. It reduces the bacterial count.[118][cxviii]

   Another cause of the bactericidal activity as stated by Bozzini et al (1986) might be due to severe plasmolysis, cell wall collapse, and finger-like extrusions as seen in Klebsiella pneumonia.[119][cxix]

2) Inert in nature-It does not interact with other components of the paste.[120][cxx]
3) Biocompatibility[115]

Different Pastes Formulations have been stated-

Sr.NO	Year	Reported by	Components	Used in cases of
1	1960 1961	Maeda et al Kurimoto et al	• Calcium hydroxide • Polyethyleneglycol 1500 Sulphisomidine • Eugenol • Same composition paste	Infected pulpless teeth with periapical lesions
2	1976	Leonardo et al.	• Calcium hydroxide (2 g), Polyethyleneglycol 400 (1.75 mL), Barium sulphate (1 g) • Hydrogenized colophony (0.05 g)	
3	1988	Lessi & Alvares et al	• Calcium hydroxide • Iodoform (30%) • Polyethyleneglycol 1500 (70%).	
4	1991	Leonardo & Leal	• Replaced the barium sulphate by zinc oxide in the same proportion.	
4	1992	Ulyssea et al. Zelante et al.	• Calcium hydroxide and Barium Sulpahte in ratio 4:1 • Calcium hydroxide (3 g) • Zinc oxide (3 g) /Iodoform (1.5 g) Polyethyleneglycol 400 (3.5 mL)	
5	1993	Bellacosa et al	• Calcium hydroxide (70%)	External/internal

			• Iodoform (30%) • Polyethyleneglycol 1500	resorption,
6	1996	Santos et al	• Calcium Hydroxide • Polyethyleneglycol 400	External cervical resorption after bleaching of pulpless teeth

PEG-coated nanoparticles were found to be most effective in killing E. coli, Staph. aureus, and multi-drug resistant clinical isolates of Shigella spp. and Vibrio cholera According, Bhattacharya in 2012.[121][cxxi]

When mixed with calcium hydroxide, it is said to enhance dissolution of calcium hydroxide and release of hydroxyl ions.

According to Chen J et al. 2005, PEG 400 is a suitable solvent for calcium hydroxide.

This is due to the complex formation as metal cations like calcium ions reacts with ethylene oxide.

The results of the first part of the study showed that compared to water, polyethylene glycol 400, when used as a solvent allows high pH values to be achieved, which are above P_H 12.4, which is the nominal limit for aqueous pastes [115]

13- RINGER LACTATE

Composition-

- Sodium chloride (8.6 g)
- Potassium chloride (0.3 g)
- Calcium chloride (0.33 g)
- Water (1L).- the United States Pharmacopeia (1989),)

Fig 10. Ringer lactate

In hospitals, it is used in regulation or maintenance of metabolic acidosis (except lactic acidosis)

Use of such a paste was first described by Granath in 1959 for Treatment of traumatic injuries, [122][cxxii] clinically, it has been evaluated in

- Indirect pulp capping (Nyborg 1955)[123][cxxiii]
- Apexification procedures
- Temporary dressing both after vital pulpectomy (Stromberg 1969)[124][cxxiv]
- Non-vital teeth

14– OTHER VEHICLES-

A) Iodoform and Methyl cellulose-

Methylcellulose was the vehicle of a paste widely used mainly in Argentina.

A paste composed of equal volumes of calcium hydroxide powder and iodoform mixed with a 5% aqueous solution of methylcellulose was introduced in 1964 by Maisto & Capurro. [125][cxxv]

it was recommended for-

- Apexification- Maisto & Capurro (1964),
- Indirect pulp capping - Krakow et al. (1974).[126][cxxvi]

A paste with the composition of by calcium hydroxide and iodoform in a ratio 2/3:1/3, two drops of camphorated parachlorophenol and a 3% aqueous solution of methylcellulose was introduced by Laurichesse in 1980.

Giro et al. (1993) proposed the use of carboxymethylcellulose [127][cxxvii]

B) Olive Oil-

Olive oil is a slight greenish water insoluble liquid with a characteristic odour.

Chemically, made up of esters of fatty acids such as oleic, linoleic, palmitoleic, estearic and linolenic acids.

Fig 11.Olive oil

It was advocated to be used as a vehicle due to low solubility, which permits low diffusion within the tissues.

C) Metacresylacetate.

Metacresylacetate is the acetic ester of metacresol with benzene.

Metacresylacetate was first introduced to dentistry by Coolidge in 1912 for the treatment of necrotic pulps.

Fig 12- Metacresylacetate

Properties-

1) Sedative
2) Antibacterial,
3) Analgesic (Lecazedieu 1986)[128][cxxviii].

The paste is used for-

- Pulp capping (Weiss 1966)[129][cxxix]
- Pulpotomy (Tenca & Tsamtsouris 1978)[130] [cxxx]
- Apexification (Levy 1980)[131] [cxxxi]
- Retreatment after endodontic and surgical failures (Stewart 1975) [132][cxxxii]
- Root resorption (Stewart 1975).

4) Some Other studies

Yoshiba et al. (1994) proposed for Pulp Capping- a paste of tricalciumphosphate, calcium hydroxide powder and saline. [133][cxxxiii]

Sazak et al. in 1996 suggested, the addition of Ledermix (Lederle Lab., MuÈnchen, Germany) to a calcium hydroxide-saline paste for reducing postoperative pain and inflammation in cases of pulp capping. [134][cxxxiv]

15- CONCLUSION

Use of these specific vehicles for dispensing intracanal medicament is vital. Studies have shown that, vehicles increase the half-life of intrcanal medicament and will help in better penetration of it inside the dentinal tubules. Hence to conclude, use of different vehicles should be in accordance with the rate of ionic dissociation. For example, aqueous vehicles should be used when rapid ionic liberation is necessary. Viscous vehicles in cases of gradual and uniform ionic liberation. Oily Vehicles are restricted to very slow ionic dissociation rate.

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