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Advances in Antimicrobial, Antibiofilm, and Remineralization Strategies against Oral *Streptococcus mutans* Found in Natural and Synthetic Agents

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Abstract

Streptococcus mutans is the most crucial cariogenic bacterium responsible for dental caries. While traditional antimicrobial agents are widely used, growing research has identified various food- and drug-derived compounds with antimicrobial, antibiofilm, and remineralization properties. These bioactive ingredients offer promising caries-preventive potential due to their effectiveness against *S. mutans*, biocompatibility, and minimal side effects. This review summarizes recent research progress in the study of these compounds and their potential applications in caries prevention and treatment.

Keywords

Dental Caries, *Streptococcus mutans*, Natural and Synthetic Agents, Antimicrobial, Antibiofilm, Remineralization

1. Introduction

Dental caries is a highly prevalent bacterial infectious disease affecting the hard tissues of teeth, posing a significant threat to oral health. According to the World Health Organization's 2022 report, dental caries affects more than 2 billion people globally, with *Streptococcus mutans* involved in a significant proportion of cases, causing the disease in 60% - 80% of children and virtually all adults [1]. *Streptococcus mutans*, a gram-positive coccus, is currently recognized as the most crucial cariogenic bacterium in the oral cavity. It contributes to caries development through acid production and adherence to the tooth surface via glucosyltransferase activ-

ity. When *S. mutans* dominates the oral microbiome, constituting approximately 50% of the total bacterial population, it significantly increases the risk of caries formation [2]. While acid production is a key factor in enamel demineralization, the ability of *S. mutans* to form biofilms plays an even more critical role in the cariogenic process, providing structural stability and resistance to antimicrobial agents [3].

In orthodontic patients with fixed appliances, maintaining oral hygiene is often challenging, leading to plaque accumulation around brackets. This in turn causes acid erosion and demineralization, ultimately resulting in white spot lesions on tooth enamel [4]. Managing caries in pediatric, elderly, and immunocompromised populations is similarly difficult. Finding effective methods that can prevent white spot lesions *in situ* and enhance the remineralization of carious lesions is crucial for improving oral health outcomes in caries prevention and treatment.

For early enamel caries, it is usually treated with topical medication. Fluoride is commonly added to water and toothpaste to prevent caries by inhibiting demineralization and promoting remineralization of enamel crystals. However, there is still controversy over the appropriate concentration of use, as higher concentrations of fluoride can lead to certain toxic and side effects, such as dental fluorosis and skeletal fluorosis. Chlorhexidine, a cationic broad-spectrum antimicrobial agent, is widely used in mouthwashes to control *Streptococcus mutans* and prevent caries. Despite its effectiveness, it has notable side effects, including tooth staining, increased supragingival calculus formation, and temporary taste disturbances [5]. In recent years, growing research on bioactive compounds has identified various food-derived and pharmaceutical agents with promising antimicrobial, antibiofilm, and remineralization properties against *S. mutans*. These alternatives offer potential clinical applications in preventing white spot lesions and promoting enamel remineralization, particularly in orthodontic patients, while minimizing adverse effects associated with conventional treatments, along with good biological properties and minimal side effects, and apply them to the prevention of white spot lesions in clinical orthodontics.

2. Microbial and Biofilm Disruptors

The following section highlights several representative compounds with antimicrobial and antibiofilm properties. The antimicrobial efficacy, mechanisms of action, and safety profiles of these compounds are listed in **Table 1**.

2.1. Matrine

Sophora (*Sophora flavescens*) is an herbaceous or subshrub plant species in the genus *Sophora* of the family Fabaceae. Yang *et al.* [6] identified four key alkaloids—matrine, oxymatrine, sophocarpine, and sophoridine—each demonstrating a concentration-dependent inhibitory effect on the metabolic activity of planktonic *Streptococcus mutans* and biofilm formation. In addition to inhibiting the growth of *Streptococcus mutans* and the formation of biofilms, sophora alka

Table 1. Bioactive compounds' properties.

