Biomaterials Journal
http://www.biomatj.com
Online ISSN: 2812-5045

Type of the Paper (Editorial)

Using nanostructure modelling for ideal dental care

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Citation: Tamer M. Hamdy. *Using nanostructure modelling for ideal dental care . Biomat. J., 2 (7),1 – 2 (2023).*

https://doi.org/10.5281/znodo.5829408

Received: 25 July 2023
Accepted: 30 July 2023
Published: 31 July 2023

Abstract: Human instinct drives us to seek out and unravel nature's mystery. In biomimicry, we use nature as a guide, benchmark, and teacher. Using either artificial or natural alternatives should make biomimicry practicable. In the past, dental restorative materials were generated at the micromolecular level of matter, but now researchers are more interested in creating materials that are more like nature by building them at the nanoscale, giving rise to the discipline of nanotechnology.

Keywords: Nanostructure; dental care; nanotechnology.

Human inclination dictates that we should try to solve the mystery that is nature. Using nature as a guide, benchmark, and teacher, biomimicry examines human behaviour. Using artificial or natural replacements should make biomimicry practicable. Prior to the development of nanotechnology, dental restorative materials were made at the micromolecular level of matter, but now that researchers are interested in creating materials that are more like nature, they are building materials at the nanoscale [1].

The most fundamental components of life systems are what biomimetic nanotechnology identifies with, as is the transfer of these components' qualities to useful human uses. The majority of natural materials, structures, and processes are thought to have nanoscale functions. From their first degree of association, the most fundamental traits and abilities of every single natural framework are characterised at the nanoscale. The main idea of nanotechnology is to use low-energy bonding to hierarchically arrange molecules into objects. Materials and methods for nanoscale fabrication and analysis are provided by nanotechnology [2].

In my opinion, all modern dental materials, especially their active ingredient, should be made at the nanoscale for the best possible replication of natural dental tissues. Nano-size will ensure that mechanical qualities are best suited to their intended use, with the best aesthetics, repairability, and energy efficiency, making materials more intelligent in how they respond to their surroundings.

Enamel, dentin, or cementum of the tooth can be painted with fluoride varnish, Clinical dental practise will change as a result of nanotechnology. Dental restoration materials will soon be extremely accurate, intelligent, and similar to natural ones. In order to accomplish dental restorative materials in nanoscle, all necessary efforts should be made. These materials include dental medication, resin composite, cements, sealers, ceramics, impression materials, remineralizing agent, dentures, bone replacement agent, root fillings, and dental implant materials.

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Biomaterials Journal
http://www.biomatj.com
Online ISSN: 2812-5045

Type of the Paper (Mini-Review)

Dental care using natural items

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Citation: Tamer M. Hamdy. Dental care using natural items. *Biomat. J.*, 2 *(7),3 – 5 (2023).*

https://doi.org/10.5281/znodo.5829408

Received: 25 July 2023
Accepted: 30 July 2023
Published: 31 July 2023

Abstract: Using natural plant extracts as medications or health-improving substances is a field of study known as phytotherapy. The use of herbs in dentistry is not just confined to the field of material sciences. A single herb exhibits numerous properties, including anti-inflammatory, antibacterial, antifungal, and many others. The natural phytochemicals hold promise as a potent antibiotic substitute as well as a potential strategy for treating and preventing dental caries and other oral infections.

Keywords: Natural plant; dental care; therapeutic strategies.

The study of using plant extracts in therapy is known as phytotherapy. Natural origin as drugs or health-improving substances. Herbs with therapeutic qualities are advantageous and efficient. a resource for treating different illness processes. (1) There is a vast collection of medicinal plants that are used in conventional medical treatments. These plants are also a great source of knowledge (2). They are classified as sedatives and anxiolytics, antimicrobial agents, anti-inflammatory agents, and sedatives in dentistry, depending on their intended function (3).

Even though root canal chemo-mechanical preparation can minimise the number of germs, intracanal antibiotic medication is necessary to maximise root canal system sanitation (4). To stop the development of caries or biofilm, a variety of antimicrobial agents and herbal items are added to dentifrice and mouthwash (5).

Curcuma zedoaria, calendula, aloe vera, and other natural remedies have all been used successfully to treat oral illnesses (6). The natural phytochemicals have promise for the treatment and prevention of dental caries and other oral infections, and they might be a good substitute for antibiotics.

Therapeutic applications

As an antibacterial agent against different endodontic infections, herbs have been employed. Besides herbs,

has long shown obtundent and soothing properties when utilised in various endodontic medicines and dressings.

Application in endodontics:

1. Endodontic irrigants

At a 15% concentration, the Salvadora persica (Miswaak) extract showed strong antibacterial activity against both aerobic and anaerobic microbes.(7) Because Azadirachta indica (Neem) is a biocompatible antioxidant and less likely to result in serious patient injuries than NaOCl accidents, using it as an endodontic irrigant may be helpful.(8).

2. Endodontic restorative surgery

For endodontic re-treatment, orange oil was recommended as a substitute to chloroform and xylol because both substances have harmful and cancer-causing effects.The main component of this is d-limonene. In addition, it contains long-chain aliphatic hydrocarbon alcohols, including octanal.

It is recommended as a substitute for xylene or chloroform when softening gutta percha and when dissolving endodontic sealants (9).

3. Drugs used intracanally

As an alternate intracanal medication, propolis showed promising in vitro antibacterial action against E. faecalis in root canals (10).

Applications for pulp capping:

In pulpotomy and pulp capping, propolis encourages bone repair and induces the creation of hard tissue bridges (11).

Periodontal applications:

Plants with anti-inflammatory properties that reduce gingival inflammation include Matricaria chamomilla (Asteraceae), Echinacea purpurea (Asteraceae), S. officinalis (Lamiaceae), Commiphora myrrha (Burseraceae), and M. piperita (Lamiaceae). Plants with immune-stimulating and anti-inflammatory properties include S. officinalis and M. piperita.

Oral mucosal healing applications:

Herbal remedies typically have a palliative purpose.Apthous ulcers heal more quickly and with less pain when treated with aloe vera gel (12).

Applications for dental trauma:

In vivo investigations revealed that teeth kept in propolis media displayed replacement resorption with substantial lengthening of the tooth, comparable to dried and saliva-maintained teeth (13). Garden sage (Salvia officinalis) extracts are used as a storage medium to preserve the viability of PDL cells in avulsed teeth (14). The best media for preserving PDL fibroblasts' cell viability were whole and skim milk, then natural coconut water and HBSS (15). Indian mulberry, or Morus rubra, is a good option for transporting avulsed teeth(16). Green tea extract from Camellia sinensis is more effective than milk and comparable to HBSS at preserving the viability of human PDL cells (17).

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Biomaterials Journal
http://www.biomatj.com
Online ISSN: 2812-5045

Type of the Paper (Mini-Review)

A New Trend in Dental Materials Is Bioactivity

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Citation: Tamer M. Hamdy. A New Trend in Dental Materials Is Bioactivity. *Biomat. J., 2 (7),6 – 7 (2023).*

https://doi.org/10.5281/znodo.5829408

Received: 25 July 2023
Accepted: 30 July 2023
Published: 31 July 2023

Abstract: An area of particular focus is the quickly developing field of bioactivity since it is a fascinating and interesting subject in the world of dentistry. Bioactive restorative materials continue to exhibit intriguing promise and provide substantial advantages to the patient and dentist. When subjected to an inorganic phosphate solution, such promising materials can develop an apatite-like surface layer along the materials' tissues' interface. Their use in dentistry includes repairing bone abnormalities, maintaining long-lasting dental bonded restorations, and remineralizing hard tissues. This article explains the idea, advancements, and evaluation of bioactivity and highlights the potential benefits of bioactive materials that have not yet been fully explored.

Keywords: Bioactivity; dental materials; remineralization.

The bioactivity is currently the topic of conversation in all areas of dentistry, but particularly in the field of dental biomaterials. It is emphasised as an important area of research for the development of new restorative materials.

What is bioactivity?

Bioactivity, in general, refers to any substances that affect, provoke, or interact with live tissues or cells, such as promoting the synthesis of hydroxyapatite[1].

The phrase "bioactive materials" was initially used by Larry Hench in 1969 to describe a new substance for bone restoration that could develop a link with bodily tissues. Hench created a wholly artificial substance known as bioglass, mostly made of calcium silicophosphate glass that the body does not reject and chemically binds to bone[2]. The original definition of bioactivity was restricted to a biomaterial that causes a certain biological reaction at the material–tissue interface and causes a link to form between them. The idea of bioactive materials has significantly evolved since then[3].

A substance becomes bioactive when it can trigger both an intracellular and extracellular reaction at its interface[4]. Dental materials that are bioactive are not regarded as novel. The initial trend in bioactivity is the adhesion of dental materials to tooth structure by an apatite-like substance with the help of fluoride-releasing materials or, more recently, by action of calcium phosphate-releasing materials. As a result, materials with varying degrees of bioactivity have been widely employed for a long time. These materials are primarily used to restore, rebuild, and regenerate dental injuries. For instance, because of their potential to remineralize tooth structure and their constant dynamic release of fluoride, which delays the development of secondary caries around restorations, glass ionomers have been referred to as bioactive materials.

The long-used calcium hydroxide can also be broken down into calcium and hydroxyl ions, which sets off a chain of events that promotes the formation of reparative dentin and tooth remineralization[6]. Glass ionomer and calcium hydroxide are among the earliest recognised bioactive dental materials as a result of these actions. When exposed to an inorganic phosphate solution, bioactive dental materials can be characterised as those that create a layer of an apatite-like substance at the tissue material interface[7].

