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Can Dental Caries Be Treated?

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Abstract

Realization that dental caries is a reversible, dynamic process at a micron level has changed the way the profession recognizes the caries disease. GV Black in 1908 in his text book "Operative Dentistry" advises the profession not to ignore the biological nature of dental caries. He stated that "this attitude of profession is an anomaly in science that should not continue." It has the apparent tendency to make dentists mechanics only. A goal of modern dentistry is to manage non-cavitated (demineralized) caries lesions noninvasively through remineralization in an attempt to prevent disease progression and improve esthetics, strength, and function. Remineralization can be described as mineral gain to the tooth structures. Commonly, fluoride was used to enhance remineralization. However, many side effects for its usage are confirmed. The aim of this chapter is to shed the light about several recent approaches for tooth remineralization.

Keywords: bioactive materials, biomimetic self-assembling peptide matrix, fluoride, low-level laser therapy, natural remedy

1. Introduction

Dental caries is a highly prevalent disease that is considered a major public health problem. Signs of the caries process extent from the first molecular changes in the apatite crystals of the tooth structure to a white-spot lesion, through dentin involvement and eventual cavitations [1].

Progression of dental caries requires a continual imbalance between pathological and protective factors that results in the dissolution of apatite crystals and the net loss of calcium, phosphate, and other ions from the tooth (demineralization) [2].

The term "remineralization" has been used previously to describe mineral gain, including the precipitation of mineral onto-enamel surfaces [3]. Cochrane et al. in 2010 define remineralization

as the process whereby calcium and phosphate ions are supplied from a source external to the tooth to promote ion deposition into voids in demineralized enamel to produce a net mineral gain [4].

1.1. Fluoride treatment

Fluoride has been established to enhance the rate and efficacy of remineralization. However, chronic low-level exposure to fluoride can cause some health problems (bone health problems, cancer, birth defects, and gastrointestinal tract problems) other than dental fluorosis. Therefore, it is still necessary to seek alternative, effective non-fluoride agents that can provide a complete cure for caries.

The action of fluoride in remineralization is the gold standard to which newer therapies are compared. The requirements of an ideal remineralization material are as follows. It must diffuse into the subsurface or deliver calcium and phosphate into the subsurface lesion [5, 6].

There are several recent approaches for remineralization:

- laser-activated fluoride (LAF)
- low-level laser therapy (LLLT)
- bioactive materials
 - Recaldent
 - NovaMin
 - tri-calcium phosphate
 - biodentine tri-calcium silicate cement
 - nano-hydroxyapatite
- Biomimetic self-assembling peptide matrix
 - curodont repair
 - icon
- Natural remedy

1.2. Laser-activated fluoride

Laser-activated fluoride (LAF) is a method to combine laser irradiation and topical fluoride application in one technique by which the resistance of the enamel to demineralization is increased. Laser irradiation has been found to reduce the critical pH of dissolution of hydroxyapatite crystals from 5.5 to 4.3. In the presence of fluoride, further reduction has been revealed [7].

1.3. Low-level laser therapy

While most applications of low-level laser therapy (LLLT) in dentistry are directed toward soft tissues, in recent times, there has been increasing interest in tooth-related or hard-tissue

applications of LLLT. There is accumulating evidence which indicates the potential of low-level laser therapy as a technique for the destruction of cariogenic bacteria without causing undue thermal stress to the tooth as well as increasing the enamel's acid resistance better than those of fluoride treatment. LLLT was shown to be efficient in the stimulation of odontoblast cells, producing reparative dentin and sealing dentinal tubules [8].

2. Bioactive remineralizing materials

2.1. Stabilized amorphous calcium phosphate systems

It combines casein phosphoproteins from milk with amorphous calcium phosphate (CPP-ACP). Amorphous calcium phosphate (ACP) induces a thin surface coating of hydroxyapatite when applied topically. This is a surface phenomenon that is basically different from the remineralization of enamel subsurface lesions which require the actual penetration of ions into enamel.

