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PHYTO-ANTIOXIDANTS: THE DENTAL PANACEA

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ABSTRACT
Oxygen is essential for the existence of human beings. Yet, in contradiction, it is also involved in harmful reactions and therefore is a constant threat to the wellbeing. Most of the potentially adverse effects of oxygen is formation of free radicals that are molecules containing at least one unpaired electrons. The antioxidants are substances that have potential to neutralize the free radicals and are able to react at the different stages of free radical formation. They are available in both synthetic and natural forms. They are also naturally available in herbs, fruits and vegetables which are rich in Polyphenols, Flavonoids, Anthocyanin, Proanthocyanidin, Vitamin C etc. and have lesser side effects compared to that of synthetic compounds. Herbal compounds have Antimicrobial, Anti-inflammatory, Sedative and Anxiolytics agents. They can be used both in restorative and endodontic procedures.

KEYWORDS: Oxygen, Free radicals, Natural antioxidants.

INTRODUCTION
Oxygen is paramount for the existence of the living organisms, as it is required in many metabolic reactions of the body. However, as per the saying "excess of everything is bad", similar is the case with oxygen. If the oxygen is present in excess, it can lead to the production of some harmful or toxic reactions by producing free radicals. In case of too many free radical molecules or "oxidants," in the body, the imbalance is called "oxidative stress".

Free radicals such as reactive oxygen species (ROS) or reactive nitrogen species (RNS) are extremely reactive chemical species, with a very short half-life and are composed of a single atom or a group of atoms that form a molecule with a free electron.[1] They are highly reactive due to free electron, which can bind other free radicals, or subtract an electron from the surrounding molecules. They are not always harmful, as they also serve useful purposes in the human body. Hence they are well recognised for playing a dual role as both deleterious and beneficial species. At low or moderate levels, ROS participate in the biosynthesis of molecules such as thyroxin, prostaglandin and are used by the immune system. Macrophages and neutrophils generate ROS in order to kill the bacteria that may engulf by phagocytosis. At high concentrations; they generate oxidative stress and nitrosative stress, a deleterious process that can damage all cell structures.[2]

Antioxidants have gained importance in recent years due to their ability to neutralize free radicals or their actions. Antioxidants are enzymes or other organic molecules that can counteract the damaging effects of reactive oxygen species in tissues. Antioxidants can be both exogenous and endogenous and synthetic or natural and they can be water soluble or lipid soluble. The term "antioxidant" is often applied to any organic molecule that act against the harmful effects of free radicals.[3] Recent studies have proved that antioxidants play an important preventive role in these diseases as potent scavenger of free radicals and protect our cells against oxidative damage and reduce the risk of developing these certain types of diseases.[4]

In the recent times natural antioxidants have gained popularity in dentistry. They are present in fruits and vegetables and are able to protect living tissue from reactive oxygen species such as superoxide anion and hydroxyl radicals and non-free radical species such as hydrogen peroxide and singlet oxygen as well as other radicals and aid in retarding the progress of many chronic disease. The role of antioxidants has attracted much interest with respect to their protective effect

against free radical damage that may cause various pathologies in body, premalignant lesions and as well as cancer. Many plant phenols, flavonols etc. other than antioxidant vitamins such as: C, E and carotenoids exert powerful antioxidant effects.[5]

In recent years there is an upsurge in the areas related to newer developments in prevention of disease especially the role of free radicals and antioxidants. So, this review compiles the possible role of 'free radicals' in disease and 'antioxidants' in its prevention, especially the current status of the antioxidants in oral diseases and future prospects and their application in dentistry.[3]

Mechanism of action of free radicals

Free radicals are chemically active atoms that have a charge due to an excess or deficient number of electrons. Free radicals containing oxygen, known as reactive oxygen species (ROS), are the most biologically significant free radicals. In the recent years the term "Reactive Oxygen Species" or "Reactive Oxygen Intermediates" is a collective term which has been adopted to include molecules like Hydroxyl radical (OH), Superoxide anion (O_2), Hydrogen peroxide (H_2O_2), Hypochlorous acid (HClO).[6]

While most reactive oxygen species have extremely short half-life, they can cause substantial tissue damage by initiating free radical chain reaction. Reactive oxygen species can cause tissue damage by a variety of different mechanism which include.