Compounds	Properties		
	Antimicrobial efficacy (MIC)	Mechanism of action	Safety profile (LD50)
Matrine	10 mg/mL	Decreased expression of genes	245 mg/kg
Xanthohumol	32 μg/mL	Increased membrane permeability	Unclear
EGCG	6.25 μg/mL	Dehydrogenase inhibition	761.5 mg/kg
Curcumin	256 μmol/L	Sortase A enzyme inhibition	5000 mg/kg
Theaflavin	500 μg/mL	Membrane disruption	2710 - 3160 mg/kg
Quercetin	16 mg/mL	Decreased expression of genes	10 g/kg
Procyanidin	12.5 mg/mL	Increased NOS synthesis into NO	3451.9 mg/kg
Glycyrrhizin	75 μg/mL	Glucosyltransferase inhibition	2000 mg/kg
Myricetin	0.8 mg/mL	Glucosyltransferase inhibition	100 μM
Baicalein	32 μg/mL	Anti-adhesive action by blocking receptors	Negligible toxicity
Peptide GH12	8 μg/mL	Decreased expression of genes	Unclear

loids also have ability to eradicate mature biofilms [7]. Moreover, various sophora alkaloids used in combination with chlorhexidine also have different degrees of synergistic inhibitory effects on *Streptococcus mutans*. Among these, matrine exhibits the strongest synergistic effect when combined with chlorhexidine, enhancing antimicrobial activity while reducing the required concentration of chlorhexidine. The combination of four sophora alkaloids with chlorhexidine can maintain high inhibitory activity while also reducing the concentration of chlorhexidine used, thereby reducing the risk of adverse reactions to some extent, and providing a new method for the combined use of sophora alkaloids with chlorhexidine to prevent dental caries. In recent years, the combined use of natural drugs and conventional antimicrobial drugs may enhance efficacy while lowering the risk of adverse reactions, offering a new avenue for caries management [8].

2.2. Xanthohumol

Xanthohumol and isoxanthohumol are the most abundant flavonoid compounds in the hops (*Humulus lupulus*) of the family Cannabaceae. Studies have found that xanthohumol and isoxanthohumol at sub minimum inhibitory concentrations can suppress various virulence factors of *Streptococcus mutans* associated with caries formation [9]. Specifically, they significantly reduce the bacterium's acidogenic ability and acid resistance while also inhibiting biofilm formation. A randomized controlled trial showed that the number of *S. mutans* in the plaque samples after volunteers used the mouthwash containing 0.1% *Humulus lupulus* polyphenols extract was significantly lower than that after they used the placebo [10]. Despite these promising findings, the safety and potential toxicity of xan-

thohumol and isoxanthohumol in the oral cavity remain unclear. In addition, there are usually complex interactions between different bacteria within the dental plaque biofilms, where microbial interactions may influence the efficacy of these flavonoids [11]. Further research is needed to evaluate their anticarious activity in multispecies biofilms and to assess their potential for clinical application.

2.3. Epigallocatechin-3-Gallate

Epigallocatechin-3-gallate (EGCG), a polyphenolic monomer extracted from green tea, not only has anti-inflammatory and antioxidant effects but also combats *Streptococcus mutans* by inhibiting the activity of dehydrogenase, thereby preventing enamel demineralization and caries occurrence [12]. Due to its strong bioactivity and low cytotoxicity, Yang *et al.* [4] investigated the incorporation of EGCG into orthodontic bonding agents. They concluded that orthodontic bonding agents containing 1 g/L EGCG demonstrated significant antimicrobial efficacy against *S. mutans* without compromising adhesion to enamel. A randomized clinical trial demonstrated that EGCG-containing mouthwash (4000 μg/mL) significantly reduced *S. mutans* counts in children aged 5 - 12 years at high caries risk [13]. These findings provide a basis for preventing white spot lesions in orthodontic patients.

2.4. Curcumin

Curcumin is a natural polyphenolic compound extracted from the root of the turmeric plant. *In vitro* studies have found [14] that curcumin combined with blue LED light can effectively reduce surviving bacteria accumulation, including common cariogenic bacteria such as *Streptococcus mutans* and *Lactobacillus acidophilus*. However, clinical application is limited by its poor bioavailability and stability. Although various strategies have been employed to improve the solubility of curcumin, challenges such as limited production and concerns over biotoxicity persist. Therefore, further research is needed to optimize its formulation and fully assess its potential for clinical use [15].