The bioavailable complexes of casein, calcium, and phosphate are created in the appropriate form for optimal remineralization of subsurface lesions in enamel, not just on the surface, for example, Recaldent is available in solutions, gums, lozenges, and creams [9].

2.2. Crystalline calcium phosphate remineralizing systems

NovaMin is technically described as an inorganic amorphous calcium sodium phosphosilicate (CSPS). It belongs to a class of materials which are known as "bioactive glasses."

Preceding the invention of bioactive glass, all biomaterials were designed to be as inert as possible in the human body. The discovery that a synthetic biomaterial could form a chemical bond with bone proved that biomaterials could be engineered to be active with the body. Bioactive glasses enable hydroxyapatite deposition when exposed to fluids containing calcium and phosphate.

Many studies have shown NovaMin particles to act as reservoirs and continuously release calcium and phosphate ions into the local environment. The calcium-phosphate complexes crystallize into hydroxycarbonate apatite, which is chemically and structurally like biological apatite. NovaMin has been incorporated into toothpastes, gels, and prophylaxis pastes.

A novel delivery system for NovaMin is through an air-polishing unit. NovaMin powder also has positive remineralization effects on partially and completely demineralized models of dentin [10].

2.3. Crystalline calcium phosphate remineralizing systems

Tri-calcium phosphate (TCP) is a bioactive and simple organic ingredient. It works synergistically with fluoride to produce superior remineralization of enamel subsurface lesions when compared to using fluoride alone. A protective barrier is created around the calcium, allowing it to coexist with the fluoride ions. When it comes in contact with saliva, it causes the barrier to dissolve and releases calcium, phosphate, and fluoride. Studies are currently underway to

demonstrate the clinical advantages of TCP. The above remineralization therapies work directly to enhance the concentration of calcium, phosphate, and fluoride [11].

2.4. Biodentine tri-calcium silicate cement

Biodentine is a new bioactive calcium silicate-based product that has been designed as dentin replacement material. It can be used in endodontic repair (root perforations, apexification, and resorptive lesions), pulp capping, as well as dentin replacement in restorative dentistry. It was formulated by taking the MTA-based technology, improving its physical and handling properties and creating a dentin replacement material with significant reparative qualities.

Biodentine penetrates the dentinal tubules forming tag-like structures that produce a micromechanical lock with the tooth. It then begins to stimulate reparative dentin. Biodentine has been revealed to enhance the formation of reparatory dentin and to create a dense dentin barrier after direct pulp capping as well as healing damaged pulp fibroblasts [12].

2.5. Nano-hydroxyapatite

Nano-hydroxyapatite (nano-HA) is one of the most biocompatible and bioactive materials and is widely applied to coat artificial joints and tooth roots. Due to the similarity to the tooth apatite in chemical composition and crystal structure, hydroxyapatite nanoparticle (nano-HA) is reported to have the potential to repair demineralized enamel lesions.

Naturally, many nano-blocks combine into self-assembled biominerals under the control of an organic matrix. Nonetheless, whether the remineralization effect of nano-HA on dentin would be better in the presence of organic component is still indistinct [13, 14].

2.6. Self-assembling peptides (enamel regeneration)

Enamel regeneration with self-assembling peptides enables a completely new treatment option for initial caries. It mimics the enamel matrix and the initiation of tooth regeneration via biomineralization. Reversal of the caries progresses toward remineralization by a three-dimensional regeneration of early enamel lesions, avoiding subsequent invasive caries treatments.

During odontogenesis, the three-dimensional amelogenin matrix enables crystallization and ordered calcium phosphate crystal growth. The matrix is subsequently degraded. Scientists from the University of Leeds found a way to mimic the enamel matrix within enamel lesions by self-assembling peptides matrix and thus enabling enamel regeneration, marketed as Curodont 2013.