Mechanisms of bioactivity:

A bioactive restorative substance exhibits at least one of the behaviours listed below[8]–[10].

1. Renewal of the hard tissues' mineral content through the release of fluoride or other minerals.
2. After being submerged in a liquid that resembles the typical physiological fluids, apatite-like development is observed along the material-tissue contact.
3. Tissue regeneration and repair by supporting the body's natural healing process.

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Biomaterials Journal
http://www.biomatj.com
Online ISSN: 2812-5045

Type of the Paper (Review Article)

Antibacterial agents and Coatings: challenges, perspectives and opportunities

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Citation: Reem A. Hany .*Antibacterial agents and Coatings: challenges, perspectives and opportunities*. *Biomat. J., 2 (7),8 – 29 (2023).*

https://doi.org/10.5281/znodo.5829408

Received: 25 July 2023
Accepted: 30 July 2023
Published: 31 July 2023

Citation:

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Abstract: Common reason for restorations failure is secondary caries, which are mainly caused by oral bacteria. In recent years, numerous research studies have been conducted with the common goal of developing a dental restorative material to be used to eradicate the microbial infection and the cause of dental caries. Today, the manufacture and use of biomaterials with antimicrobial effects in medical and dental treatment plans is rapidly progressing. Therefore, manufacturing products containing antimicrobial agents or applying antimicrobial coatings on different material has become an interesting topic for research in the dental field.

Keywords: *antimicrobial, bacteria, antibiotics, herbal, smart materials, implants.*

Introduction

Antibacterial agents are a class of materials that act against pathogenic bacteria and microorganisms either by killing or reducing their metabolic activity. A therapy reducing their pathogenic effect in the biological environments.(1) Antibacterial agents can be classified according to their mode of action into:

1. Inhibition of peptidoglycan biosynthesis.
2. Selective disruption of cytoplasmic membrane.
3. Interfere with DNA replication, transcription, or translation.
4. Positively charged molecules.
5. Reactive oxygen species (ROS) induced oxidative stress.
6. Interfere with bacterial enzymes and enzymatic activity.
7. Increasing tooth mineralization.
8. Containing natural constituents.
9. Combined mechanisms.

1. Inhibition of peptidoglycan biosynthesis:

Peptidoglycan is a vital component of all bacterial cell walls. The peptidoglycan polymer is responsible for the shape, mechanical strength, and integrity of bacterial cells. If the synthesis of peptidoglycan is selectively blocked, bacteria undergo a number of changes in shape, the cell wall is greatly weakened and they ultimately die as the result of cell lysis. Mammalian cells do not possess a cell wall or macromolecular structures that resemble peptidoglycan. Consequently, antibacterial agents that interfere with peptidoglycan synthesis have excellent selective toxicity and can be used systemically.(2)

1.a. Antibiotics (ß-Lactams):

- **Penicillin:**

Is the most widely used β-lactam antibiotic, it can inhibit the synthesis of the peptidoglycan layer of the bacterial cell walls.

Uses in dentistry:

- Caries prevention: The first use of penicillin to treat dental caries dated from 1946, when McClure and Hewitt reported that penicillin inhibited caries in rats. Four years later, Zander reported that penicillin showed caries inhibition in children.

Limitations:

However, the use of penicillin can cause some side effects, such as diarrhoea, hypersensitivity, nausea, rash, neurotoxicity, and urticaria. Another major problem is the bacterial resistance.(3)

2. Selective disruption of cytoplasmic membrane:

The integrity of the cytoplasmic membrane is vital for normal cell function, but it is a much more difficult structure to target by antibiotics because it is chemically similar in all cell types with few differences to exploit.

Gram-negative bacteria contain an additional outer-membrane structure which provides a protective penetration barrier to potentially harmful substances. The stability of all membranes is maintained by a combination of non-covalent interactions between the constituents involving ionic, hydrophobic and hydrogen bonding. The balance of these interactions can be disturbed by the intrusion of membrane-active agents, which destroy the integrity of the membrane, thereby causing leakage of cytoplasmic contents or impairment of metabolic functions associated with the membrane. Most membrane-active agents which function in this way have very poor selectivity. They cannot be used systemically because of their damaging effects on mammalian cells; instead they are used as skin antiseptics, disinfectants and preservatives.(2)

2.a. Chlorhexidine (CHX):

Chlorhexidine is active against gram-positive and gram-negative bacteria, facultative anaerobes and aerobes.

Uses in dentistry:

- Caries prevention: It has proved to be the most effective for dental caries. Combining CHX in polymeric matrices have been attempted for sustained delivery specifically in glass ionomer cements (GIC). Although incorporation of CHX in GIC enables better protection against caries, it results in cements with inferior mechanical properties that exhibit a less than optimal period of sustained release.(3)

Also, chlorhexidine incorporated in composite resin was released faster in media of lower pH values due to its higher solubility at lower pH. Release rate also was affected by hydrophilicity of resin. Composites with hydrophilic resin tended to release chlorhexidine faster and the chlorhexidine-containing resin lost its antibacterial activities after storage in water for 2 weeks.(1)

- Plaque and gingivitis control: To date, chlorhexidine remains the “gold standard” of antiplaque agents. Chlorhexidine can reduce the binding of bacteria to tooth surfaces adsorbing chlorhexidine. It is a key component in oral formulations such as mouthwashes and oral gels that can be used topically in the management of oral biofilms.

- Endodontic irrigant: 2% is the concentration of root canal irrigating solutions usually found in the endodontic literature. Despite its usefulness as an endodontic irrigants , it cannot be advocated as the main irrigant in standard endodontic cases, because it lacks a tissue dissolving capacity. (4)

Limitations:

Chlorhexidine causes genotoxicity by inducing DNA damage in leukocytes, kidney cells and oral mucosal cells. When in contact with tissues, CHX is irritant and can delay healing, thus care must be taken to prevent its accidental extrusion into soft tissues.(3)

2.b. Alcohols:

The mechanism of action of alcohols depends on coagulation of protein, dehydration of cells and disruption of bacterial membranes.

Uses in dentistry:

- Disinfectant: Disinfectants are substances that are applied to non-living objects to destroy microorganisms that are living on the objects. The efficacy of these disinfectants depends on contact time, temperature, type and concentration of the active ingredient. A 70% aqueous solution of alcohols (usually ethanol or isopropanol) is more effective at killing microbes than absolute alcohols because water facilitates diffusion through the cell membrane. Additionally, 70% ethyl alcohol can also be safely used as antiseptic on skin.(5)

3. Interfere with DNA synthesis, replication, transcription or translation:

Living cellular systems store the genetic information associated with their growth, division, and survival as a sequence of bases within their DNA. Thus, the DNA must be capable not only of accurate self-replication and segregation into daughter cells, but also of accurate transcription and eventual translation into protein. Double-stranded DNA is not only replicated for cell division, but also transcribed into single-stranded RNA. This RNA provide templates for the biosynthesis of protein (mRNA).(2)

3.a. Antibiotics:

- **Metronidazole:**

Can inhibit nucleic acid synthesis and disrupt DNA through DNA strand breakage. The metronidazole is more effective against anaerobic organisms.

Uses in dentistry:

- Caries prevention: More than 99% of the bacteria present in carious lesions and infected root dentin were not recovered in the presence of metronidazole in in vitro experiments.

- Oral infections and lesions: Metronidazole is available as a topical cream for the mouth and has a wide spectrum of bactericidal action against oral obligate anaerobes.

Limitations:

Side effects of metronidazole, include nausea, a metallic taste, headaches, flushing of the skin, tachycardia, loss of appetite, and shortness of breath.(3)

- **Tetracycline:**

Are a group of broad-spectrum antibiotics with the ability to inhibit protein synthesis in bacteria through blocking 30S ribosomal subunit.

Uses in dentistry:

- Caries prevention: Effective against S.mutans and Lactobacilli.

Limitations:

However, tetracycline appears to become incorporated into human teeth, causing discoloration. In 1963, the United States Food and Drug Administration issued a warning regarding the use of such antibiotics for pregnant women and young children since teeth are most susceptible to tetracycline discoloration during their formation.

The side effects of tetracycline include cramps or burning of the stomach, diarrhoea, sore mouth or tongue, skin photosensitivity, headache rarely, and vision problems, with damage to the kidneys also having been reported.(3)

3.b. Aldehydes:

The aldehydes that act through alkylation of amino, carboxyl-or hydroxyl group, and finally damage nucleic acids.

Uses in dentistry:

- Sterilization an disinfectant: They have a wide microbiocidal activity and are sporocidal and fungicidal. The most popular of this subgroup are 40% formaldehyde (used for surface disinfection) and 2% gluteraldehyde (exposure of at least 3 hours can be used to sterilize anasethetic equipments and other medical equipments such as thermometers and cystoscopes). (5)

3.c. Ethylene oxide:

Ethylene oxide is an alkylating agent. It causes alkylation of proteins, DNA, and RNA in microorganisms, which prevents normal cellular metabolism and replication and thus renders affected microbes nonviable.

Uses in dentistry:

- Sterilization: It is a highly effective agent capable of killing spores rapidly. It can be used for sterilization of complex instruments, delicate materials, dental equipments, heat labile materials as rubber and plastics.

Limitations:

Ethylene oxide should be used with high care as it is highly flammable, highly toxic, irritating to eyes and skin, mutagenic and carcinogenic.(5)

4. Positively charged molecules:

Bacterial cells have a negative surface charge cell membrane phosphate that attracts the positively charge molecules. Attachment to these molecules disturb the electric balance, disrupt the membrane functions and the bacterial cell bursts under osmotic pressure. (6)

4.a. Quaternary Ammonium compounds (QACs):

The positive charge of QACs is due to the presence of N+ (nitrogen) in quaternary ammines.