- DNA damage.
- Lipid peroxidation (through activation of cyclogenase and lipo oxygenase pathway).
- Protein damage including gingival hyaluronic acid and proteoglycans.
- Oxidation of important enzymes e.g. Antiprotease such as 1 antitrypsin.
- Stimulation of pro inflammatory cytokine release by monocytes and macrophages by depleting intracellular thiol compounds and activating nuclear factor.[7] (Fig:1)

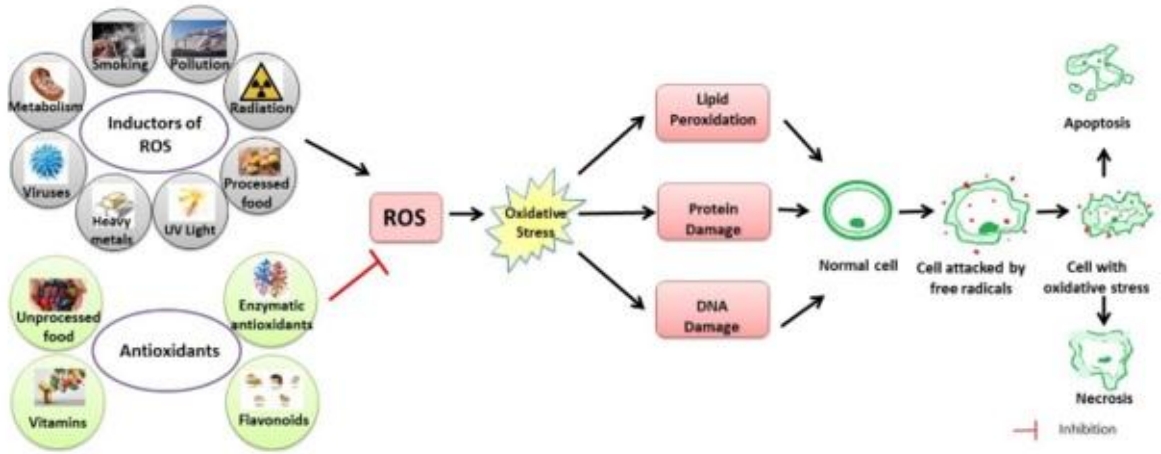

Fig 1: Mechanism of action of free radicals.

Free Radicals and Diseases

Other than being responsible for causing various Inflammatory, Cardiovascular, Respiratory diseases, Diabetes, Ageing, Neurological diseases and Nephropathy, ROS has been associated in the following oral pathologies (Fig 2).

1. PERIODONTITIS: Periodontitis is induced by bacteria and bacterial products of dental plaque and is characterized by destruction of tooth supporting connective tissues and alveolar bone. Reactive oxygen species have been implicated to participate in the pathogenesis of periodontitis by 2 ways :

A. DIRECT ACTION: Stimulation by bacterial antigen, PMN produces free radicals via respiratory burst as a part of host response to infection, degrading bone proteoglycans and collagen degradation, resulting in a reduction of collagen gelation, increased aggregation, cross-linking and collagen insolubility and this could lead to significant attachment loss.

B. INDIRECT ACTION: In addition to direct intracellular and extracellular damage, ROS enhance pro-inflammatory gene expression, including cytokines (e.g. TNFα. IL-1), chemokines (e.g. IL-8) and cellular adhesion molecules. Other than PMNs, fibroblasts, gingival epithelial cells and osteoclasts are also sources of ROS in periodontal tissues.[2]

2. ORAL SUBMUCOUS FIBROSIS: Oral submucous fibrosis (OSMF) is a crippling slowly progressive precancerous lesion of oral cavity that predominantly affects people habit of consuming areca nut and its commercial preparations generating high levels of reactive oxygen species (ROS) during their metabolism. It can progress to invasive squamous cell carcinoma.[8]

3. ORAL LICHEN PLANUS (OLP): It's a pre malignant lesions-like leukoplakia and submucous fibrosis which can proceed to oral cancer. Free radicals and reactive oxygen species play important roles in its pathogenesis.[2]
4. ORAL CANCER: Free radicals can damage DNA and cause mutagenicity and cytotoxicity and thus play a key role in carcinogenesis. Lipid Peroxidation plays an important role in control of cell division as its end product, Malondialdehyde (MDA) act as a tumor promoter and a co carcinogenic agent.[9]
5. DENTAL CARIES: Antioxidant capacity of saliva has been shown to have a linear relation with caries.[10]
6. PERI-IMPLANT DISEASE- Studies show that gram-negative, anaerobic or microaerophilic bacteria in inflamed area produce ROS which may be responsible for it.[2]