Hu *et al.* [16] found that 30 μmol/L of curcumin could significantly reduce the adhesion and biofilm formation of *Streptococcus mutans* and *Streptococcus sanguis* monocultures without exerting antimicrobial pressure. This effect is mediated by the inhibition of the Sortase A enzyme in both bacteria. However, in complex biofilms where these species coexist, curcumin does not significantly alter the adhesion rate of *S. mutans*, suggesting that bacterial interactions may counteract its inhibitory effect. The interactions between bacteria might offset the changes in the adhesion capability of *Streptococcus mutans* caused by curcumin. While *in vitro* biofilm models provide mechanistic insights, they lack the complexity of oral microbiota interactions, the specific mechanism underlying further research. These findings highlight a key challenge in translating curcumin's biofilm-disrupting properties into effective caries prevention strategies.

2.5. Theaflavin

Theaflavin, the main component of black tea, is a benzotropolone compound that

has antimicrobial, anti-inflammatory, antioxidant, and anti-mutagenic effects [17]. Research by Wang *et al.* [2] showed that theaflavin can inhibit the growth and acid production of *Streptococcus mutans*, demonstrating good antimicrobial activity. Similarly, in the study by Zheng *et al.* [3], theaflavin exhibits significant inhibitory activity against pre-formed biofilms of *Streptococcus mutans* UA159, suggesting its potential application in caries prevention. Despite its promising bioactivity, further research is needed to determine the optimal and safe dosage for oral use. Establishing appropriate concentrations will be critical for translating theaflavin into clinical dental treatments.

2.6. Quercetin

Quercetin, also known as 3,3,4,5,7-pentahydroxyflavone, is widely found in the flowers, leaves, and fruits of various plants. In addition to anti-inflammatory and antioxidant effects [18], quercetin can also counteract *Streptococcus mutans* by effectively reducing biofilm formation through the inhibition of related gene expression. Sun *et al.* [19] found that adhesives containing 0.5 mg/mL quercetin can exert long-lasting antimicrobial effects without interfering with the polymerization and shear strength, suggesting potential for preventing white spot lesions. However, further studies are needed to analyze the cytotoxicity of quercetin and its long-term antimicrobial effects more thoroughly, ensuring its safety and efficacy in clinical applications.

2.7. Grape Seed Procyanidin

Recent studies have highlighted the high nutritional and medicinal value of grape seed extracts, primarily due to its rich procyanidin content. Procyanidin has antioxidant, free radical scavenging, immune system boosting, and anti-tumor effects [20]. Wang *et al.* [21] conducted experimental research on the antimicrobial activity of grape seed procyanidins against *Streptococcus mutans* and its inhibitory effect on the biofilm. The results showed that procyanidins can effectively inhibit the growth metabolism and biofilm of *Streptococcus mutans*, and suppress virulence factors, demonstrating its potential in preventing and reducing the occurrence of dental caries. However, further research is required to elucidate their specific mechanisms of action more deeply and assess their efficacy *in vivo*.

2.8. Glycyrrhizin

Glycyrrhiza glabra, commonly known as licorice, is a medicinal plant containing glycyrrhizin, a triterpene glycoside with antimicrobial properties. Glycyrrhizin has been shown to inhibit the activity of glucosyltransferase, suppressing the synthesis of extracellular polysaccharides, thereby reducing extracellular polysaccharide synthesis and reducing dental plaque biofilm formation, ultimately limiting *Streptococcus mutans* activity [22]. Wang *et al.* [23] further demonstrated that glycyrrhizin significantly inhibits acid production, adhesion, and biofilm formation of *Streptococcus mutans*. Analysis of enzyme kinetics revealed the mechanism by which

glycyrrhizin inhibits enzyme activity, indicating that glycyrrhizin is a noncompetitive inhibitor of glucosyltransferase [1]. While this study confirmed the inhibitory effects of glycyrrhizin on *Streptococcus mutans* in planktonic and biofilm states *in vitro*, further *in vivo* studies are necessary to determine its potential for clinical applications in caries prevention.