Uses in dentistry:

- Caries prevention: Incorporation of Benzalkonium chloride (BAC) in etchants and dental adhesives owing to its antibacterial activity. BAC is a positively-charged quaternary ammonium compound (QAC). The antibacterial activity of BAC results from its amphiphilicity as it bears both hydrophobic (long alkyl carbon chain) and hydrophilic (cationic ammonium group).

BAC's hydrophilic cationic region destabilizes the pathogen's surface by interacting with negatively charged components, which is followed by penetration of the hydrophobic long alky group into the bacteria leading to cell leakage and lysis.

BAC is stable in acidic media and has been added into commercial phosphoric acid etchants to a final concentration of 1%. Examples of such products include ETCH-37a or UNI-ETCHa. (1)

Sabatini et al., added BAC into All-Bond Universal, a universal dental adhesive with final BAC concentrations of 0.5%, 1%, and 2% (wt/ wt). These BAC-containing adhesives delivered higher bond strength than did the control after 1-year storage in artificial saliva, probably because of their ability to inhibit MMPs. (7)

Methacryloylox-dodecyl-pyridinium (MDPB) is a derivative og QACs and has been added to composite resin restorations owing to its antibacterial effect. MDPB is composed of a compound of dodecyl-pyridinium which is an antibacterial agent, and a methacryloyl group which is able to copolymerize with other dental monomers. MDPB-containing composites demonstrated significant antibacterial effects even after 90 days of immersion in water. Also, MDPB was included in self-etching adhesive systems include (MDPB) present in commercially available Clearfil Protect Bond®. (6)

- Plaque and gingivitis control: In the 1970s, quaternary ammonium salts were first administered to inhibit oral plaque by being incorporated into mouth rinses.

Limitations:

However, administration of Quaternary ammonium salts may have many side effects as gastrointestinal symptoms, coma, convulsions and hypotension.(3)

4.b. Triclosan

Triclosan is a synthetic phenol derivative used as a topical antimicrobial agent. It has a broad spectrum of action including both gram positive and gram negative bacteria.

Uses in dentistry:

- Plaque and gingivitis control: Triclosan is included in tooth paste and mouth washes to reduce plaque formation. In addition to its antimicrobial action, triclosan possess an anti-inflammatory action by inhibition of formation of prostaglandins and leukotrienes.(8)

4.c. Essential oil mouth washes:

Uses in dentistry:

- Plaque and gingivitis control: Over-the-counter mouth rinses consisting of thymol, menthol, and eucalyptol with methyl salicylate can exert an antimicrobial activity and antioxidant activity.

Limitations:

The main concern related to the use of essential oils mouth rinses is their alcoholic content that causes dry mouth and their burning sensation.(8)

5. Reactive oxygen species (ROS) induced oxidative stress:

Reactive oxygen species (ROS) induce oxidative stress. The four ROS types are the superoxide radical (O_2^-), the hydroxyl radical (-OH), hydrogen peroxide (H_2O_2), and singlet oxygen (O_2). Under normal circumstances, the production and clearance of ROS in bacterial cells are balanced. However, with excessive production of ROS, this unbalanced state produces oxidative stress, which damages the individual components of bacterial protein and DNA. Also, Oxidative stress is a key contributor to changing the permeability of the cell membrane which can result in bacterial cell membrane damage and subsequently bacterial cell apoptosis.(9)

5.a. Hydrogen peroxide:

Uses in dentisrty:

- Root canal disinfection: H_2O_2 is a commonly used for canal disinfectant at a concentration of 3–6% as it is the strongest oxidizer.

In addition, the elevated oxygen concentration is un-favorable for the growth of strict anaerobes in root canals. Moreover, H_2O_2 generates effervescence which provides physical clearance of microbial deposits.

- Sterilization and disinfection: Hydrogen peroxide is used in hospitals to disinfect surfaces and it is used in solution alone or in combination with other chemicals as a high level disinfectant. It is used at 6% concentration to decontaminate the instruments, equipments such as ventilators. 3% Hydrogen Peroxide Solution is used for skin disinfection.

- Plaque and gingivitis control: 1.5-2 % Hydrogen peroxide is used as mouthwashes. It is often preferred because it causes far fewer allergic reactions than alternative disinfectants.(10)

Limitations:

The limitation of its use is that the produced hydroxides are inherently caustic.(11)

6. Interfere with bacterial enzymes and enzymatic activity:

6.a. Iodine potassium iodine:

Iodine potassium iodine has a wide-spectrum antimicrobial activity. It is The iodine is the oxidizing agent of this substance, it reacts with free sulfhydryl groups of bacterial enzymes cleaving the disulfide bonds.

Uses in dentistry:

- Endodontic irrigant: It is a traditional root canal disinfectant used in concentrations ranging from 2% to 5%.

Limitations:

A mojor disadvantage of iodine is a possible allergic reaction in some patients.(11)

7. Increasing tooth mineralization:

7.a. b.1. Fluoride (inc mineralization)

The popular mechanism in the antimicrobial action of fluoride is that fluoride ions contact the mineral of the tooth surface and increase remineralization to prevent the acid-induced demineralization caused by cariogenic bacteria. Another proposed mechanism is its ability to inhibit enolase enzyme. Inhibition of enolase results in growth inhibition and reduced acid production of oral streptococci, such as S. mutans.

Uses in dentistry:

- Caries prevention: Fluoride is the simplest anion of fluorine but is one of the most successful cavity prevention agents especially for preventing dental caries. Fluoride is typically supplemented in small quantities to drinking water or products such as mouthwashes, toothpastes, and oral supplement.

Examples for restorations containing fluoride for caries prevention, Glass ionomer cements' (GIC) antibacterial activity is due to its fluoride release. In addition, there is a claim that the low pH of GICs during setting may contribute more than the fluoride leached to their antibacterial properties.

Similarly, resin modified glass ionomer cements (RMGIC) have also been shown to exhibit antimicrobial activity. This antimicrobial activity is due to the release of fluoride and the low initial pH. Also, the release of strontium ions may also produce a synergistic antibacterial effect with fluoride.

Also, fluoride was incorporated in composite resin resulting in fluoride-releasing dental composites. Despite some success in the development of dental composites with sustained fluoride release, the levels achieved are generally very much lower compared to those gained with GICs and compomers.(12)

Limitations:

However, there is a concern regarding dental and skeletal fluorosis, as well as the development of fluoride resistant oral bacteria.(6)

8. Containing natural constituents:

The search for more biocompatible and dentin friendly agents that can overcome the limitations of the chemical antimicrobial agents is the current trend. Herbal products are gaining popularity in every field of medicine, mainly due to their biocompatibility and not likely to cause the severe injuries to patients that might occur. The herbal extracts also possess high medicinal properties such as anti-oxidant, antimicrobial, and anti-inflammatory properties due to their saponins, flavonoids, iso-flavonoids, chalcones, coumarins, aurones, benzofurans, phenols, pterocarpans, and stilbenes content which contribute to its pharmacological properties.(13)

8.a. Tea tree oil:

Tea tree oil's is a native Australian plant with many properties such as being an antiseptic, antibacterial and an antifungal agent.

Uses in dentistry:

Cavity disinfection: The use of tea tree oil and many natural products have shown anti-microbial properties which can be used as cavity disinfectant in the field of dentistry. A study compared the efficacy of herbal antibacterial agents (Tea Tree Oil (TTO)) with commercially available 2% chlorhexidine (CHX) as cavity disinfectant for use in minimally invasive dentistry. Post-disinfection, 2% chlorhexidine showed highest reduction in bacterial count followed by 1% tea tree oil. Therefore, natural antibacterial agents like tea tree oil could be effectively used as cavity disinfectants which will help in minimizing secondary caries and rendering a long-term restorative success.(10)

8.b. Liquorice:

It has an anti-inflammatory, antibacterial, antifungal, antiviral and anticarcinogenic.

Uses in dentistry:

- Caries prevention: Recently, liquorice has been studied extensively for its anticaries properties. He et al.,(14) concluded that liquorice had the highest antimicrobial activity against S. mutans bacteria and therefore has an anti-cariogenic effect.

- Based on this observations, Hu et al.,(15) developed a sugar-free orange flavoured liquorice lollipop for caries prevention. They found that liquorice lollipops are safe and effective against S. mutans when consumed for 10 days (twice daily) by pre-school children.

Limitations:

But, due to the anticoagulant and antiplatelet effects of liquorice there is a potential risk of increased bleeding for patients taking conventional anti-clotting medications for cardiovascular or cerebrovascular diseases.(16)

8.c. Propolis:

Propolis is a resinous hive product collected by bees. Different components of propolis contribute to its antimicrobial acions. Caffeic acid phenethyl ester (CAPE) have anticarcinogenic, antimitogenic and immunomodulatory properties.

Uses in dentistry:

- Caries prevention: Propolis is superior in reducing the salivary levels of S. mutans and Lactobacilli spp. compared to that of chlorhexidine (CHX) mouthwash. The residual beneficial effect of propolis could be observed for a further 45 days. Propolis containing chewing gum also reduced bacterial counts compared to xylitol chewing gum.(17)

- Plaque and gingivitis control: Propolis-containing mouth rinse reduces supragingival plaque and insoluble polysaccharides. Moreover, propolis in toothpaste improves oral health and exhibits inhibitory effect on dental plaque formation. Topical application of propolis improves periodontal health due to reduced P. gingivalis in the gingival crevicular fluid (GCF), probing pocket depth (PPD), and clinical attachment level (CAL) in periodontitis patients.