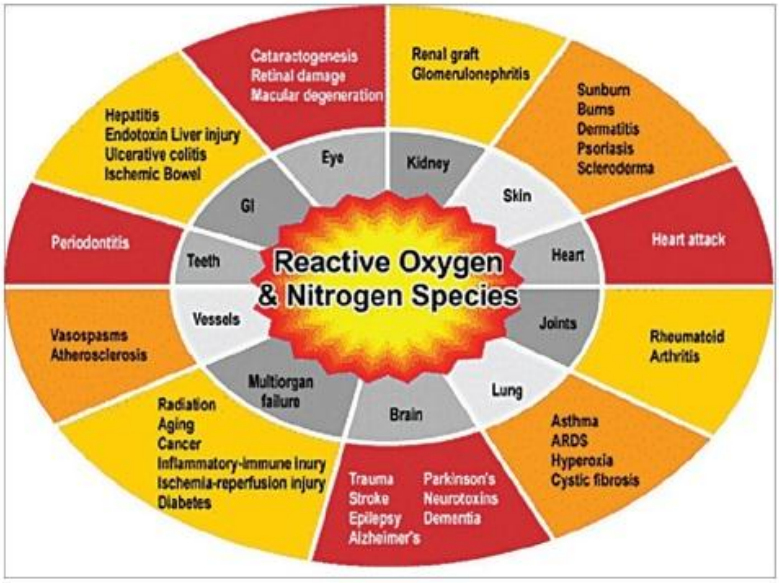

Fig 2: Diseases caused by free radicals

Mechanism of Action of Antioxidants

Antioxidants neutralise free radicals by donating one of their electrons, which ends the electron stealing reaction. Important antioxidants include the following:

1. Chain breaking or scavenging ones, such as Vitamin E (alpha tocopherol), Vitamin C (ascorbic acid), or Vitamin A (beta carotene)
2. Preventative antioxidants that function largely by sequestering transition metal ions and preventing Fenton reactions and are therefore largely proteins by nature (e.g., albumin, transferring, or lactoferrin).[11] (Fig 3)

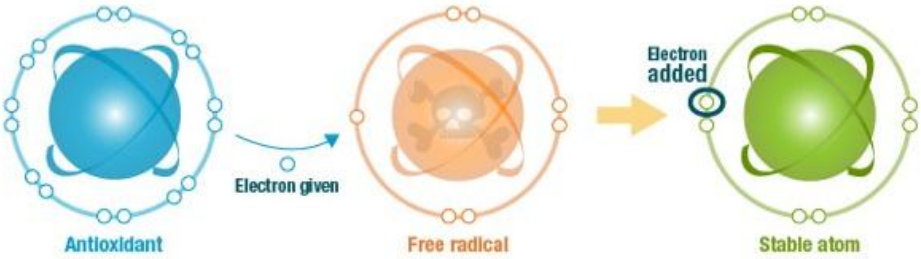

Fig 3: Mechanism of action of antioxidants.

Classification Of Antioxidants

The antioxidants defense systems of the human body are complex and various classification systems exist. Antioxidants can be categorized as (Fig 5,6).

1. Their mode of function.
2. Their location of action.
3. Solubility.
4. Their structural dependents.
5. Their origin/source (Dietary or Non-dietary sources).

I. According to mode of action

It can be classified as.

a) Intracellular: Superoxide dismutase enzyme 1 and 2, catalase, glutathione peroxidase, DNA repair enzymes e.g. poly (ADP-ribose) polymerase, others, reduce glutathione, ubiquinone (reduced form).

b) Extracellular: Superoxide dismutase enzyme3, selenium, glutathione peroxidase, lactoferrin, transferring, ascorbate, uric acid, carotenoids, ceruloplasmin.

II. According to location of action

It can be classified as.

a) Preventive antioxidants

i. Enzymes: Superoxide dismutase enzymes (1,2 and 3), catalase, glutathione peroxidase, DNA repair enzymes.

ii. Metal ion sequestrators: Albumin, lactoferrin, transferrin, haptoglobin, ceruloplasmin, hemopexin, carotenoids, superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, uric acid, polyphenolic flavonoids.

b) Scavenging antioxidants: Ascorbate, carotenoids, uric acid, α – tocopherol, polyphenols, bilirubin, albumin, ubiquinone, reduced glutathione and other thiols.

III. According to solubility

a) Lipid soluble: Haptoglobin, cerulopasmin, albumin, ascorbate, uric acid, polyphenolic flavenoids, reduce glutathione, and other thiols.

b) Water soluble: α- tocopherol, carotenoids, bilirubin, quinines.

IV. According to structures they protect:

a) DNA protective antioxidants: Superoxide dismutase enzyme 1 and 2, glutathione peroxidase, DNA repair enzymes [poly (ADP) ribose polymerase], reduced glutathione, cysteine.

b) Protein protective antioxidants: Sequestration of transition metals by preventative antioxidants.

c) Lipid protective antioxidants: α- tocopherol, ascorbate, carotenoids, reduced glutathione, glutathione peroxidase, bilirubin

V. According to their origin

a) Exogenous antioxidants: Carotenoids, ascorbic acid, tocopherols (a,b,c,d), polyphenols, folic acid cysteine.

b) Endogenous antioxidants: Catalase, superoxide dismutase, glutathione peroxidase, glutathione –S-transferase, reduce glutathione, ceruloplasmin, transferrin, ferritin, glycosylases.

c) Synthetic: N-acetylcysteine, penicillinamine, tetracylines.

d) RH Liu in 2004 classified antioxidants in to two major groups.