Self-assembling peptides are widely used in tissue engineering and to produce three-dimensional cell cultures. Self-assembling peptides form spontaneously a biocompatible three-dimensional matrix that mimics the enamel matrix. Around the newly formed matrix, calcium phosphate from saliva crystallizes, forming new enamel. The process uses the natural remineralization process that is in a healthy tooth.

When Curodont repair is applied onto a carious lesion, the monomers diffuse through the pores into the subsurface lesions. In the subsurface cavities, they form the three-dimensional matrix around which the crystallization of calcium phosphate occurs.

This process is comparable to the mineralization process that occurs during odontogenesis, or the remineralization process which is in equilibrium with the demineralization process. Curodont repair arrests initial caries and initiates the natural, three-dimensional regeneration of enamel, the tooth heals [15, 16].

2.7. Peptide-based infiltrate

The technique uses a peptide-based fluid (e.g., Icon) which is painted onto the tooth's surface to infiltrate inside the pores of the demineralized enamel to fill the spaces and enhance remineralization. It enables immediate treatment of lesions not yet advanced enough for restoration. It arrests caries progress without unnecessary loss of healthy tooth structure and cosmetic treatment of cariogenic white lesion. No drilling or anesthesia is required [17].

2.8. Natural remedy for dental caries

There is a great trend nowadays to use natural materials as cure for many diseases. Alternative medicine has made a lot of contributions to modern medical practice.

Dental plaque plays an essential role in the pathogenesis of dental caries. The occurrence of dental bacteria depends on the bacteria coherence, acidogenicity, and acid resistance. Control of the oral biofilm includes removal or reducing the biofilm mass or acidogenicity through mechanical and/or chemical interventions. Previously, chemical synthetic agents such as chlorhexidine gluconate and tri-closan have demonstrated their efficiency as antibiofilm agents [18, 19].

However, the excessive use of synthetic agents leads to side effects including alteration of the oral cavity environment and the bacterial tolerance. A natural anti-plaque agent with safe efficacy and potent activity may be attractive for daily oral care.

2.8.1. Green tea

Many reports in experimental animals and humans suggested that green tea consumption (without added sugar) reduces dental caries as it acts as an antibacterial agent.

In addition, green tea decoctions inhibit α -amylase in human saliva, reducing maltose release by 70% and effectively lowering the cariogenic potential of starch-containing food. Apart from their polyphenol content, both green and black tea are a natural source of fluoride as well as an effective vehicle for its delivery in the oral cavity. Many studies revealed that by using tea as a mouthwash, approximately 34% of the fluoride is retained and shows a strong binding ability to interact with the oral tissues and their surface integuments [20, 21].

2.8.2. *Propolis resinous mixture*

Propolis is a nontoxic natural substance collected by *Apis mellifera* bees from various plant sources and has been used in folk medicine for centuries. It is known that propolis exhibits several biological activities, such as antimicrobial, anti-inflammatory, anesthetic, cytostatic, antitumor, hepatoprotective, antioxidant, hematostimulative, immunomodulatory, and cariostatic properties.

The chemical composition of propolis is complex; flavonoids and (hydroxyl) cinnamic acid derivatives have been considered the primary biologically active compounds. Propolis has also been used in dentistry for surgical wound healing, root canal treatment, pulp capping, and tooth hypersensitivity. Different commercial propolis products are available in market. Propolis has a promising role in future medicine [22].

Dental caries was markedly decreased by the multiple actions of propolis which had an antimicrobial activity against *S. sobrinus*, *S. mutans*, and *S. cricetus*, inhibited water-insoluble glucan synthesis, and inhibited glucosyltransferase activity.

Propolis has a wide range of biological activities; the potential of propolis and its compounds as cariostatic agents is a thought-provoking contribution to develop bioactive products to control caries activity. Therefore, guidelines for quality control should be implemented since the high variability in the chemical composition of propolis is an important obstacle to be overcome before it can be recommended for routine application in dentistry clinics [23].