- Endodontic irrigant.

8.d. Siwak powder:

Uses in dentistry:

- Siwak powder containing denture base material: The effect of adding siwak powder with average particle size of (75 μm) in different concentrations by weight to PMMA on certain mechanical properties was evaluated. The results showed that addition of low concentrations (3%, 5%) Siwak to the heat polymerizing acrylic resin imparted antimicrobial properties to the acrylic resin denture base material and did not affect significantly the tensile, compressive, impact strength or surface roughness. While the addition of (7 %) Siwak powder revealed a significant decrease in tensile, impact and compressive strength.(18)

9. Combined mechanisms:

Some antibacterial agnents relie on the concept of having a combination of more than one mechanism of antibacterial actions together for additional therapeutic effect.

9.a. Nanoparticles incorporation in dental materials:

Nanoparticles (NPs) with their enhanced and unique physicochemical properties, such as ultrasmall sizes, large surface area/mass ratio, and increased chemical reactivity, have led research toward new prospects of treating and preventing dental infections.(19)

Mechanism of action of nanoparticles:

i. Interacting with peptidoglycan cell membrane content of bacteria causing increased permeability and cell lysis.

ii. Interacting with bacterial proteins and disrupting protein synthesis.

iii. Interacting with bacterial DNA causing DNA & RNA damage and preventing DNA replication.

iv. Increase the production of reactive oxygen species (ROS) resulting in increased respiratory stresses.(20)

Uses in dentistry (12, 21):

- **Quaternary ammonium polyethylene-imine (QPEI):**

- Nano-particles containing dental composite: QPEI mechanism of action is a combined mechanism. Being a nano-particle sized and containing positively charged N+ (nitrogen) in quaternary ammonium compounds that attack the negative surface charge in bacteria. Antibacterial activity of quaternary ammonium polyethylene-imine (QPEI) nanoparticles embedded in composite resins and restorative materials has been proven with effects lasting for a month. Moreover, the QPEI nanoparticles did not affect the material's mechanical properties and no leaching of the nanoparticles was detected.

- **Chitosan nanoparticles:**

- Nano-particles containing dental composite: Similarly, chitosan has a positive surface charge of chitosan. The nontoxic and antibacterial effects of chitosan have rendered this material to have multiple uses in dentistal restorations. Chitosan has been analyzed in resin-based composites and results showed that it promoted the antibacterial effects without deteriorating the mechanical properties such as surface hardness.

- Nano-particles containing intracanal medications: Incorporating chitosan NPs into a Ca(OH)2 based paste and zinc-oxide eugenol based sealer had the potential of increasing its antibacterial effect against E. faecalis . The chitosan NPs showed superior penetration into the dentinal tubules and proven antibacterial efficacy.(19)

• **Zinc oxide nanoparticles:**

- Nano-particles containing dental composite: ZnO is able to react with the moisture available in the oral cavity and creates active oxygen species such as H2O2, causing bacterial inhibition in addition to its nanosized properties. The addition of zinc oxide nanoparticles also resulted in antibacterial activity against S. mutans without compromising mechanical properties, on the contrary its addition increased compressive and flexural strength.

- Nano-particles containing intracanal medications: The bactericidal effect of zinc oxide nanoparticles was shown to be related to size and concentration. The smaller the size, the higher the antibacterial effect and the production of reactive oxygen species such as hydrogen peroxide when in contact with an aqueous medium. Also, the higher the concentration, the maximum antibacterial effect is obtained. Varying degrees of antibacterial effects against P. aeruginosa, E. faecalis, C. albicans and S.aureus were shown when zinc oxide nanoparticles were incorporated into polyethylene glycol to form a creamy mix and used as an intra-canal medicament.(22)

• **Silver nanoparticles:**

- Nano-particles containing dental composite: Silver has been used as a broad-spectrum antibacterial agent for centuries and is still one of the most frequently used antibacterial fillers for dental materials.

Silver interacts with thiol group compounds found in the bacterial cell wall, resulting in the inhibition of the respiration process. Also, Silver interferes with bacterial enzymatic activity. Silver nanoparticles have been incorporated in the formulations of dental composites and adhesives and were reported to inhibit S. mutans. Using particles on a nanoscale reduces the amount of silver compounds needed to achieve antibacterial properties, which eliminates the discoloration caused by large amounts of these compounds, and better aesthetics are acquired.

- Nano-particles containing intracanal medications: Nanonsilver root canal irrigation solution has showed high efficiency against E. faecalis. Also, incorporation of silver nanoparticles in Calcium silicate cement such as MTA showed a significant increase in their antimicrobial effects.(19)

• **Titanium dioxide nanoparticles:**

- Nano-particles containing dental composite: Titanium dioxide nanoparticles have been added to composite resin and glass ionomer cements and resulted in improved mechanical and antibacterial properties. But, even small amounts of titanium oxide (0.1–0.25 (wt.%)) can lower aesthetic properties such as translucency and discoloration of resin-based composites, which could be one of the reasons they are not added to these materials.

9.b. Photodynamic therapy (PDT):

PDT is a new antimicrobial strategy that has a combined antibacterial mode of action. The first mechanism involves the combination of a nontoxic photosensitizer (PS) and a light source. The excited PS reacts with molecular oxygen to produce highly reactive oxygen species, which induces injury and death of bacteria. The second mechanism relies on the positive charge of PDT can rapidly bind and penetrate the bacterial cells and therefore, shows a high degree of selectivity for killing microorganisms.

Uses in dentistry:

- Recent advance in root canal disinfection: When conventional endodontic therapy was followed by PDT, there was significantly more bacterial killing and less bacterial growth than endodontic therapy alone.(11)

9.c. Probiotics:

Currently, the known mechanisms of probiotic activity can include the following:

i. Competing for binding sites on the tooth surface;

ii. Competing for nutrients;

iii. Producing antimicrobial compounds to inhibit other oral bacteria, such as hydrogen peroxide.(3)

Uses in dentistry:

Probiotics are available in medicinal preparations as mouth rinses, tablets, capsules, powder, and lozenges or in the form of functional foods, in the form of culture concentrations added to beverages, dairy products such as yogurt.

The dietary probiotics are intolerant to low pH as it decreases their survival. Therefore, the commercial probiotics are needed. The commercially available probiotics are in the form of tablets or capsules which are used as a drug carrier.(23)

9.d. MTAD (Mixture of Tetracyclin Acid Detergent):

Uses in dentistry:

MTAD is an antibacterial commercially available root canal disinfectant. MTAD is a mixture of 3% tetracycline isomer (doxycycline), and 4.25% acid (citric acid), and 0.5% detergent.

One of the characteristic of this solution is a high binding affinity of the doxycycline to dentin which results in sustained antimicrobial activity. Moreover, it was reported to remove the smear layer due to its citric acid content.(11)

9.e. Sodium hypochlorite (NAOCL):

NaOCl possesses a broad spectrum antimicrobial activity against microorganisms and biofilms difficult to eradicate from root canals such as Enterococcus faecalis , Actinomyces and Candida species. Sodium hypochlorite mediate its antimicrobial action by reacting with fatty acids and amino acids. It acts as an organic and fat solvent, degrading fatty acids. Also, it acts by denaturing proteins in the biofilm matrix and inhibiting major enzymatic functions in bacterial cells. The antimicrobial effectiveness of sodium hypochlorite is also based on its high pH (pH>11). Such high pH results in an irreversible enzymatic inhibition and an alteration in cytoplasmic membrane integrity. (4, 24)

Uses in dentistry:

- Endodontic irrigant: Sodium hypochlorite (NaOCl) has been the most widely used root canal irrigant. This is due to its excellent antimicrobial activity and its ability to dissolve pulpal remnants and organic components of dentin. The concentration of NaOCl that is considered both safe and effective is still controversial. Concentrations of NaOCl ranging from 0.5% to 5.25% have been evaluated. Studies reported that higher concentrations of NaOCl resulted in a more rapid and greater bactericidal effect, but unfortunately, more cytotoxic effects were evident.(4, 24)

9.f. Calcium hydroxide:

Antimicrobial activity of calcium hydroxide is related to the release of hydroxyl ions (OH-) in an aqueous environment causing damage to the bacterial cytoplasmic membrane, protein denaturation and damage to their DNA content. The high pH of calcium hydroxide alters the biologic properties of bacterial lipopolysacharide present in the cell walls of gram-negative species.

Uses in dentistry:

- Pulp capping material: Calcium hydroxide is a white odorless powder that was originally introduced to the field of endodontics as a direct pulp-capping agent. It is the most commonly used inter-appointment dressing. (11)

Recent advances and future perspectives in dental restorations with antibacterial properties

Smart dental materials for antibacterial applications (Bioresponsive antimicrobial restorations)

The last 20 years have witnessed a transformative evolution of antimicrobial dental materials. The field is switching from offering "passive" treatments to "smart" antimicrobial biomaterials that are triggered by different internal and external stimuli to deliver "on-demand" therapies with improved control of dosage, location, duration, and efficacy. Smart biomaterials can sense and react to physiological or external environmental stimuli (e.g., mechanical, chemical, electrical, or magnetic signals).

The last decades have seen exponential growth in the use and development of smart dental biomaterials for antimicrobial applications in dentistry. Recent advances in technology and manufacturing tools are enabling the development of "smart" dental materials that offer multiple functionalities for different therapies.(25)

Classification of smart biomaterials according to its smartness:

Four levels of smart biomaterials were defined, including

- **Bioinert:** Bioinert biomaterials cause minimal interaction with surrounding tissues and have minimal harm or toxicity to the surrounding tissues after implantation. For example, polymethyl methacrylate (PMMA).