A. Enzymatic antioxidants.

B. Non enzymatic antioxidants.

Antioxidants are grouped into two namely:

1. Primary or natural antioxidants.
2. Secondary or synthetic antioxidants.

Primary or natural antioxidants

Antioxidants minerals: Selenium, copper, iron, zinc and manganese.

Anti oxidants vitamins: Vitamin C, Vitamin E, Vitamin B.

Phytochemicals: Flavonoids.

Secondary or synthetic antioxidants

Butylated hydroxyl anisole (BHA).

Butylated hydroxyrotoluene (BHT).

Propyl gallate (PG) and metal chelating agent (EDTA).

Tertiary butyl hydroquinone (TBHQ).

Nordihydro guaretic acid (NDGA).[12]

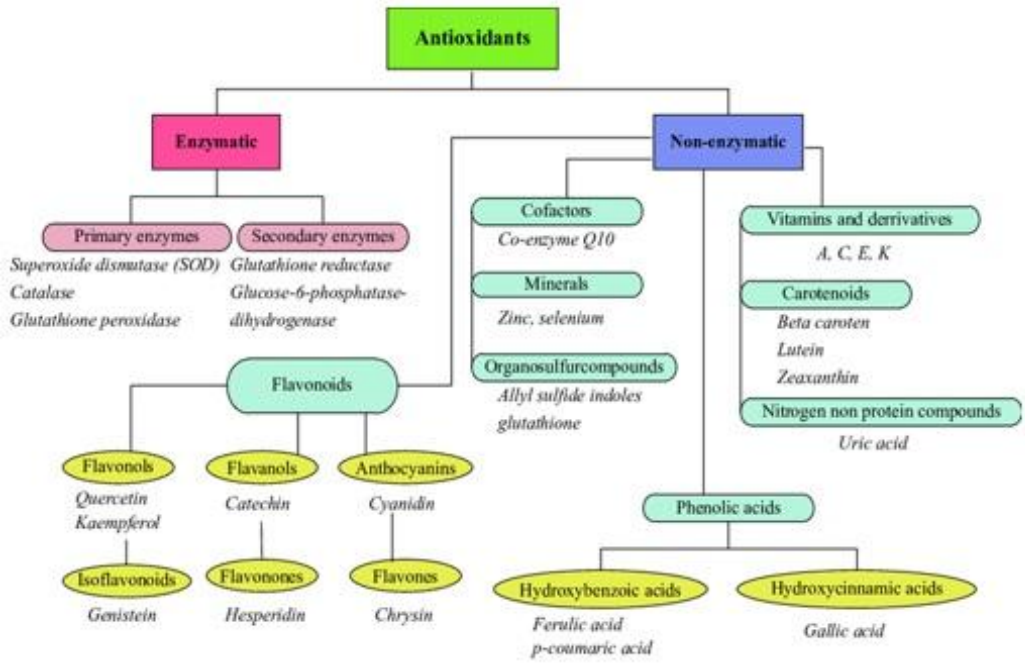

Fig 4: Classification of antioxidants.

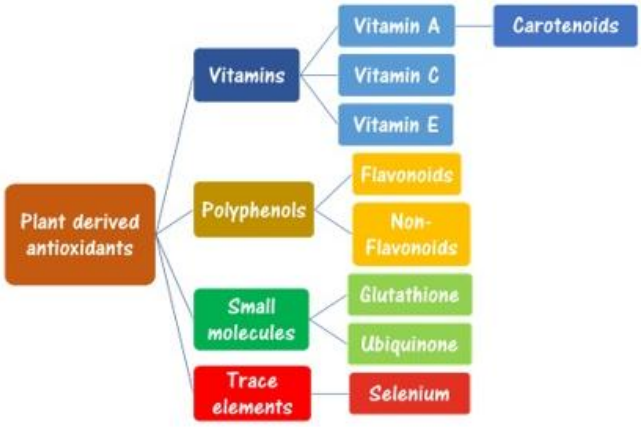

Fig 5: Classification based on plant derivatives.

Antioxidants in Restorative Dentistry and Endodontics

Restorative Dentistry

Bond strength after bleaching

Dental bleaching is a cosmetic procedure that is often requested in clinical practice. The bleaching procedure can be classified into two groups as vital bleaching and nonvital bleaching.[13]

Bleaching agents can cause side effects, such as pulpal sensitivity, microleakage in restorations, external root resorption, and changes in the composition of tooth structure. Vital dental bleaching agents contain H_2O_2 or carbamide peroxide ranging from 3% to 40%.

Some cases require aesthetic treatments such as replacement of old restorations with tooth colored restorations followed by bleaching. But due to the presence of residual peroxide liberating oxygen, it interferes with resin tags formation and inhibits free-radical polymerisation which compromises the bond strength on composite resin to enamel. and placement of laminates and veneers and even the orthodontic treatment. The free reactive oxygen is the culprit for genesis of various diseases, thereby antioxidants stabilizes or deactivates the free oxygen radicals and controls the damage caused by it. To overcome the post-operative bleaching effects, bonding procedure should be delayed by 24 hours to 3 weeks.