2.8.3. *Coconut oil*

Coconut oil has received much attention of late; coconut oil is the richest sources of saturated fat. Most of these fatty acids are medium-chain triglycerides.

They are metabolized differently than the long-chain fatty acids found in most other foods and have many potential health benefits.

A medium-chain fatty acid (lauric acid) makes up almost 50% of coconut oil. This oil breaks down into a compound called monolaurin. Both lauric acid and monolaurin can kill harmful bacteria, fungi, and viruses in the body [24]. According to research, many of the health benefits associated with coconut oil are directly caused by lauric acid [25].

Lauric acid is particularly effective against harmful bacteria in the mouth that can cause bad breath, dental caries, and gum disease [26].

The most popular ways to use coconut oil for your teeth are using it in a process called “oil pulling,” or making toothpaste. Oil pulling is the act of using oil as a mouthwash for 15–20 min and then spitting it out.

Coconut oil has an antibacterial effect against *Streptococcus mutans* and *Lactobacillus*, which are the primary bacteria responsible for dental caries [27].

Several studies suggest that coconut oil can be compared to chlorhexidine which is the active ingredient used in many mouth rinses in reducing these cariogenic bacteria [28–31].

For these reasons, coconut oil can help prevent plaque formation and dental caries.

2.8.4. *Turmeric (haldi)*

Turmeric is a flavorful yellow-orange spice. Turmeric has been attributed for several medicinal properties in the traditional medicine. Components of turmeric include mainly curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin. The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane) and various volatile oils including tumerone, atlantone, and zingiberone. Other constituents include sugars, proteins, and resins. Curcumin has been used extensively in medicine for centuries, as it is nontoxic, antioxidant, analgesic, anti-inflammatory, antiseptic activity, and anticarcinogenic activity [32].

Many researches were performed to compare the effect of turmeric mouthwash to that of standard treatment—chlorhexidine gluconate mouthwash in treating gingivitis and plaque. A significant reduction in plaque index and microbial count was observed with turmeric mouthwash. However, chlorhexidine gluconate mouthwash was more effective when antiplaque property was considered [33].

2.8.5. *Licorice root*

The main active ingredient in licorice root is glycyrrhizin. However, over 600 active components have been identified in the plant, including 10 bioflavonoids which act to strengthen the immune system [34].

Two antibacterial ingredients were extracted from licorice root: licoricidin and licorisoflavan A. In 2012, an international published research by the American Chemical Society linked these chemicals to oral health.

The researchers found that each chemical strongly inhibited two major cariogenic bacteria—*S. mutans*, which is the most important bacterium, induces dental caries, and *S. sobrinus*. The chemicals also had a major inhibitory effect on two common gum disease bacteria: *Porphyromonas gingivalis* and *Prevotellaintermedia*. In addition, the licoricidin moderately inhibited a third bacterium, *Fusobacterium nucleatum*, which is often associated with periodontal disease [35].

2.8.6. *Miswak Alvadora Persica*

Miswak has been used as a natural toothbrush for centuries. The World Health Organization has also promoted its use for oral hygiene. Many researches revealed that Miswak can prevent dental caries, bad breath, and it can be used in toothache [36].

Miswak contains the following compounds: lauric, myristic, and palmitic acids; polysaccharide and lignin derivatives of phenols and furans; sterols. The benzylisothiocyanate isolated from the Meswak showed an antiviral activity and acts as an agent for controlling dental caries, even when used without any other tooth-cleaning methods. The use of Meswak extract chewing gum may promote a decrease in plaque, bleeding, and gingival indices. The tannins and resins in Meswak have an astringent effect on the mucus membrane and form a layer over the enamel which indeed gives protection to the teeth [37, 38].

Silica in Miswak acts as an abrasive material to remove plaque and stains. Tannins present in Miswak exert an astringent effect on the oral mucous membrane, thus reducing gingivitis and other dental pathologies [39].