2.9. Myricetin

Myricetin, as the primary active pharmacological component in bayberries, exhibits an effective ability to inhibit the activity of glucosyltransferase, thereby disrupting *Streptococcus mutans* biofilm formation [24]. Xu *et al.* [25] has demonstrated that myricetin inhibits biofilms and reduces the cariogenic ability of *Streptococcus mutans*, supporting its potential application in treating biofilm-induced dental caries. However, its cytotoxic effects on oral cells and the precise molecular mechanisms underlying its antimicrobial activity require further investigation to assess its safety and therapeutic viability.

2.10. Baicalein

Baicalein, also known as 5,6,7-trihydroxyflavone, a flavonoid isolated from the roots of *Scutellaria baicalensis* and *Scutellaria lateriflora*, known for its wide range of biological properties [26]. Liu *et al.* [27] found that although baicalein exhibits weaker antimicrobial activity compared to chlorhexidine, it demonstrates a superior inhibitory effect against *Streptococcus mutans* biofilms. Nevertheless, its precise antimicrobial mechanism remains unclear, necessitating further research to elucidate its mode of action and potential clinical applications.

2.11. Antimicrobial Peptide

Swedish scientists Boman *et al.* first discovered an antimicrobial peptide (AMP) capable of inhibiting bacterial proliferation in 1972, and the term AMPs was officially introduced in 1981. Antimicrobial peptides are a class of short, positively charged bioactive molecules, widely distributed in human saliva, epithelium, and neutrophils, with broad-spectrum antimicrobial activity. However, natural antimicrobial peptides have disadvantages such as toxicity, hemolytic properties, high cost, and limited availability. To overcome these challenges, researchers have developed synthetic AMPs with improved stability, reduced cytotoxicity, and enhanced activity against cariogenic bacteria. Researchers have designed and synthesized an amphipathic α-helical antimicrobial peptide GH12 (GLLWLHLHLLH-NH2) [5]. Wang *et al.* [28] selected the peptide GH12 from three short antimicrobial peptides which has the most stable secondary structure and strongest antimicrobial activity, studied its antimicrobial activity against eight major planktonic cariogenic bacteria, and investigated its effect on the biofilm of single *Streptococcus mutans*, Their study confirmed that GH12 effectively inhibits *S. mutans* growth at low concentrations and disrupts biofilm formation by downregulation of *ldh*, *atpD*, *gtfB*, *gtfC*, *gtfD* gene expression [5], making it a promising agent for caries prevention.

3. Remineralizers

3.1. Catechin

Catechins, a subgroup of flavonoids, are the primary pharmacologically active compounds in green tea. Among them, epigallocatechin-3-gallate (EGCG) accounts for approximately 50% of catechins, with the highest content [29]. Studies have found that EGCG has a remineralization effect on dental caries by binding with calcium ions to form complexes, which penetrate dentinal tubules and facilitate calcium deposition. This process supports the growth of dissolved enamel crystals and enhances remineralization [30]. Additionally, dental adhesives with an appropriate amount of EGCG not only inhibit *Streptococcus mutans* growth and biofilm maturation but also improve adhesive strength and exhibit remineralization properties. These characteristics make EGCG a promising additive in dental materials for caries prevention and enamel restoration.

3.2. Gallic Acid

Gallic acid is a cost-effective, widely available compound naturally found in a variety of fruits and vegetables. Similar to EGCG, the pyrogallol groups contained in gallic acid have been proven to facilitate remineralization by binding with calcium ions, which are key components of hydroxyapatite found in saliva, accelerating hydroxyapatite regeneration [31]. Building on this property, Niu *et al.* [32] developed a biocompatible, stable, novel dual-function antimicrobial peptide GA-KR12 by grafting gallic acid onto the active peptide KR12. GA-KR12 exhibits both anti-*Streptococcus mutans* activity and remineralization potential, making it a promising candidate for enamel caries prevention and treatment.