- **Bioactive**: Active or bioactive materials induce a specific biological response at the material-tissue interface after implantation or contact with tissues, cells, or body fluids. These biomaterials release the therapy "uncontrollably" after being installed in the body. For example,"fluoride-releasing compounds".

- **Bio responsive**: Responsive, bioresponsive, or stimuli-responsive biomaterials can "sense" a specific stimulus (e.g., light, temperature, pH changes, enzymes) and then "respond" by releasing a pre-programmed therapy. For example, a dental composite is fabricated with pH-sensitive NPs that deliver antimicrobial agents under certain pH levels (acidic) to treat caries.

- **Autonomous:** autonomous biomaterials can sense, react and adapt to multiple stimuli. They adjust their response accordingly to offer an appropriate response for each need at different time points. This class of biomaterials is the smartest.(25)

Bio-responsive (smart) antimicrobial therapies

Generally, the antimicrobial agent is incorporated into a carrier/ vehicle (a biomaterial), designed to respond to the specific stimulus by changing its properties (e.g., degradation). To release the antimicrobial agent, some carriers may vary their structure or properties after responding to the stimulus.

a. pH-responsive biomaterials:

They respond to the changes in the pH level of the surrounding medium or microenvironment. Depending on their design, biomaterials may expand, collapse, or change a specific property. For example, in an acidic environment, some hydrogels may expand (structural change) to release the drugs, while basic pH levels force the hydrogel’s collapse and the drugs remain protected and unreleased.For example, the pH range of the microenvironment of active dental caries is 4.5–5.5, while in physiological conditions, saliva has a normal pH range of 6.2–7.6. As a result, pH-responsive biomaterials have become an attractive choice to be used in the treatment of caries, periodontitis, and peri-implantitis.

A recent work designed a N-dimethylaminoethylmethacrylate (DMAEMA)-co-2-hydroxyethyl methacrylate (HEMA) (poly(DMAEMA-co-HEMA) hydrogel capable of releasing CHX in response to pH levels to prevent and treat dental caries. This bioresponsive biomaterial inhibited the development of S. mutans biofilm and regulated the oral microecosystem.(25)

b. Enzyme responsive biomaterials:

Salivary and bacterial enzymes act as trigger (or signal) to release antimicrobial agents (as antibiotics or NPs) for treatments. Bacteria and fungi secrete various enzymes, including lipase, esterase, phosphatase, urease, gelatinase, and many more. Some of these enzymes have been established as the marker to indicate active stage of disease. For example, a bacterial by-product in chronic periodontitis is the enzyme matrix metalloproteinase-8 (MMP-8).

This enzyme has been used as a stimulus in bioresponsive delivery systems for managing periodontitis. Activation using MMP-8 has been used in a hydrogel made of gelatin methacrylate (GelMA) loaded with CHX and aluminosilicate nanotubes. The presence of MMP-8 degrades the hydrogel in 20 days and provides a sustained release of CHX for dental infection treatment.(25)

c. Electrically responsive biomaterials:

The effect of electrical currents on microbial biofilms has been studied for several years as an alternative to chemical therapy without leading to antibiotic resistance. The capacity of electrical charges to destroy pathogens depends on the the electrical charge magnitude, density, and polarity. Several mechanisms are proposed to explain the killing ability of electrical charges. These mechanisms include the direct contact theory, in which the electric current directly results in bacterial death by disrupting the integrity of the cell membrane.

For example, The concept of using electrical current as an antibacterial mechanism has been mostly tested in metallic implants. Electrically polarized materials possess electrical charges at the surface due to polar or electric properties. The use of polarized substrates such as HAp has antibacterial activity against gram-positive and gram-negative bacterial strains.(25)

d. Magnetic responsive biomaterials:

In antimicrobial applications, magnetic NPs have been used mainly for positioning or moving the antibacterial agent closer to the infection site. This is highly attractive in dentistry since infected sites are usually deep within tissues and inaccessible to treatment. For example, a urethane dimethacrylate (UDMA)-HEMA system filled with CHX loaded with magnetite Fe_3O_4 NPs showed a significant antimicrobial effect against P. gingivalis for periodontal disease treatment. Under a magnetic field, the CHX/Fe_3O_4 compounds not only can move to the site of infection, but also the movement releases the CHX to the targeted place.(25)

Antibacterial coatings

Titanium and titanium alloys are widely used in orthopedic and dental implants, but infection associated with these implants still poses serious threat leading to possible complications. The implant surface is susceptible to infection because of two main reasons: formation of a surface biofilm and compromised immune ability at the implant/tissue interface. A surface protein layer is formed under physiological conditions on the implant surface. This protein layer actually makes the surface suitable for bacterial colonization and biofilm formation.

Biofilms are defined as a microbially derived sessile community characterized by cells irreversibly attached to a substratum. The biofilm protects adherent bacteria from the host defense system and bactericidal agents. However, the low sensitivity of bacteria to antibiotics induced by the biofilm growth, together with the increasing number of resistant strains, makes the use of antibiotics currently less effective than it has ever been. To prevent such infections, one approach is to improve the antibacterial ability of the materials. Therefore, as an alternative to the use of antibiotics to prevent bacterial infection or to treat established biofilms, surface coatings that prevent viable bacteria from adhering has been developed.(26)

Many different chemical strategies and technologies for antibacterial coatings are described in the literature. For example, antibacterial coatings may contain active eluting agents (e.g. ions or nanoparticles of silver, copper, zinc, or antibiotics, chloride, iodine, etc.), immobilized molecules that become active upon contact (e.g. quaternary ammonium polymers or peptides). In addition to surface and chemical modifications.(26)

Strategies to achieve antimicrobial coatings can be classified as:

1. Safe-by-design strategy (passive).

2. Toxic by design strategy (active).

1. Safe-by-design strategy (passive):

The topography of a surface can by itself significantly affect its hygienic status in a beneficial manner (reducing microbial retention). This is known as the "Anti-adhesive strategy". Anti-adhesive surfaces "Repellant surfaces" or "Antifouling surfaces" can reduce the adhesion force between bacteria and a solid surface to enable the easy removal of bacteria before a biofilm layer is formed on the surface (but they will not reduce the number of germs by killing them).

Attachment of bacteria starts with an initial adsorption of proteins onto the material surface. Hence, elimination of bacterial attachment is achieved by prevention of protein adsorption through; superhydrophobicity and nanostructures or repellant action induced by electrostatic repulsion. (26, 27) Therefore, anti-adhesive/passive strategy is based on the prevention of bacterial adhesion on the implant surface and can be classified into:

1.a. Superhydrophobicity and nanostructures.

1.b. Electrostatic repulsion.

1.a. Superhydrophobicity and nanostructures:

Superhydrophobic surfaces are characterized by a water contact angle of over 150° and they are inspired by natural mimimcingof the Lotus leaf in nature and animals skin architecture as sharks. It was further revealed that the Lotus leaf has a hierarchical micro/nanostructure surface. In general, topographies at the micro-scale do not have bactericidal effects but may limit bacterial adhesion. While in contrast, nano-topographic features cause high deformational stresses on the bacterial membrane leading to their rupture.

Also, effective air entrapment in the three-dimensional nanomorphology in nanostructures renders them superhydrophobic and slippery enables bacteria to “roll off” the surface. Immobilization of superhydrophobic molecules that can resist protein adsorption such as; Poly Ethylene Glycol (PEG), have demonstrated great anti-adhesion properties in vitro and considered as the standard approach for antiadhesive coatings. (25, 26, 27)

1.b. Electrostatic repulsion:

Electrostatic repulsion is a mechanism used in some implant coatings to prevent bacterial adhesion. The electrostatic repulsion mechanism is based on the principle that like charges repel each other. When the surface charge of the implant coating is negative, it repels negatively charged bacteria and prevents them from attaching to the surface. This mechanism can be effective in preventing bacterial colonization and biofilm formation, which are key steps in the development of implant-associated infections.

Coating titanium surfaces with a negatively charged polymer and then exposing them to Staphylococcus aureus, a common bacterial pathogen. The negatively charged surface repelled the bacteria and prevented them from adhering to the surface. (28)

2. Toxic by design strategy (active):

This strategy aims to kill bacteria that exist on the material surface through the release of a toxic substance. It is known as “Bactericidal/Biocide release strategy” and can be classified into:

2.a. Release of antibacterial substances from the materials.

2.b. Contact killing.

2.a. Release of antibacterial substances from the materials:

These coatings typically incorporate antibacterial agents such as antibiotics, antimicrobial peptides, or metal ions that are released from the coating and diffuse into the surrounding tissue to kill bacteria. The bactericidal mechanism of these coatings is based on the ability of the antibacterial agent to disrupt bacterial cell membranes or interfere with essential cellular processes, leading to bacterial death. When incorporated into implant coatings, these agents can prevent bacterial colonization and biofilm formation, reducing the risk of implant-associated infections.

However, one of the challenges of using bactericidal coatings is the potential for the development of bacterial resistance to the antibacterial agent over time. This can limit the long-term effectiveness of the coating and increase the risk of infections. Additionally, there are concerns about the safety and biocompatibility of some antibacterial agents, particularly those that are highly toxic or have off-target effects. Also, they will gradually become inactive (26, 27)

2.a.1. Hydroxyapatite (HA) and Calcium Phosphate (CP) coatings:

Dental implant coatings incorporating hydroxyapatite (HA) and calcium phosphate (CaP) have been studied for their antibacterial properties due to their biocompatibility and osteoconductive properties. The antibacterial activity of these coatings is attributed to their ability to release ions, such as calcium and phosphate, which can interfere with bacterial metabolism and growth.