Methods to overturn the reduced shear bond strength which occurs during bleaching include treatment of bleached enamel surface with alcohol before restoration, utilisation of organic solvents that contain adhesives, removal of outermost layer of enamel and the utilisation of antioxidants.[14]

A study was done by using 5% Grape seed solution, 5% Pine bark solution and 5% Pomegranate solution as antioxidants. As a result they found that use of antioxidants immediately after bleaching completely neutralizes the deleterious effects of bleaching and increases shear bond strength. 5% pine bark extract showed better bond strength.[15]

In a study 10% Sodium ascorbate, 5% Pomegranate seed extract and 5% Tomato seed extract were used as antioxidants. They concluded that use of tomato seed extract and pomegranate seed extract can be used as an alternative to sodium ascorbate and tomato seed extract showed best result of all.[16]

An in vitro study examined the shear bond strengths of composite resins to bleached enamel using 10% sodium ascorbate, 10% alpha tocopherol, 10% grape seed extract, and 10% guava seed extract as antioxidants. The results showed that guava seed extract was the most effective antioxidant increasing the bond strength. With the use of these antioxidants, the bonding strengths of the bleached enamel were effectively increased.[17]

Natural antioxidants that can overturn the reduced shear bond strength are.

Neem, Cranberry, Aloe vera, Green tea, Clove, Cinnamon, Grape seed extract, Guava seed extract, Turmeric, Tomato, Morinda citrifolia, Pomegranate, Pine bark, Propolis, Triphala.

Remineralization

Remineralization was defined by Cochrane et al. as "the process whereby calcium and phosphate ions are supplied from a source external to the tooth to promote ion deposition into crystal voids in demineralized enamel to produce net mineral gain."[18]

Proanthocyanidins are found in grape seed extracts. Silva et al. compared the remineralization effect of grape seed extract and fluoride under cariogenic challenge on enamel and dentin. The samples that were treated with grape seed extract and fluoride showed better remineralization than the untreated group.[19]

Hesperidin is a citrus flavonoid antioxidant. Hiraishi et al. compared the effect of hesperidin on the remineralization of dentin lesions with chlorhexidine. Their study showed that hesperidin enhances remineralization by protecting the collagen structure.[20]

Dentinal Hypersensitivity

Dentinal hypersensitivity is defined as a short and sharp pain arising from exposed dentin in response to a thermal, evaporative, tactile, osmotic, or chemical stimulus and cannot be associated with any other form of dental pathology or defect. The most widely accepted theory behind the mechanism of dentin hypersensitivity is the hydrodynamic theory given by Brannstrom.[21-23]

The treatment modalities of hypersensitivity include occluding the dentinal tubules or impeding or diminishing neural transmission. For this purpose, several strategies, such as lasers, iontophoresis, dentin sealers and soft tissue grafting are used. The use of toothpastes is widely preferred in delivering the desensitizing agents. Desensitizing agents, such as potassium, fluoride, hydroxyapatite, copal varnishes, and $Ca(OH)_2$, or dentin bonding agents are used. There has been a growing interest in the use of natural products and antioxidants for the treatment of dentin hypersensitivity.[21-25]

Propolis, a bee product, has been a striking natural agent for the treatment of dentin hypersensitivity. Sankari et al. stated that propolis occludes dentinal tubules and reduces dentinal hypersensitivity of periodontally involved teeth. Purra et al. compared the desensitizing effect of propolis with 5% potassium nitrate and distilled water. Their results showed that propolis is the most effective desensitizing agent in the intermediate relief of sensitivity.[26]

Madhawan et al. compared the clinical efficiency of propolis with sodium fluoride, casein phosphoprotein-amorphous calcium phosphate fluoride and distilled water and found that propolis is the most rapid agent in treating dentinal hypersensitivity.[23]

Pulp capping

When dental pulp is exposed either traumatically or because of caries, direct pulp capping technique is used for protecting pulpal health and function, allowing the patients to retain their teeth longer and at lower costs than root canal treatment, which is an alternative invasive technique. The materials used should control infection, prevent microleakage, promote hard tissue formation, and should be handled easily.[27]

The high pH value also made $Ca(OH)_2$ a toxic material and prone to dissolve soft tissue that causes chronic inflammation and cell necrosis. Al-Shaher et al. found that propolis, an antioxidant agent, has superior properties than $Ca(OH)_2$ and does not produce pulpal inflammation, necrosis, and infection while inducing tubular and high qualified dentin production.[28]

In a study they have reported that the response of dental pulps to propolis as a pulp capping agent is comparable to that of ProRoot MTA and Dycal. They have reported that the response of dental pulps to propolis as a pulp capping agent is comparable to that of ProRoot MTA and Dycal.[29]