3.3. Xylitol

Xylitol is a polyol obtained from plant fibers by hydrolyzing and hydrogenating the xylose contained, also known as pentitol. Xylitol inhibits cariogenic bacteria and remineralizes early demineralized dental caries to achieve caries prevention [33]. Chen *et al.* [34] found that sucrose and glucose significantly promote microbial growth, while xylitol has no promotional effect on microbial growth. Xylitol-containing toothpaste has been shown to reduce the fermentation and growth of *Streptococcus mutans*, thereby limiting acid production. Additionally, xylitol is considered to promote remineralization by shifting the balance in favor of mineral deposition, aiding the natural repair of demineralized tooth structures. This ability to promote remineralization while preventing further demineralization underscores its potential as a key component in caries prevention strategies.

4. Limitation and Outlook

Given the anticarious activity against oral *Streptococcus mutans* and the ability to promote remineralization, certain bioactive food and drug ingredients may serve as future alternatives to antibiotics and fluoride. The compounds mentioned above serve as merely a selection of representative examples and do not encompass all the

identified effective components. These compounds could be incorporated into mouthwashes, toothpaste, or dental adhesives to aid in caries prevention and treatment. However, most of the current research is still in the *in vitro* stage. To fully understand their potential, more studies are needed to replicate real-world oral microbial environments through advanced *in vivo* models. When translating *in vitro* findings to clinical practice, some compounds may not be effective due to oral microbiota interactions. Additionally, large-scale clinical trials are essential to assess their long-term efficacy in biofilm disruption and caries prevention within the complex conditions of the oral cavity. Future research should focus on optimizing these compounds for safe and effective clinical application [5].

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Atazhanova, G.A., Levaya, Y.K., Badekova, K.Z., Ishmuratova, M.Y., Smagulov, M.K., Ospanova, Z.O., *et al.* (2024) Inhibition of the Biofilm Formation of Plant *Streptococcus mutans*. *Pharmaceuticals*, **17**, Article No. 1613. https://doi.org/10.3390/ph17121613

[2] Wang, Y.N., Zhang, J. and Xu, G.C. (2020) Inhibitory Effect of Theaflavin on *Streptococcus mutans*: An *in Vitro* Study. *Preventive Medicine*, **12**, 1287-1289, 1292.

[3] Zheng, P., Zhang, Y. and Wang, S. (2021) Inhibitory Effects of Theaflavin on Planktonic and Sessile Bacterial Cells of *Streptococcus mutans in Vitro*. *Shanghai Journal of Stomatology*, **1**, 33-37. https://doi.org/10.19439/j.sjos.2021.01.007

[4] Yang, L.Q., Wang, B.H. and Xie, L.L. (2021) Evaluation of Antibacterial Ability of Epigallocatechin-3-Gallate-Modified Adhesive. *Journal of Oral Science Research*, **2**, 131-134. https://doi.org/10.13701/j.cnki.kqyxyj.2021.02.009

[5] Wang, D.N. and Zhao, Y.P. (2021) Research Progress of Synthetic Peptide GH12 for Caries Prevention and Treatment. *Hainan Medical Journal*, **6**, 782-784.

[6] Yang, R.C., Zhao, G.P., Wang, C.D., *et al.* (2021) Combinatorial Effects of Four Alkaloids with Chlorhexidine on *Streptococcus mutans*. *Research and Practice on Chinese Medicines*, **3**, 34-38. https://doi.org/10.13728/j.1673-6427.2021.03.008

[7] Yang, R.C., Wang, J. and Zhang, Y.Y. (2021) Study on the Inhibitory Effect of Matrine on the Biofilm of *Streptococcus mutans*. *Anhui Agricultural Science*, **9**, 168-171. https://doi.org/10.3969/j.issn.0517-6611.2021.09.045

[8] Karygianni, L., Al-Ahmad, A., Argyropoulou, A., Hellwig, E., Anderson, A.C. and Skaltsounis, A.L. (2016) Natural Antimicrobials and Oral Microorganisms: A Systematic Review on Herbal Interventions for the Eradication of Multispecies Oral Biofilms. *Frontiers in Microbiology*, **6**, Article 1529. https://doi.org/10.3389/fmicb.2015.01529

[9] Yang, R.C., Li, Q., Wang, T., *et al.* (2021) Inhibitory Effects of Xanthohumol and Isoxanthohumol on Cariogenic Virulence Factors of *Streptococcus mutans*. *Journal of Shaanxi University of Science & Technology*, **5**, 62-68.

