

NATURAL REMEDIES FOR CHRONIC PERIODONTITIS: A PLANT-BASED INTERVENTION STRATEGY

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Abstract

Chronic periodontitis, a widespread dental condition characterized by inflammation and destruction of periodontal support tissue and alveolar bone, has seen a growing trend among younger individuals, affecting 10% - 15% of the global population. Left untreated, it can lead to tooth loss and significantly impact patients' quality of life. Oral health is a vital aspect of overall health and well-being, making effective periodontitis treatment imperative. Traditional treatments often rely on mechanical methods, such as subgingival curettage and root surface leveling. However, due to the intricate nature of root anatomy, these approaches alone may not fully control the disease, necessitating adjuvant drug therapies.

Various antibiotics have been used as adjuvant treatments for periodontitis, but concerns about antibiotic resistance and systemic side effects persist. Recently, a combination of traditional Chinese and Western medicine has gained prominence in periodontitis treatment, employing natural plant extracts known for their anti-inflammatory, antioxidant, and anti-tumor properties. This article reviews studies exploring the therapeutic potential of natural plants such as Skullcap, Curcuma longa L, Pueraria lobata, Naringin, Paeoniflorin, and resveratrol in the treatment of periodontitis, shedding light on the promising role of plant-based compounds in managing this condition.

Keywords: chronic periodontitis, dental health, natural plant extracts, adjuvant treatment, antibiotics, periodontal support tissue, inflammation, alveolar bone, root anatomy, oral health, tooth loss, drug therapy.

Introduction

Chronic periodontitis is occurring in the periodontal support tissue of periodontal inflammation and alveolar bone destruction as the main characteristics of chronic disease^[1], its number accounts for 10% -15% of the total number of the world^[2], and gradually younger age trend, if not timely treatment, with the further development of periodontal inflammation, will lead to missing teeth, seriously affect the life of patients^[3]. Oral health not only reflects the oral state of patients, but also has a certain impact on the physiology and psychology. Good oral health has become one of the ten standards of human health, so the treatment of periodontitis is very important^[4]. The traditional treatment of chronic periodontitis is based on mechanical methods, including subgingival curettage and root surface leveling^[5]. Due to the complexity of root anatomy, the complete control of periodontitis can not be achieved by mechanical treatment alone, so it is necessary to use drugs as adjuvant treatment on the basis of previous treatment^[6]. At present, the clinical treatment of periodontitis adjuvant antibiotics, such as amoxicillin and metronidazole^[7-9], metronidazole and azithromycin^[7], azithromycin^[8], metronidazole^[9], levofloxacin^[9], moxifloxacin^[9], erythromycin^[9], etc. But still need to pay attention to the possibility of antibiotic resistance and antibiotics on the human microbial

environment^[10], and systemic adverse reactions when antibiotics is more^[9]. In recent years, the combination of traditional Chinese and western medicine is more and more extensive in the treatment of periodontitis, such as Xipayi mouth rinse + minocycline hydrochloride^[11,12], erythritol^[13,14], rehabilitation new fluid + minocycline^[15], etc. Numerous studies have shown that natural plants have anti-inflammatory, antioxidant and anti-tumor effects, and these extracts may exert their potential medicinal value in the treatment of periodontitis^[16]. Many scholars have chosen a large number of natural plants to study the treatment of periodontitis, such as Skullcap, Curcuma longa L, Pueraria lobata, Naringin, Paeoniflorin, resveratrol, etc. In recent years, the recognition of natural drugs in countries around the world has been increasing^[17]. It is not only widely used in traditional medicine countries such as China and India, but also shows great potential in medical care in the European Union, Singapore, the United States, the United Kingdom and other regions. The research on chronic periodontitis treatment has gradually attracted attention. The natural plants for the treatment of chronic periodontitis are briefly summarized.

1. Cistanche deserticola Ma

Cistanche deserticola Ma, is one of the "nine Chinese herbs", known as "desertginseng", its chemical structure is complex, has purified and identified more than 150 kinds of chemical family, including Phenylethanoid glycosides, Benzylglycosides, secoiridoid, lignin, oligosaccharides and polysaccharides, etc. Among them, Phenylethanoid glycosides has received wide attention worldwide due to its favorable pharmacological properties^[18]. Modern pharmacology has found that Cistanche deserticola Ma has anti-inflammation, anti-fatigue, anti-oxidation, anti-tumor, enhancement of immunity and other effects of^[19], and has a good safety profile^[20].

The extract of Cistanche has been reported^[21] that through prevent the receptor activator of nuclear factor Kappa B ligand (RANKL) / receptor activator of nuclear factor Kappa B (RANK) / tumor necrosis factor receptor (TNFR)-associated factor 6 (TRAF6) induced nuclear factor Kappa B activation, promote the upregulation of the phosphoinositide 3-kinase (PI3K) / Protein kinase B (Akt), activation of the proto-oncogene c-fos, and inhibition of nuclear factor of activated T cells 2 (NFATC2), final inhibition of osteoclast differentiation and corresponding bone resorption was inhibited. Li^[22] demonstrated through in vitro and in vivo studies that the Cistanche extract can promote bone formation and the expression of alkaline phosphatase (ALP), osteocalcin (OCN), bone morphogenetic proteins 2 (BMP2) and bone mineralization.