Endodontics

Root canal irrigant

The main goal of root canal treatment is to prevent or treat apical periodontitis which is achieved by proper chemo-mechanical preparation, root canal disinfection followed by three dimensional obturation of root canal system.[30]

The most popular root canal irrigant currently used is Sodium Hypochlorite because of its tissue dissolving ability along with being antimicrobial and potent lubricant. But some disadvantages of Sodium Hypochlorite are unpleasant taste, high toxicity, inability to remove smear layer properly.[31]

The bond strength of root canal sealers to dentin is important for maintaining the integrity of the seal in root canal filling in both static and dynamic situations. The physical properties necessary to maintain integrity include adaptation and adhesion of filling materials to root canal walls, as gutta percha does not directly bond to dentin surface and ideal sealer should be capable of producing bond between core material and dentin wall.[32]

The oxidative by-products of Sodium Hypochlorite are Hypochlorous acid and Hypochlorite ions which inhibits the free radicular polymerization of methacrylate resin and adhesion of epoxy resins used in the canals. This eventually compromises bond strength of sealer to root dentin and hinders its sealing ability and causes microleakage. To overcome the situation, pre-treatment of the root canal with antioxidants or neutralizing agents should be done before adhesive bonding of resin sealers as it is capable of reversing the Sodium Hypochlorite induced reduction in bond strength.[33]

Herbal extracts are more biofriendly and suited as dental irrigants. They are rich in antioxidants, antimicrobial, sedative and anti-inflammatory properties, thereby making them ideal for root canal irrigation.[34]

Kumar PS et al have done a An In – vitro study by using 6.5% Proanthocyanidin (Grape Seed Extract) and 25% Bamboo Salt were used as irrigants. They concluded that Sodium Hypochlorite significantly decreases dislocation resistance of AH Plus sealer and use of Proanthocyanidin and Bamboo Salt as final irrigant solutions reverses compromised Push out bond strength of AH Plus to NaOCL- treated dentin.[33]

An In – vitro study was done by using 10% Grape Seed Extract and 10% Green Tea were used as irrigants. They were divided into 3 groups: No agent; Grape seed extract and Green Tea were used for final rinse after irrigating with 5% NaOCL or 2% CHX and 17% EDTA. The least push out bond strength was seen in group with NaOCL

and EDTA as final irrigant. Other groups had significantly same bond strength. They concluded that irrigation protocol and naturally derived reducing agents did not have much effect on push out bond strength of resin based sealer to root dentin.[35]

An In – vitro study was done by using 2% Chlorhexidine and 15% Proanthocyanidine as irrigants. It included six groups: AH Plus; CHX+AH Plus; PA+AH Plus; EndoREZ; CHX+EndoREZ; PA+EndoREZ. Dentin was treated for 1 or 5 mins with 2% CHX or 15% PA respectively. They found that at 24 hours, AH Plus had bond strength than EndoREZ. At 6 months, AH Plus and EndoREZ had higher bond strength for CHX and PA. They concluded that bond strength decreases with time and AH Plus had higher bond strength than EndoREZ in untreated dentin. However CHX and PA enhanced long term Bond strength of EndoREZ.[36]

Herbs with antioxidant properties that can be used as irrigants : Neem, Triphala, Propolis, Azardiracta Indica, Green tea, SalvadoraPersica, Tea tree oil, Garlic, Lemon solution, Turmeric, Grape seed extract, Acacia nilotica, Morinda citrifolia.[37-39]

Intracanal Medicament

The micro-organisms are the prime cause for the root canal and periradicular infections. Complete debridement and disinfection of the canals from the microflora is essential for the success of endodontic treatment. However, due to some factors like, complex nature of the root canals, there is incomplete disinfection of the root canal system and retained microflora in the root canal are one of most common causes for failed root canal treatment. Hence, additional methods such as the use of intra-canal medicaments are required to maximize disinfection of root canal system and kill as many bacteria as possible.[40]

Calcium hydroxide has been the prototype of any intracanal medicament used. Although CH is proven to be good intracanal medicament in reducing the microbial growth, literature (Doyon et al.,Yassen and Platt Zarei et al.) have shown that there is decrease in mechanical properties of radicular dentin when CH is used as intracanal medicament for more than 5 weeks. Study by Prabhakar et al. has shown that when CH is mixed with 0.2% CHX, there is no alteration in fracture resistance of radicular dentin after 30 days.