It was concluded that, amorphous CP and HA nanoparticles displayed antibacterial effect against a number of bacterial species including; S. aureus, S. epidermis, E. coli and P. aeruginosa. Also they have similar levels of activity against Gram-negative bacteria, however, ACP was more effective against the Gram-positive ones. (29, 30)

2.a.2. Chlorhexidine based coating:

Chlorhexidine-based coatings have been studied for their antibacterial properties in dental implant applications. Several studies investigated the use of a chlorhexidine coating on titanium implants. The chlorhexidine coating was found to significantly reduce bacterial adhesion and biofilm formation on the implant surface, while also promoting osteoblast activity and bone formation. (31)

2.a.3. Carbon nanotubes, Graphene oxide or Diamond-like carbons coatings:

Surface coating with carbon nanotubes (CNTs), graphene oxide (GO) or diamond-like carbons (DLCs) showed interesting antibacterial activity since these materials show relatively low cytotoxicity towards mammalian cells. It seems that GO based materials show higher antibacterial activity. The most commonly mechanisms of action are: oxidative stress induction, protein dysfunction, transcription arrest and membrane damage.(27)

2.a.4. Metal nanoparticles based coatings:

Metallic coatings based on metal nanoparticles as silver, copper and golsd has been successful because of their extensive antimicrobial activity. The main disadvantage of metallic nanoparticles coatings are cytotoxicity and resultant decreased biocompatibility.(32)

Examples:

- Silver nanoparticles (AgNPs) coating: A study compared the bactericidal effects of Ag NPs-coated polyethylene terephthalate (PET) mesh against S. aureus and E. coli, with an uncoated one. It was found that Ag NPs-coated PET mesh displayed excellent antibacterial property against Staph. aureus and Escherichia coli with 99% bacterial reduction rate compared to the untreated PET mesh.(33)

- Copper nanoparticles (CuNPs) coating: Possess a lower antibacterial efficacy than that of AgNPs and hence a higher doping of CuNPs is always desired to achieve the similar effect. (34)

- Gold nanoparticles (AuNPs) coating: Biocompatible, exhibited low toxicity to mammalian cells. Proved to be effective against both Gram-negative and positive pathogens and the development of resistance to these NPs was very low. Only AuNPs with size below 3nm are cytotoxic.(35)

2.b. Contact killing:

In contact-active surfaces, the biocidal group is attached to the surface through a polymer chain allowing the biocide to reach the cytoplasmic membrane of the bacteria and to perforate them. Bacteria secrete signaling molecules enabling cell to cell communication and regulation of several bacterial processes (quorum-sensing, QS). Consequently, molecules that target and disrupt QS have been considered antibacterial agents. QS-inhibiting molecules demonstrated excellent in vitro antibacterial properties. Moreover, they are less likely to induce the development of resistance. The most effective compounds for contact-killing coatings are quaternary ammonium compounds (QACs), antimicrobial enzymes (AMEs), chitosan and antimicrobial proteins (AMPs) derived from human salivary proteins.(36)

Recent advances and future perspectives in antibacterial implant coatings

Recent developments in antibacterial implant coatings have focused on improving their effectiveness, biocompatibility and longevity. They include:

1. Hybrid coatings/Combination coatings:

Sometimes two functional strategies are combined to achieve synergistic effects, e.g. by embedding antibacterial substances into antiadhesive surfaces. This is known as "Hybrid coating". Combining different types of antibacterial coatings can improve their overall effectiveness and reduce the risk of bacterial resistance. For example, nanostructured hydroxyapatite (nHA) coating was prepared on titanium (Ti) surface and then the antibacterial agent of chitosan was loaded on the HA surface. The results showed that the hybride nHA/chitosan coating against E. coli inhibited the bacterial growth, and improved biological and antibacterial properties.(37)

2. Smart antibacterial coatings:

Smart implant coatings are coatings that can respond to external stimuli, such as changes in temperature, pH, or chemical composition. These coatings are designed to provide a controlled release of antibacterial agents in response to specific conditions, allowing for targeted and efficient antibacterial activity.

- **pH-responsive coating** can release antibacterial agents in response to acidic conditions. This type of coating can be particularly useful in preventing bacterial infections associated with acidic conditions, such as those that occur in the mouth. For example, coating made from chitosan which has amino groups that can be protonated or deprotonated depending on the pH of the surrounding environment. At acidic pH, the amino groups on chitosan are protonated, giving the coating a positive charge. At neutral or basic pH, the amino groups are deprotonated and the coating becomes neutral or negatively charged. This pH-dependent charge switch can be used to control the release of drugs or other molecules from the coating.(38)

- **Temperature-responsive coating** can release antibacterial agents in response to changes in temperature. This type of coating can be used to prevent bacterial infections associated with inflammation and fever, which can increase the temperature of the implant site.

- **Enzyme-responsive coating** can release antibacterial agents in response to specific enzymes produced by bacteria as phospholipase A2 (PLA2). This type of coating can be used to target specific types of bacteria and prevent biofilm formation, which can be particularly difficult to treat with traditional antibiotics.(39)

- **Photosensitizer implant surface coatings** are a type of antibacterial coating. It is a polymeri containing photosensitizers, such as toluidine blue, immobilized within a polymer matrix. The phoosensitizer is a molecule that can absorb light energy and become excited to generate ROS, which can then damage bacterial cells and lead to bacterial death. These coatings have several advantages, including their ability to selectively target and kill bacteria without damaging host cells and their potential for reducing the development of antibiotic-resistant bacteria. However, there are also some challenges associated with these coatings. One major challenge is ensuring that the photosensitizer remains stable and effective over time, as it can degrade and lose its antibacterial activity if not properly stored or handled. Additionally, the use of light as an activation mechanism may limit the applicability of these coatings in certain clinical settings.(40)

N.B: Stimuli-responsive materials are considered controlled release coatings that release therapeutic agents in a controlled and sustained manner, which can enhance the effectiveness of these agents and reduce the risk of systemic side effects. Controlled release coatings can also minimize the risk of toxicity to surrounding tissues.

3. Zwitterionic coatings:

Zwitterionic dental implant coatings refer to a type of coating composed of molecules that contain both positive and negative charges, which allows them to form a stable layer on the surface of the implant. The term "zwitterionic" comes from the German word "zwitter," which means hermaphrodite or hybrid. In the case of zwitterionic coatings, the molecules have both positive and negative charges, which makes them highly resistant to protein adsorption and bacterial attachment. Zwitterionic coatings can also enhance the biocompatibility of dental implants by reducing inflammation and promoting tissue integration. They can also improve the mechanical properties of the implant surface by increasing its hardness and wear resistance.

The coatings work by creating a repulsive force that prevents bacterial adhesion to the implant surface, as well as promoting the adsorption of proteins that enhance tissue integration. One proposed mechanism is the hydration layer model, which suggests that zwitterionic coatings create a hydrated layer on the implant surface that repels proteins and bacteria. This layer consists of water molecules that are attracted to the positive and negative charges on the zwitterionic molecules, creating a barrier that prevents protein and bacterial adhesion. One example of a zwitterionic coating for dental implants is poly(sulfobetaine methacrylate) (PSBMA). (41)

Challenges of antibacterial coatings (25):

Despite these recent advances, there are still several challenges that need to be addressed in the development of antibacterial implant coatings before they can be widely used in clinical practice. More research is needed to understand their long-term effectiveness and safety, as well as to develop coatings that are effective against multiple bacterial mechanisms and have good biocompatibility.

1. Long-term effectiveness: Typically, the antimicrobial effect of a leachable agent is less than 1 year. Once depleted, the agent could not be recharged. Uncontrolled release of antimicrobial agents challenges the delivery of an appropriate dose. This uncontrolled release can speed up the agent depletion or provide insufficient amount of agent for therapy. This has been avoided to some degree by using nano-carriers and stimuli responsive smart coatings.

2. Bacterial resistance: Antibacterial coatings can also lead to the development of bacterial resistance, which can reduce their effectiveness over time. The lack of bacterial targeting can cause collateral damage (killing of commensal species) and a potential imbalance in the oral microbiota since the therapy will "attack" everything it encounters in the microenvironment. To address this challenge, coatings that target multiple bacterial mechanisms and combinations of coatings should be investigated.

3. Biocompatibility: Some antibacterial coatings (bactericidal release strategy) that leach and release antibacterial agents can be toxic to surrounding tissues, leading to inflammation and other complications. Therefore, Biocompatibility of coatings should be carefully studied to avoid adverse reactions.

Although several clinical trials have successfully evaluated the use of NPs in different dental materials as antimicrobial agents , the wide use of NPs in clinical practice is limited due to concerns regarding the release of toxic ions that could cause inflammation, immunotoxicity, cytotoxicity, and genotoxicity in healthy cells.

4. In the case of safe by design strategy: Antimicrobial polymers have significant limitations regarding the high selectivity against gram-positive strains, the lack of standardized methods for testing the performance of the antibacterial coatings under representative environmental conditions and high cost of manufacturing.

(Although they overcome some drawbacks of the leachable chemical therapies such as long-term activity, no leaching or exhaustion of the antimicrobial compound, limited toxicity against mammalian cells, reduced antimicrobial resistance, and increased chemical stability)

5. Regulatory approval: To be used in clinical settings, antibacterial implant coatings must meet regulatory approval. It can be a long and expensive process, which can delay the development and implementation of new coatings.