In vitro experiments^[23] have found that Cistanche can reduce the formation of osteoclasts and the expression of osteoclasts marker genes Matrix metalloproteinase 9 (MMP 9), cathepsin K (CTSK) and tartrate-resistant acid phosphatase 5 (TRACP5), and inhibit the production of the reactive oxygen species (ROS) mediated by RANKL in vitro, the activation of nuclear factor of activated T-cell (NFATc) and mitogen-activated protein kinase (MAPK). In conclusion, Cistanche has potential value in the treatment of the alveolar bone loss in chronic periodontitis.

2. Curcuma

Curcuma is a traditional Chinese medicine, derived from the dried root of Curcuma longa L, mainly produced in Chinese Sichuan, Fujian, Guangdong, Guangxi, Yunnan, Xizang and other provinces and regions. Curcuma first contained in the Tang Dynasty "new herbal", warm, bitter, spicy, return to the spleen, liver meridian, has the effect of breaking blood, dysmenorrhea and pain relief^[24]. The main components of Curcuma are essential oil and curcumin. A large number of experiments and clinical studies have shown that

curcumin antioxidant, anti-inflammatory, anti-cancer and antiviral infection pharmacological effects^[25]. A meta-analysis of^[26] evaluated the clinical effect of curcumin and chlorhexidine for the treatment of chronic periodontitis. Since curcumin is a natural food, it is a good candidate for adjuvant periodontitis treatment. Sha^[27] confirmed by in vivo experiments that curcumin reduced bone resorption and osteoclast formation by inhibiting RANKL expression and increasing osteoprotegerin (OPG) release, alleviated alveolar bone loss, and attenuated periodontal inflammation, we also found that curcumin had less side effects on periodontal tissue compared with chlorhexidine. Some scholars^[28] have confirmed through experiments in vitro that curcumin has no toxic effect on human periodontal ligament stem cells at moderate concentration, and can promote the osteogenic differentiation of human periodontal ligament stem cells (hPDLSCs) through PI3K / AKT signaling pathway.

3. Puerariae Lobatae Radix

Puerariae Lobatae Radix is the tuber of the legume, which is a strong vine, which was written in Shennong Materia Medica Classic. Puerariae Lobatae Radix has a long history of application in China. The ancient Chinese, it has the functions of relieving muscle fever, quenching thirst, penetrating rash, and relieving alcohol poison, modern pharmacological studies show that it has bacteriostatic, anti-myocardial ischemia, antioxidant, anti-tumor, anti-convulsant, puzzle and other effects. Some scholars showed through systematic evaluation that puerarin can be used as an effective osteogenic promoter, but also as an inhibitor of RANKL-induced osteoclastogenesis, and through in vitro and in vivo studies, puerarin was found to have a great effect on the osteogenic capacity of osteoblasts.

Some studies found through in vitro and in vivo experiments that puerarin can reverse the bone destruction of glucocorticoids, improve the viability of osteoblasts, and promote the differentiation of osteoblasts and the expression of osteogenesis-related genes; through in vivo experiments found that puerarin can reduce the activity of Alkaline phosphatase (ALP) in osteoblasts under high glucose and promote the expression of type I collagen (Col-1). Chinese scholar Zhao Bing found through the curative effect observation of clinical trials that after basic periodontal treatment, the depth and attachment of periodontal pockets were significantly improved after oral puerengqin decoction treatment, periodontal tissue was restored, and the decoction had high safety, which is worthy of clinical promotion. Thus, puerarin could be a more selective and safer drug to slowing alveolar bone loss in chronic periodontitis.

4. Resveratrol

Resveratrol is a natural polyphenol non-flavonoid compound, which is widely found in a variety of plants, mainly derived from grapes, soybeans, peanuts and berries. Its pharmacological effects include anti-oxidation, anti-inflammatory, anti-tumor, antibacterial, bone protection, cardiovascular protection and so on. Based on a large number of experimental studies, it is found that resveratrol promote the proliferation and differentiation of osteoblasts in vitro and in vivo, and inhibit the differentiation of osteoclasts to protect bone tissue. The configuration of drug delivery system in the form of scaffold can improve and optimize the efficacy of resveratrol.

After the successful establishment of the mouse model of periodontitis, due to the severe destruction of periodontal tissue, the extraction of ligated molar teeth and local intervention of resveratrol. Compared with the control group, the alveolar socket of the treatment group had significantly increased bone tissue, the periodontal tissue also recovered, and the inflammatory factors decreased significantly. Scholar has also found

through in vitro experiments that resveratrol can improve the inflammatory microenvironment and enhance the osteogenic differentiation of hPDLSCs by activating the Extracellular signal-regulated kinase (ERK (1/2)) pathway. Thus, resveratrol may be a good candidate for anti-inflammatory agents that can ameliorate the inflammatory microenvironment-induced bone remodeling.