2.8.7. *Gallachinensis*

Gallachinensis has been widely used as a natural traditional Chinese medicine. *Gallachinensis* exhibits antibacterial, antiviral, antioxidant, hepatoprotective, antidiabetic, antithrombin, antidiarrheal, anti-inflammatory, antitumor activity, and detoxification properties [40–42].

Gallachinensis extract contains significant quantities of monomeric and polymeric polyphenols (gallotannin and gallic acid), carbohydrates, and proteins. Gallotannins was found to be bactericidal for cariogenic bacteria [43–47].

Extracts from *gallachinensis* (Ellagic acid) has been proposed to reduce the glucan-mediated adhesion of *S. mutans* to saliva-coated hydroxyapatite. The bioactivity of *gallachinensis* extract is a result of synergistic effects and/or antagonistic effects of several compounds [48, 49].

Previous studies revealed that *gallachinensis* has anticariogenic and outstanding effects in promoting hard-tissue remineralization [50, 51].

3. Concluding remarks

A goal of modern dentistry is the noninvasive management of non-cavitated caries lesions involving remineralization systems to repair the enamel. In individuals at risk of disease, procedures should be instituted to prevent the onset of disease, and those in whom disease is already evident, the lesions should be treated noninvasively by remineralization.

Interest in the discovery of natural, safe, and novel anti-infective compounds derived from plants is ongoing in the scientific community.

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References

- [1] Buzalaf MR. Fluoride and the oral environment. Monographs in Oral Science (Basel, Karger). 2011;**22**:97-114

- [2] Fejerskow O, Kidd EA, Nyvad B, Baclum V. Defining the Disease: An Introduction: Dental Caries—The Disease and its Clinical Management. 2nd ed. Oxford: Blackwell Munksgaard; 2008. pp. 3-6
- [3] Featherstone JD. Dental caries: A dynamic disease process. *Australian Dental Journal*. 2008;**53**(3):286-291
- [4] Cochrane NJ, Cai F, Huq NL, Burrow MF, et al. New approaches to enhanced remineralization. *Journal of Dental Research*. 2010;**89**:1187
- [5] Zero DT, Fontana M, Martinez- Mier EA, et al. The biology, prevention, diagnosis and treatment of dental caries. *Journal of the American Dental Association* (1939). 2010;**140** (Suppl. 1):25S-34S
- [6] Walsh L. Evidence that demands a verdict: Latest developments in remineralization therapies. *Dental Economics*. 2009
- [7] Cecchini RM, Zezell DM, Oliverira E, Freitas PM, et al. Effect of Er:YAG laser on enamel acid resistance: Morphological and atomic spectrometry analysis. *Lasers in Surgery and Medicine*. 2005;**37**:373-380
- [8] Sanjeev KV, Sandhya M, Ray KS, Prabhat KC. Laser in dentistry: An innovative tool in modern practice. *National Journal of Maxillofacial Surgery*. 2012;**3**(4):124-132
- [9] Ruchi V, Rajamani I, Ramachandran S, Anil K, et al. Role of casein phosphopeptide amorphous calcium phosphate in remineralization of white spot lesions and inhibition of *Streptococcus mutans*. *Journal of Conservative Dentistry*. 2013;**16**(4):342-346
- [10] Wang Z, Jiang T, Sauro S, Wang Y, et al. Dentine remineralization induced by two bio-active glasses developed for air abrasion purposes. *Journal of Dentistry*. 2011;**39**(11):10-16
- [11] Karlinsey RL, Mackey AC, Walker ER, Frederick KE. Enhancing remineralization of subsurface enamel lesions with functionalized TCP. In: *Biomaterials Developments and Applications*. cdeworld.com: EDS H Bourg, A Lisie; 2010. pp. 353-374
- [12] Qi Y-P, Li N, Niu L-N, Caolyn M, et al. Remineralization of artificial dentinal caries lesions by biomimetically modified mineral trioxide aggregate. *Acta Biomaterialia*. 2011; **8**(2):836-842
- [13] Allaker RP. The use of nanoparticles to control. oral biofilm formation. *Journal of Dental Research*. 2010;**89**(11):1175-1186
- [14] Asa R. Proactive prevention: Treating caries disease with remineralization. *AGD Impact Journal*. 2011;**39**(2):20-24
- [15] Matteo C, Maria M, Riccardo B, Marco C, et al. Effect of self-assembling peptide P11-4 on enamel erosion: AFM and SEM studies. *The Journal of Scanning Microscopies*. 2016;**38**(4): 344-351
- [16] Burke JL. In Situ Engineering of Skeletal Tissues Using Self-Assembled Biomimetic Scaffolds. Leeds: The University of Leeds; 2011