Finally, many antibacterial coatings have been shown to be effective in vitro or in animal models, but their long-term effectiveness in humans is still unclear. More research is needed to understand the long-term outcomes of these coatings in clinical settings.

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Biomaterials Journal

http://www.biomatj.com

Online ISSN: 2812-5045

Type of the Paper (Review Article)

Bonding of posts to tooth structure

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Citation: Reem A. Hany . ***Bonding of posts to tooth structure*** . *Biomat. J., 2 (7),30 – 37 (2023).*

https://doi.org/10.5281/znodo.5829408

Received: 25 July 2023
Accepted: 30 July 2023
Published: 31 July 2023

Citation:

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Abstract: The prognosis of endodontically treated teeth depends not only on the success of the endodontic treatment, but also on the type of reconstruction. These considerations include the decision of whether or not to use posts. While metal posts have been the standard for many years, nonmetallic posts have been introduced to address the need for a more esthetic material in the anterior region. One of the most important factors affecting post retention is the luting agent and the bonding procedure steps.

Keywords: Metal posts, fiber posts, resin based cements, self etch, total etch, dual cured resin cements

Introduction

In the recent years there have been significant advances in the development of bondable, fiber-reinforced and ceramic esthetic posts to reinforce endodontically treated teeth. The survival and long- term success of endodontically treated teeth with posts are affected by many different factors:

i. Factors related to the surface properties of the post that if not optimized, failure at cement-post interface may occur.

ii. Factors related to the adhesion strategy that if not adequately applied failure at cement-dentin interface could occur.(1)

Luting agent:

One of the most important factors affecting post retention is the luting agent. The use of resinous cements has increased, and studies have reported higher retention values and resistance to fatigue for these cements compared to brittle zinc phosphate cements used widely in the past. This is due to, the modulus of elasticity of resin cements approaches that of dentin, and therefore they may have the potential to clinically reinforce thin-walled roots. On the other hand, resin cements are technique-sensitive because of their short working time, the number of operating steps involved, and the sensitivity to moisture, compared to zinc phosphate cements.(1)

Bonding of post to tooth structure:

a. Cement-post interface.

b. Cement-dentin interface.

a. Cement-post interface:

a.1. Bonding to fiber-reinforced posts:

Fiber-reinforced posts consist of fibers (glass, carbon, quartz, or polyethylene) embedded in a polymer–epoxy resin matrix. The purpose of the fibers is to increase the tensile and fatigue strength of the post and to enhance its volumetric stability. The epoxy matrix is highly cross-linked, with a very high degree of polymerization conversion. Its purpose is to support and protect the fibers.

Since fiber posts are passively retained into the root canal, the effectiveness of the adhesive cement and the luting procedure plays a relevant role in the overall clinical performance of the restorations. The most common technical complication of endodontically treated teeth restored with fiber posts is post debonding. This is due to:

◎ The high degree of polymerization conversion of the resin matrix in fiber posts that result in a poor bond between resin cements and the post surface because of the lack of free functional groups.(2)

To overcome this issue, ultra-high molecular weight polyethylene fibers coated with a dentine bonding agent (which contains free functional groups) are used to build-up endodontic posts and cores. As the fibers adapt to the root canal, canal enlargement is not required. The woven fibers have a modulus of elasticity similar to that of dentine and are claimed to create a dentine-post-core mono-block, through chemical bonding with the resin based adhesive system, allowing for a more favorable stress distribution along the root.(3)

Surface treatment of fiber posts:

Many techniques suggest surface treatment of the fiber post surface to increase the adhesion of resin cements. Surface treatment is a common method for improving the adhesion properties of a material, by facilitating chemical and micro-mechanical retention between different constituents. These procedures fall into three categories:

1) Chemical bonding between a composite and post:

Silane coupling agent is a hybrid organic-inorganic compound that is able to increase surface wettability and create a chemical bridge between the methacrylate groups of resin and the hydroxyl groups of the exposed quartz and glass fibers. A chemical bond may be achieved between the core resin matrix and the exposed glass fibers of the post at the interface level. Using silanization as a preparation of the post before the cementation is well investigated and it's known that the interfacial strength is still low because of the absence of chemical union between the methacrylate-based resin composites and the epoxy resin matrix of fiber posts (fiber posts don't have enough free functional groups to react with silane). However, silane could be effective when it follows other post pretreatment techniques.(1, 2)

2) Surface roughening of the post:

Non-treated fiber posts have a smooth surface area that limits mechanical interlocking between the post surface and resin cement.

◎ Sandblasting with alumina particles or silica oxide results in an increased roughness of the surface. In addition, by using silicate-coated alumina particles, surface area is not only increased, but also a silicate layer is welded onto the post surface. This silicoating that is followed by silanization is referred to as 'tribo-chemical coating' can be performed in the laboratory (Rocatec system) or at the chairside (Cojet system).

However, the treatment was considered too aggressive for fiber posts and the main problem related to this technique is that there is lack of selectivity; both the matrix and the fibers of the post are affected.(1, 4)

◎ Acid etching using hydrofluoric acid, because silica and quartz present in fiber posts are comparable in chemical structure with ceramic material, hydrofluoric acid has recently been proposed for etching fiber glass posts. It is intended to create a rough pattern on the glass fiber posts surface, which allows for micromechanical interlocking with the resin cement and composite. Despite the improvement in post-to composite bond strength, a remarkable surface alteration, varying from microcracks to longitudinal fractures was found. Although the bond strength was increased by prolonged acid etching, the microstructure of the FRC posts might have been damaged. Also, etching by 37% phosphoric acid (H3PO4) for 15 second is a better and comfortable alternative to other methods in improving the adhesion of fiber post to root canal dentin.(1)

Because these above-mentioned techniques can sometimes damage the glass fibers and affect the integrity of the posts, substances that selectively dissolve the epoxy matrix without interfering with the fibers have been studied. Potassium permanganate, methyl chloride, sodium ethoxide, and hydrogen peroxide (H2O2) remove the epoxy resin and expose the fibers which are then available to be silanated. H2O2 at concentrations of 10% and 24% effectively removes the surface layer of the epoxy resin. The main disadvantage in using H2O2 is the prolonged time for etching (20 minute).(1, 2)

The application of surface treatments might negatively affect the light transmission property of fiber posts which limits the curing rate. Also, the unreacted monomers as a result of incomplete polymerization of the resin cements, might leak through the apical root filling and could result in inflammatory, cytotoxic, and mutagenic reactions of periodontal tissue.

3) Combination of micromechanical and chemical components by using the two above-mentioned method:

◎ For example, Hydrofluoric acid in combination with a silane-coupling agent is often employed to increase the bond strength between composite resins and feldspathic ceramics.(1)

a.2. Bonding to zirconia posts:

High flexural strength, high fracture toughness, chemical stability, biocompatibility, and favorable optical properties are advantageous characteristics of zirconia as a restorative material. However, when used for endodontic posts, zirconia has revealed some major limitations. In relation to its rigidity zirconia posts are more prone to cause root fractures than fiber posts. Also, the surface of zirconia posts does not bond to resin composite materials. Zirconia posts can be pre-treated by silicoating followed by salinization which results in an increased surface. However its main disadvantages are the high modulus of elasticity of zirconia that can lead to vertical root fracture and it is practically impossible to grind off luted zirconia post if endodontic retreatment is required.(3)

a.3. Bonding to metallic posts:

Metallic posts can be fabricated from high noble alloys or various types of base metal alloys (nickel-chromium alloys, stainless steel, and titanium). A resin-based cement material could bond to a metal oxide layer through hydrophilic bonds. However, this bond is relatively weak and prone to hydrolysis. Techniques attempting to enhance the bond quality between metal surfaces and resin-based cements can be mainly divided into 2 categories: surface modification techniques and techniques involving the application of primers containing functional monomers.(2)

a.3.i. Surface modification techniques (2):

Generally, surface modification techniques could be used for both noble and base metal alloys:

◎ Include pyrochemical silica coating techniques, tribo-chemical coating systems, titanium dioxide coating systems, and spark erosion. These techniques create a silicified oxide layer on the metal surface.

◎ The tinplate technique increases the bond strength of composite resins to noble alloys through the electrochemical deposition of a layer of tin.

◎ The disadvantage of those techniques is that they are more complicated procedures and require special equipment. Also, they cannot be easily applied chairside.

a.3.ii. Techniques involving the application of primers containing functional monomers (2):

Functional monomers contain groups of atoms or bonds that are responsible for a specific chemical reaction. These functional monomers have a chemical affinity to metals and copolymerize with the structural monomers of resin-based materials. Primers can be divided into primers for base metal alloys/titanium, primers for noble alloys, and universal primers.

◎ Base metal alloy primers include functional monomers that contain phosphate or carboxylic acid functional groups. Examples include 10-methacryloyloxydecyl dihydrogen phosphate and 4-methacryloyloxyethyl trimellitate anhydride, which create an ionic bond with resin-based products.

◎ Noble metal alloy primers include functional monomers that contain thionic groups. An example is 6-(4-vinylbenzyl-n-propyl) amino 1,3,5-triazine-2,4-dithiol, dithione tautomer, which also creates an ionic bond.

Finally, the universal primers consist of a combination of monomers, one for base metal alloys and one for noble alloys. They may consist of dual functional monomers, which contain both phosphate and thionic functional groups in a single molecule. An example is thiophosphate methacryloyloxyalkyl. The main advantage of universal primers is that only one primer is necessary and can be applied to any kind of alloy.