Recently, there has been growing interest in evaluating the effect of natural antioxidants in dentistry. Studies by Arumugam et al., Abraham et al. have shown that addition of antioxidants like lycopene (LP). It was concluded that addition of LP to CH and CHX mixture has not decreased the fracture resistance of radicular dentin after 1-month.[41]

A study done by Aly et al. has shown that Moringa oleifera could be removed easily from the root canals and showed increase in the microhardness of root canal dentin similar to the commonly used calcium hydroxide when used as intracanal medicament.[42]

In a study by Parashar V et al has concluded that Aloe vera shows promising results in terms of good antimicrobial properties and fewer effects on microhardness of the root dentin.[43]

Herbs with antioxidant properties that can be used as intracanal medicament. Propolis, Aloe vera, Articum lappa, Liquorice, Cranberry, Turmeric, Triphala.[37]

Antioxidants in Dentistry

Periodontology

Oxidative stress stays at the heart of the periodontal damage that happens from host-pathogen interactions. This stress is a result of excess ROS activity, antioxidant deficiency or activation of redox- sensitive transcription factors and the creation of inflammatory stage. It is known that there are significant relations between oxidant status and periodontal status, the oxidative stress can play important role in the pathology of periodontitis.[44]

Antioxidants change the progress of oral problems such as periodontitis, gingivitis by compromising antioxidant capacity of crevicular fluid and plasma. One of the conditioning factors for gingivitis is ascorbic acid deficiency. So, antioxidant support are preferred against struggling periodontal diseases. Plant oils and green leafy vegetables can break free radical chain reactions thus may contribute in reducing periodontal inflammation. Flavanoids acquired from antioxidants can possess anti-inflammatory properties that reduce inflammatory molecule expressions in immune system warriors such as monocytes within the gingival connective tissues.[45]

Matricaria chamomilla (Asteraceae) has Anti-inflammatory properties that reduce gingival inflammation; Echinacea purpurea (Asteraceae) stimulates immune response; S. officinalis (Lamiaceae) has antihemorrhagic properties; Commiphora myrrha (Burseraceae) has natural antiseptic properties and M. piperita (Lamiaceae) has analgesic, antiseptic and Anti-inflammatory properties.[46]

Punicia granatum (Pomegranate) extract decreased the number of colony forming units of dental plaque bacteria by 84%, comparable to chlorhexidine.[47] Use of Salvadora persica(Miswaak) mouthwash resulted in improved gingival health and lower carriage rate of cariogenic bacteria when compared with the pre-treatment values.[48]

Orthodontics

In orthodontics, similar agents can be used to increase bond strength of brackets. In bracket bonding, to increase

bond strength values ascorbic acid solutions that were hard to prepare were used.

In a recent study, it was reported that the usage of pine bark extract solution could be used instead of ascorbic acid solution. For maxillary expansion, there are several studies researching the effect of antioxidant agents on bone formation or maturation. Uysal et al. researched the effect of Vitamin C and resveratrol in the expanded premaxillary suture. They concluded that the effect of antioxidants on bone formation was statistically significant. Similarly, Altan et al. revealed that systemic propolis usage stimulates bone formation in the expanded suture area.[45]

Oral-Maxillofacial Surgery

According to Ohnishi et al. reactive oxygen such as hydrogen peroxide, are responsible for the alveolar bone loss that is accompanied by decreased endothelial nitric oxide synthase expression in mice and they stated that the generation of oxidative stress is an underlying systemic condition that enhances alveolar bone loss. Peri-implantitis is initiated by gram negative, anaerobic bacteria that accomodates in the subgingival area. Treating peri-implantitis involves antioxidant supplemention. Sheresta et al. stated that grape seed extract has positive effect on treating peri-implantitis. For bone healing and bone formation, it was reported that caffeic acid phenethyl ester which can be found in propolis have significantly improved bone healing in rat models.[45]

Surgical applications

Antioxidants can be used to control bleeding and promotes fast wound healing.

Ankaferd Blood Stopper (ABS) is a standardized extract from the following plants: Thymus vulgaris, Glycyrrhiza glabra, Vitis vinifera, Alpinia officinarum and Urtica dioica in a weight ratio of 6:8:7:7:5, respectively. The basic mechanism of action of ABS is through the formation of encapsulated protein network providing focal points for vital erythrocytes to aggregate on. ABS was found to be effective within 10–20 min in controlling bleeding in most of the patients after dental surgery.[49]

Calendula officinalis (English marigold) flower extract treatment promotes wound to heal much faster attributable to its capability to enhance the synthesis of connective tissue, especially collagen.[50]

Curcumin longa (Turmeric) was shown to be effective in reducing wound-healing time and acts as proangiogenic agent, playing a role in remodeling phase of wound repair.[51]

Dental trauma applications

Antioxidant extracts can be used as storage media for avulsed tooth in case of trauma.