[10] Shinada, K., Tagashira, M., Watanabe, H., Sopapornamorn, P., Kanayama, A., Kanda, T., *et al.* (2007) Hop Bract Polyphenols Reduced Three-Day Dental Plaque Regrowth. *Journal of Dental Research*, **86**, 848-851. https://doi.org/10.1177/154405910708600908

[11] Lamont, R.J., Koo, H. and Hajishengallis, G. (2018) The Oral Microbiota: Dynamic Communities and Host Interactions. *Nature Reviews Microbiology*, **16**, 745-759. https://doi.org/10.1038/s41579-018-0089-x

[12] Besingi, R.N., Wenderska, I.B., Senadheera, D.B., Cvitkovitch, D.G., Long, J.R., Wen, Z.T., *et al.* (2017) Functional Amyloids in *Streptococcus mutans*, Their Use as Targets of Biofilm Inhibition and Initial Characterization of SMU_63c. *Microbiology*, **163**, 488-501. https://doi.org/10.1099/mic.0.000443

[13] Vilela, M.M., Salvador, S.L., Teixeira, I.G.L., Del Arco, M.C.G. and De Rossi, A. (2020) Efficacy of Green Tea and Its Extract, Epigallocatechin-3-Gallate, in the Reduction of Cariogenic Microbiota in Children: A Randomized Clinical Trial. *Archives of Oral Biology*, **114**, Article ID: 104727. https://doi.org/10.1016/j.archoralbio.2020.104727

[14] Chen, D.H., Liu, Q. and Wu, B.L. (2021) Research Progress of Curcumin in Stomatology. *Chinese Journal of Prosthodontics*, **3**, 216-221. https://doi.org/10.19748/j.cn.kqxf.1009-3761.2021.03.012

[15] Chen, Y., Lu, Y., Lee, R.J. and Xiang, G. (2020) Nano Encapsulated Curcumin: And Its Potential for Biomedical Applications. *International Journal of Nanomedicine*, **15**, 3099-3120. https://doi.org/10.2147/ijn.s210320

[16] Hu, P., Zeng, P.P., Zhang, Y.Y., *et al.* (2021) Study on the Adhesion of Curcumin to *Streptococcus mutans* and *Streptococcus sanguis*. *Journal of Clinical Stomatology*, **1**, 11-14.

[17] Singh, B.N., Prateeksha, Rawat, A.K.S., Bhagat, R.M. and Singh, B.R. (2017) Black Tea: Phytochemicals, Cancer Chemoprevention, and Clinical Studies. *Critical Reviews in Food Science and Nutrition*, **57**, 1394-1410. https://doi.org/10.1080/10408398.2014.994700

[18] Li, Y., Yao, J., Han, C., Yang, J., Chaudhry, M., Wang, S., *et al.* (2016) Quercetin, Inflammation and Immunity. *Nutrients*, **8**, Article No. 167. https://doi.org/10.3390/nu8030167

[19] Sun, Y.H., Li, K., Yang, H.Y., *et al.* (2020) Study on Antibacterial Property of Quercetin Modified Adhesive. *Journal of Guangxi Medical University*, **10**, 1837-1841. https://doi.org/10.16190/j.cnki.45-1211/r.2020.10.013

[20] Rajakumari, R., Volova, T., Oluwafemi, O.S., Rajesh Kumar, S., Thomas, S. and Kalarikkal, N. (2020) Grape Seed Extract-Soluplus Dispersion and Its Antioxidant Activity. *Drug Development and Industrial Pharmacy*, **46**, 1219-1229. https://doi.org/10.1080/03639045.2020.1788059

[21] Wang, J. and Wang, H. (2017) Antibacterial Activities of Grape Seed Procyanidins against *Streptococcus mutans in Vitro*. *Journal of Nanjing University of Traditional Chinese Medicine*, **2**, 173-176. https://doi.org/10.14148/j.issn.1672-0482.2017.0173

[22] Messier, C., Epifano, F., Genovese, S. and Grenier, D. (2011) Licorice and Its Potential Beneficial Effects in Common Oro-Dental Diseases. *Oral Diseases*, **18**, 32-39. https://doi.org/10.1111/j.1601-0825.2011.01842.x

[23] Wang, Y.B., Song, L.Q., Yang, J.Y., *et al.* (2021) *In Vitro* Study on the Antibacterial Effect of Glycyrrhizin on *Streptococcus mutans*. *Gansu Medical Journal*, **7**, 577-579, 582.