- [17] Fonseca BM, Pucci CR, Duarte A, Arantes A, et al. Enamel artificial caries: Influence of infiltration and re-mineralization in bond strength. In: IADR Congress Abstract; 2012. #676
- [18] Wilson M. Susceptibility of oral bacterial biofilms to antimicrobial agents. *Journal of Medical Microbiology*. 1996;**44**:79-87
- [19] Wilson M, Patel H, Fletcher J. Susceptibility of biofilms of *Streptococcus sanguis* to chlorhexidinegluconate and cetylpyridinium chloride. *Oral Microbiology and Immunology*. 1996;**11**:188-192
- [20] Katiyar SK. Skin photoprotection by green tea: Antioxidant and immunomodulations effects. *Current Drug Targets*. 2003;**3**:234-242
- [21] Lee MJ, Lambert JD, Prabhu S, Meng XF, et al. Delivery of tea polyphenols to the oral cavity by green tea leaves and black tea extract. *Cancer Epidemiology, Biomarkers & Prevention*. 2004;**13**:132-137
- [22] Duailibe SA, Goncalves AG, Ahid FJ. Effect of a propolis extract on streptococcus mutans counts in vivo. *Journal of Applied Oral Science*. 2007;**15**:420-423
- [23] Simon-Finsrom M, Spivak M. Propolis and bee health: The natural history and significance of resin use by honey bees. *Apidologie*. 2010:295-311
- [24] Bruce Fife MD. *The Healing Miracle of Coconut Oil*. 1st ed. Health Colorado Springs: Wise publications Co; 2000. pp. 1-46
- [25] DebMandal M, Mandal S. Coconut (*Cocosnucifera* L: Arecaceae): In health promotion and disease prevention. *Asian Pacific Journal of Tropical Medicine*. 2011;**4**:241-247
- [26] Amith HV, Ankola AV, Nagesh L. Effect of oil pulling on plaque and gingivitis. *Journal of Oral Health and Community Dentistry*. 2007;**1**:12-18
- [27] Asokan S, Emmadi P, Chamundeswari R. Effect of oil pulling on plaque induced gingivitis: A randomized, controlled, triple-blind study. *Indian Journal of Dental Research*. 2009;**20**:47-51
- [28] Lobene RR, Weatherford T, Ross NM, Lamm RA, et al. A modified gingival index for use in clinical trials. *Clinical Preventive Dentistry*. 1986;**8**:3-6
- [29] Löe H. The gingival index, the plaque index and the retention index systems. *Journal of Periodontology*. 1967;**38**(6):610
- [30] Newman MG, Takei HH, Klokervold PR. *Carranza's Clinical Periodontology*. 10th ed. Vol. 2006. Elsevier. p. 241
- [31] Marsh PD. Dental plaque: Biological significance of a biofilm and community life-style. *Journal of Clinical Periodontology*. 2005;**32**:7-15
- [32] Chainani-Wu N. Safety and anti-inflammatory activity of curcumin: A component of turmeric (*Curcuma longa*). *Journal of Alternative and Complementary Medicine*. 2003;**9**: 61-68