In vivo studies showed that teeth maintained in propolis medium exhibited replacement resorption with significant reduction in tooth length, similar to teeth maintained in saliva and dried teeth. Salvia officinalis (Garden sage) extracts serve as a storage medium for the maintenance of PDL cell viability of avulsed teeth. Skimmed and whole milk, followed by natural coconut water and HBSS, were the most effective media in maintaining cell viability of PDL fibroblasts. Morus rubra (Indian mulberry) can be recommended as a suitable transport medium for avulsed teeth. Efficacy of Camellia sinensis (Green Tea) extract in maintaining the viability of human PDL cells is similar to that of HBSS and higher than that of milk.[46]

Oral Cancer

Antioxidants show preventive and therapeutic potential in many stages of oral carcinogenesis. Researchers have recently stated there is inhibition of oral cancer phenotypes after antioxidant intakes. The administrations of proanthocyanidins that can be found in flavonoid structures of antioxidants have an ability to reduce cell growth and proliferation of oral carcinomas. Dietary antioxidants can protect the lipids and other membrane molecules against oxidative damage by intercepting oxidants before they try to destroy the tissues.[45]

CONCLUSION

The use of plants and herbs for dental care is a very common indigenous system of medicine and it must be included in everyday life. The major advantages of using natural alternatives are easy availability, cost‑effectiveness, increased shelf life, low toxicity and lack of microbial resistance reported so far. Herbal agents have been used in dentistry for reducing inflammation, as antimicrobial plaque agents, antiseptics, antioxidants, antimicrobials, antifungals, antibacterials, antivirals, and analgesics. The active principles of plants should be incorporated into modern oral health-care practices and dentists should be encouraged to use natural remedies in various oral health treatments.

ANTIOXIDANTS OF DENTAL SIGNIFICANCE					
Antioxidant	**Source**	**Action**	**Mechanism**	**Clinical use**	**Benefits**
Ascorbic acid (Vitamin C)	Citrus fruits, Mangoes, Honey dew, Papaya, Strawberry	Scavenging radicals anticarcinogenic Enhances chemotaxis, phagocytosis, collagen synthesis	1. Decrease nitrosation 2. Effect leukocytes and macrophages	1. Deficiency cause gingivitis. 2. Prevention and treatment of oral premalignant lesion and oral cancer. 3. Increase bond strength of resins to bleached enamel	1. Improves gingival health. 2. Improves bonding of resin when used on bleached enamel.
β Carotene	Dark green, orange or yellow vegetables and fruits	1. Immunomodulation 2. Inhibit mutagenesis 3. Induction of cytotoxic and cytostatic effects on cancer cells scavenging the peroxyl radical	Increased activity of TNF-α increases cell mediated immune response	1. Regression of oral premalignant lesions 2. Periodontal disease treatment	1. Improves periodontal condition.
α Tocopherol	Plant oil, green leafy vegetables, wheat germ	Scavenges free radicals anti-inflammatory	Reduce oxidative damage caused by hydroxyl radicals	1. Prevention of periodontal pathology. 2. Increases bond strength of resin to bleached enamel.	1. Improves bonding of resin to bleached tooth enamel.
Proanthrocyanidin	Red wine, pigmented fruits, nuts and chocolate, grape seed extract, Cranberry	Antimicrobial, anti-inflammatory.	1.Reduce cell proliferation in human oral cancer cells induce apoptosis 2. Inhibit glucan synthesis. 3. Decrease adhesion of S. mutans to tooth	1.Oral cancer chemo preventive 2. Dental caries prevention 3. Periodontal disease 4.In endodontics to increase bond strength of resins to bleached enamel	1. Improves bonding of resin to bleached tooth enamel. 2. Causes remineralisation of tooth.
Epigallocatechin-3-Gallate (EGCG) (Catechins)	Green tea, oolong tea, black tea	Anti-carcinogenic activity	1.Bactericidal to S. Mutans 2. Decrease acid production in dental plaque 3. Inhibit the production of important MMP 4. Increase acid resistence of teeth	1. Preventive role in dental caries. 2. Periodontitis treatment 3. Prevent oral cancer 4. Treatment of dental erosion 5. Endodontic irrigant 6. As a storage medium for avulsed tooth	
Lycopene	Tomatoes	Anticarcinogenic, Antibacterial, Antifungal	1. Inhibit cancer cell proliferation 2. Effective against candida albicans	1. Prevention of OSMF 2. Oral leukoplakia 3. Oral lichen planus 4. Gingivitis	Inhibits free reactive oxygen after vital bleaching.
Eugenol	Clove	Scavenging		Effective in toothache	
Curcumin	Turmeric, aloe vera	Antibacterial, Antifungal, Anti-inflammatory		1. Wound healing 2. Endodontic irrigant 3. Intracanal medicament	High antibacterial property against micro-organisms.
Spirulina	Blue green microalgae	scavanging		Effective in buccal squamous carcinoma	
Flavanoids	Morinda citrifolia	Anti-inflammatory, Anti-allergenic, Anti-viral,	Regulate nitric-oxide	1. Cancer treatment 2. Endodontic irrigants	1. Inhibits free reactive oxygen

		Antiaging, Anticarcinogenic activity	production of LPS-stimulated human gingival fibroblasts.	3. Intracanal medicaments 4. Increase bond strength after bleaching	after vital bleaching.

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