[24] Rocha, G.R., Florez Salamanca, E.J., de Barros, A.L., Lobo, C.I.V. and Klein, M.I. (2018) Effect of *tt*-Farnesol and Myricetin on *in Vitro* Biofilm Formed by *Streptococcus mutans* and Candida Albicans. *BMC Complementary and Alternative Medicine*, **18**, Article No. 61. https://doi.org/10.1186/s12906-018-2132-x

[25] Xu, X.Y., Guo, M.Q., Yu, H.J., *et al.* (2022) Effect of Myricetin on Virulence Factor and

Biofilm of *Streptococcus mutans*. *Journal of Oral Science Research*, **4**, 344-349. https://doi.org/10.13701/j.cnki.kqyxyj.2022.04.011

[26] Vijayakumar, A., Sarveswari, H.B., Vasudevan, S., Shanmugam, K., Solomon, A.P. and Neelakantan, P. (2021) Baicalein Inhibits *Streptococcus mutans* Biofilms and Dental Caries-Related Virulence Phenotypes. *Antibiotics*, **10**, Article 215. https://doi.org/10.3390/antibiotics10020215

[27] Liu, L., Lin, H., Huang, R.S., *et al.* (2017) Study on Inhibitory Effect of Baicalin and Baicalein on the Formation of *Streptococcus mutans* Biofilm. *Traditional Chinese Drug Research & Clinical Pharmacology*, **4**, 464-467. https://doi.org/10.19378/j.issn.1003-9783.2017.04.011

[28] Wang, Y., Fan, Y., Zhou, Z., Tu, H., Ren, Q., Wang, X., *et al.* (2017) De Novo Synthetic Short Antimicrobial Peptides against Cariogenic Bacteria. *Archives of Oral Biology*, **80**, 41-50. https://doi.org/10.1016/j.archoralbio.2017.03.017

[29] Yang, L.Q., Wang, B.H. and Liang, J.M. (2021) Research Progress of Epigallocatechin Gallate in the Treatment of White Spot Lesions. *China Medicine and Pharmacy*, **12**, 29-32. https://doi.org/10.3969/j.issn.2095-0616.2021.12.008

[30] Chen, K., Ruan, J.Y., Yi, D.Z., *et al.* (2012) Remineralization of Artificial Demineralized Enamel by Extracts from Galla Chinensis and Galla Halepensis. *Journal of Dali University*, **9**, 22-24.

[31] Prajatelistia, E., Ju, S., Sanandiya, N.D., Jun, S.H., Ahn, J. and Hwang, D.S. (2016) Tunicate-Inspired Gallic Acid/Metal Ion Complex for Instant and Efficient Treatment of Dentin Hypersensitivity. *Advanced Healthcare Materials*, **5**, 919-927. https://doi.org/10.1002/adhm.201500878

[32] Niu, J.Y., Yin, I.X., Wu, W.K.K., Li, Q., Mei, M.L. and Chu, C.H. (2021) A Novel Dual-Action Antimicrobial Peptide for Caries Management. *Journal of Dentistry*, **111**, Article ID: 103729. https://doi.org/10.1016/j.jdent.2021.103729

[33] Xu, Y.H., Li, C.J., Yang, S., *et al.* (2020) Application Status of Xylitol in Toothpaste. *Oral Care Industry*, **5**, 37-38.

[34] Chen, M.S., Lin, Y.G., Li, Y.P., *et al.* (2004) Bacteriostatic Test of Xylitol and Xylitol-containing Toothpaste. *Toothpaste Industry*, **4**, 32-33.