Air-particle abrasion with aluminum oxide (Al2O3) particles is necessary for the primers to be effective. The chemical affinity of aluminum particles to phosphate monomers may be responsible for the improved performance of primers after air-particle abrasion. It may act through increasing the surface area (micromechanical retention), decrease of surface tension (adhesion and wettability) and/or oxidization of base metal alloys (chemical bond). However, air-particle abrasion may alter the character of the metal surface. Aluminum oxide particles may get trapped and partially cover the original alloy elements in the superficial layer.

b. Cement-dentin interface (bonding to radicular dentin):

Procedures related to endodontic treatment, post space preparation, and post cementation may further impact the quality of the adhesive interface and there are ways to overcome some of these potential problems.(2)

◎ Achieving stable adhesion to intra-radicular dentine, particularly at the apical level, remains a clinical challenge, due to the negative influence of several intervening factors. Chemo-mechanical preparation materials containing peroxides, sodium hypochlorite and glycol (RC-Prep) may decrease the bonding capability of resin cements to radicular dentin. Residual peroxides may oxidize the dentin collagen network or may further break down into oxygen, inhibiting the polymerization of resin-based products. Glycol lubricant may be difficult to be removed and may inhibit proper monomer polymerization. Therefore, the solution is using ascorbic acid or sodium ascorbate which act as reducing agents and may reverse the negative oxidizing effects of sodium hypochlorite (NaOCl) or RC-Prep on certain adhesive systems.(5)

◎ The use of eugenol-based sealers during endodontic treatment has adverse effects on the polymerization of composite resin materials. The effect of eugenol is also time dependent because it may continue to penetrate the dentin tubules over time. Therefore, the solution is that the remnants of eugenol in the root canal can be removed by irrigating ethyl alcohol or etching with 37% phosphoric acid. In addition, the use of eugenol based sealers has been limited in favor of resin based sealers or ceramic sealers that do not inhibit the polymerization of composite resins.(6)

◎ During post space preparation, reamers are used to remove gutta-percha (GP), which results in a heat-plasticized smear layer (secondary smear layer) rich in endodontic sealer and GP remnants. There is no scientific data to suggest that this type of smear layer can be successfully removed by etching. Also, the absence of a chemical bond between the polyisoprene component of GP and the methacrylate component of resin cements may further jeopardize the bond to dentin. Therefore, the solution is using EDTA, phosphate etching and sodium hypochlorite (NaOCl) or chlorhexidine irrigation that may eliminate the radicular smear layer more efficiently. However, the oxidizing effect of NaOCl may not be compatible with all bonding agents. In addition, the use of ultrasonic instrumentation in association with EDTA rather than rotary instruments has been suggested.(2, 5)

◎ Etchants may not flow completely in the root canal, causing inadequate exposure of the collagen fibers. Furthermore, etchants cannot be removed completely, and residual etchants (self-etch adhesive that contains acidic monomer etchant & no rinsing) may cause low pH-related inhibition of polymerization of resin-based materials (due to the reaction between acidic components and amide groups present in the resin system. The amide groups are susceptible to protonation under acidic conditions, leading to a change in their chemical structure and they become less reactive towards the polymerization reaction. This protonation reaction can inhibit the polymerization reaction at low pH levels). Also, the presence of excessive amounts of moisture is another challenge in the root canal environment and voids between posts and root canal walls are evident when resin cement is used. Therefore, the suggested solutions are:

1. Self-etching and self-adhesive systems with co-initiator/co-activator may perform better than etch-and rinse systems in the root canal because they are less sensitive to the moist radicular environment. These alternative co-initiators/co-activators offer advantages in terms of stability, reactivity, and compatibility with acidic environments. By incorporating these initiators into self-etch adhesives, manufacturers aim to ensure efficient polymerization and enhance the overall performance of the adhesive systems. In addition, the adhesion mechanism of self-adhesive systems is related with the micromechanical bonding and chemical interaction between the acid monomers and hydroxyapatite.(1)

2. Intracanal air-drying could be more effective than paper points in the removal of solvents and water, resulting in improved push-out bond strength when a self-etching adhesive is used.(2)

3. The use of an injection delivery cement system or a rotary spiral paste filler may also reduce voids and air entrapment, resulting in enhanced bond strength of fiber posts to dentin.(2)

4. Preparation of radicular dentin with chlorhexidine solution or ethanol may improve the durability of the bond when a self-etching system is used. Chlorhexidine inhibits degradation caused by dentin matrix metalloproteinases, and ethanol facilitates better penetration of hydrophobic monomers into dentin.(2)

◎ Incomplete light penetration in the post space can result in incomplete polymerization of both the adhesive agent and the resin cement. Therefore, the solution is using translucent glass or quartz fiber posts that allow more transmission of light into the root canal space, resulting in increased cure depth. In addition, enhanced light penetration combined with dual cured resin cements may result in improved polymerization and provide the most reliable option for achieving proper cement polymerization all along the dowel space. Self-cured is not advisable because they have worse handling characteristics because of their fast and uncontrolled polymerization.(3, 7)

◎ Even if there was successful etching and monomer penetration into the radicular dentin, the configuration of the root canal (C-factor) may not be favorable. The root canal simulates a very deep class I cavity in which the c-factor value may exceed that of 200, resulting in uncontrolled resin polymerization contraction. The resulting stress from volumetric shrinkage may exceed the bond strength with radicular dentin. Therefore, the solution may be using slow setting cements which have the potential to provide stress relief during polymerization. Some manufacturers claim that self-adhesives have lower polymerization stresses. In addition, others suggested that using low filled composite resin results in lower stresses due to its lower modulus of elasticity.(2)

Microleakage and Degradation of Adhesive Systems (2):

Microleakage is a phenomenon that happens in both adhesive and non-adhesive systems with a gap size of 10–20 μm. Microleakage follows nanoleakage, which occurs in non-visible gaps within the hybrid layer that have an approximate size of 20–100 nm. Nanoleakage may be due to incomplete polymerization of the adhesive or the presence of nanometric spaces around the collagen fibers that were not completely infiltrated by the adhesive monomers. These phenomena have been identified in teeth restored with fiber posts in which gaps occur between the dentin and the cement and not between the cement and the post surface. Microleakage results in the presence of water molecules in the adhesive interfaces. Both composite resin materials and fiber posts absorb water over time through a process called diffusion. Hygroscopic expansion of composite resin materials may partially counteract polymerization shrinkage stress, which causes the cement to fill shrinkage-related voids.

Degradation of the endodontic adhesive systems can be chemical or mechanical. Chemical degradation is a direct result of microleakage and is related to the presence of water and enzymes. These enzymes can cause hydrolysis of resin components, detachment of resin fillers, and hydrolysis of the exposed collagen fibers. Mechanical degradation is related to the forces that an adhesive interface is subjected to while chewing. The materials used in adhesive systems exhibit different moduli of elasticity, causing stress concentration at the various interfaces. When the adhesive interface degrades, separation and micromovement between different bonded materials may occur then further leakage and caries are expected. In addition, subsequent contamination of the apical terminus can occur. (7) Also, thermal changes that occur due to the differences in the coefficient of thermal expansion and contraction of the materials at the adhesive interfaces can induce further stress. Therefore, the chance of failure increases as the number of participating interfaces increases.

Additional factors affecting post retention(1):

a) Post length:

The length of the post influences stress distribution in the root, and thus affects its resistance to fracture. When the length of the post is increased the retentive capacity also increases, but a long post preparation increases the risk of root perforation. A common recommendation has been that the length of the post should be equal to or bigger than the length of the crown. Other criteria concern is the apical seal of the root canal. It has been suggested that leaving at least 4-5 mm of root-filling material is necessary to maintain the apical seal.

b) Post diameter and remaining dentin:

Ideally, the post diameter should be less than one third the diameter of the root at the cementoenamel junction and 1 mm or more of dentin should remain around the post. Post removal, internal resorption, or current coronal flaring to gain access to the apical aspect may result in decreased dentin thickness at the coronal part. The reduced thickness of the coronal walls may reduce the effect of the ferrule. The restorative procedures required for endodontically treated teeth are dependent upon the amount of coronal dentin remaining.

c) Post design

The design of the post affects the retention and the success of the restoration. Regarding the post taper, parallel-sided posts are more retentive than tapered posts and they distribute stress more uniformly along their length during function. The greater the taper, the less the retention. The shape of the post can be cylindrical, conical or combined. The combined shape is preferred because the cylindrical half is placed at the coronal part of the root and the conical half of the post is positioned in the apical part of the root. Double-tapered posts better adapt to the shape of the endodontically treated canal, thus limiting the amount of dentine tissue to be removed in post space preparation. Some marketed posts exhibit a coronal head or serrations for retentive purposes.

Oval-shaped glass fiber posts were recently introduced for better adaptation into ovoid-shaped canals. For ovoid-shaped canals, the use of an ultrasonic oval-shaped tip has been suggested for a more conservative post space preparation.(3)

Conclusion:

The adhesive system used to bond a fiber post to tooth structure is a dual cure self-adhesive system with co-initiator/co-activator which involves several steps. Firstly, the tooth is prepared, and the root canal space is shaped. Then, an acidic etchant is applied to the tooth to create a micro-retentive surface. A bonding agent is subsequently applied and light-cured to form a hybrid layer on the etched tooth surface. The fiber post is coated with dual-cure resin cement and carefully inserted into the prepared root canal. Excess cement is removed, and the cemented post is light-cured for complete polymerization. Proper isolation, moisture control, and meticulous technique are crucial for achieving a durable and reliable bond between the fiber post and the tooth structure.

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