- [33] Chaturvedi TP. Uses of turmeric in dentistry: An update. *Indian Journal of Dental Research*. 2009;**20**:107-109
- [34] Belt D. Licorice root lollipop shows sweet promise in reducing tooth decay. Licorice root lollipop shows sweet promise in reducing tooth decay. *Journal of the California Dental Association*. 2008;**36**(4):243-249
- [35] Messier C, Epifano F, Grenier D. Licorice and its potential beneficial effects in common oro-dental diseases. *Oral Diseases*. 2012;**18**(1):32-39
- [36] Farooqi MIH, Srivastava JG. The tooth-brush tree (*Salvadora persica*). *Quarterly Journal of Crude Drug Research*. 1968;**8**:1297-1299
- [37] Peddi VR, Whiting J, Weiskittel PD, Alexander JW, et al. Characteristics of long-term renal transplant survivors. *American Journal of Kidney Diseases*. 1998;**32**:101-106
- [38] Lamey PJ, Darwaza Fisher BM, Samaranayake LP, MacFarlane BM, et al. Secretor status, candidal carriage and candidal infection in patients with diabetes mellitus. *Journal of Oral Pathology*. 1988;**17**:354-357
- [39] Babak A, Akbar MA, Soozan B, et al. Extract chewing gum and gingival health: Improvement of gingival and probe-bleeding index. *Complementary Therapies in Clinical Practice*. 2010;**16**:121-123
- [40] Djakpo O, Yao W. *Rhuschinensis* and *Gallachinensis*-folklore to modern evidence: Review. *Phytotherapy Research*. 2010;**24**:1739-1747
- [41] Tong SS, Fu M, Cao X, Kesse C, et al. Lipid raft stationary phase chromatography for screening anti-tumor components from *Gallachinensis*. *Chromatographia*. 2014;**77**:419-429
- [42] Wang Z, Lin S, Wang D, Huang L. Anti-epidermal growth factor receptor tyrosine kinase activities of traditional Chinese medicine for cancer treatment. *Journal of Integrative Medicine*. 2014;**6**:565-570
- [43] Wu-Yuan CD, Chen CY, Wu RT. Gallotannins inhibit growth, water-insoluble glucan synthesis, and aggregation of mutans streptococci. *Journal of Dental Research*. 1988;**67**: 51-55
- [44] Haslam E. Gallic acid and its metabolites. In: Hemingway RW, Laks PE, editors. *Chemistry of Vegetable Tannins*. New York: Plenum Press; 1992. pp. 169-172
- [45] Xie Q, Li J-Y, Zuo Y-L, Zhou X-D. The effect of *Gallachinensis* on the growth of cariogenic bacteria in vitro. *West China Journal of Stomatology*. 2005;**23**:82-84
- [46] Xie Q, Li J, Zhou X. Anticaries effect of compounds extracted from *Gallachinensis* in a multispecies biofilm model. *Oral Microbiology and Immunology*. 2008;**23**:459-465
- [47] Tian F, Li B, Ji B, Zhang G, et al. Identification and structure-activity relationship of gallotannins separated from *Gallachinensis*. *LWT - Food Science and Technology*. 2009;**42**:1289-1295

- [48] Loo WT, Jin L, Cheung MN, Chow LW. Evaluation of ellagic acid on the activities of oral bacteria with the use of adenosine triphosphate (ATP) bioluminescence assay. *African Journal of Biotechnology*. 2010;**9**:3938-3943
- [49] Huang X, Cheng L, Exterkate RA, et al. Effect of pH on Gallachinensis extract's stability and anti-caries properties in vitro. *Archives of Oral Biology*. 2012a;**57**:1093-1099
- [50] Tang B, Yuan H, Cheng L, Zhou X, et al. Control of hydroxyapatite crystal growth by gallic acid. *Dental Materials Journal*. 2015a;**34**:108-113
- [51] Tang B, Yuan H, Cheng L, Zhou X, et al. Effects of gallic acid on the morphology and growth of hydroxyapatite crystals. *Archives of Oral Biology*. 2015b;**60**:167-173