5. *Salvia miltiorrhiza* Bge

Salvia miltiorrhiza Bge is a traditional Chinese medicine, first contained in "Shennong Materia Medica", is a lip plant, is the dry root and root of *Salvia miltiorrhiza* Bge, bitter taste, slightly cold, liver meridian has blood circulation and blood stasis, clear heart and remove annoyance and other functions. The major tanshinones isolated from *Salvia miltiorrhiza* Bge included 15, 16-dihydrotanshinone, tanshinone I, cryptotanshinone, and tanshinone IIA with anti-inflammatory and anti-osteoporotic effects. Foreign researchers collected a large number of studies to show that tanshinone promotes bone remodeling by inhibiting osteoclastogenesis and bone resorption, while promoting osteobogenesis and bone differentiation. Some studies have found that tanshinone can improve bone loss and bone metabolism and promote osteogenesis through in vitro and in vivo experiments. Chinese scholar Jiang Saifang through clinical observation of the efficacy of Danshen tablets in chronic periodontitis patients after basic treatment found that the control of periodontal inflammation and the recovery of periodontal tissue in patients taking Danshen tablets had obvious effects, with good short-term clinical efficacy.

6. Summary

In conclusion, the adjuvant drug of chronic periodontitis is still dominated by antibiotics. Due to the antibiotic resistance and its impact on the microbiota, natural plants gradually enter the attention of researchers. Studies on natural plants mainly focus on the control of inflammatory factors, bone metabolic pathways, and tissue destruction mediated by inflammatory mediators, so as to control periodontitis and promote tissue regeneration.

When natural plants are used as adjuvant drugs, the agent status, purification method, concentration and frequency of use are also our concern. Clinicians topical application of curcumin nanoparticles in the adjuvant treatment of chronic periodontitis, did not observe the beneficial effect of the patient's condition; however, others topical curcumin gel as the adjuvant drug after mechanical treatment of chronic periodontitis was observed the periodontal pocket depth and attachment level were significantly improved after a month. Chinese scholar Yuan Yuan through meta-analysis, short-term (during a month) follow-up observation of patients with topical curcumin gel and chlorhexidine, and the attachment level of the former improved more significantly. It is expected that future experiments will consider this issue more comprehensively.

Natural plant composition is complex and there are numerous experimental studies showing that natural drugs can be used to treat chronic periodontitis, but clinical applications is still limited. Natural drug single-combination use is also a problem that we need to think about. In China, chronic periodontitis is mainly treated in the form of combined Chinese medicine. It is expected that future studies can combine drugs to a single form or active ingredient to realize the precision of adjuvant drug therapy.

References

He W, You M, Wan W, Xu F, Li F, Li A. Point-of-Care Periodontitis Testing: Biomarkers, Current Technologies, and Perspectives. Trends Biotechnol. 2018, 36(11): 1127-1144.

- Kassebaum NJ, Bernabé E, Dahiya M, Bhandari B, Murray CJ, Marcenes W. Global burden of severe periodontitis in 1990-2010: a systematic review and meta-regression. *J Dent Res*. 2014, 93(11): 1045-1053.
- Saglam E, Canakci CF, Sebin SO, Saruhan N, Ingec M, Canakci H, SezerU. Evaluation of oxidative status in patients with chronic periodontitis and polycystic ovary syndrome: A cross-sectional study. *J Periodontol*. 2018, 89(1): 76-84.
- Chen Jia, Mengnan Li, Qingnan Liu, Jie Li. Significance analysis of tea polyphenol mouthgargle combined with self-continuation rehabilitation guidance inpatients with chronic periodontitis. *Chinese Journal of Modern Drug Application*, 2020, 14(17): 245-246.
- Koptur S. Plant-Animal Interactions in the Face of Disturbance - keynote address. Proceedings of the 1st Joint Symposium on the Natural History and Geology of the Bahamas. Gerace Research Centre, San Salvador, Bahamas.[J]. 2017.
- Elashiry M, Morandini AC, Cornelius Timothius CJ, Ghaly M, Cutler CW. Selective Antimicrobial Therapies for Periodontitis: Win the "Battle and the War". *Int J Mol Sci*. 2021, 22(12):6459-6472. 2017, 24(1): 1148-1158.
- Teughels W, Feres M, Oud V, Martín C, Matesanz P, Herrera D. Adjunctive effect of systemic antimicrobials in periodontitis therapy: A systematic reviewand meta-analysis. *J Clin Periodontol*. 2020, 22: 257-281.
- Zhang Z, Zheng Y, Bian X. Clinical effect of azithromycin as an adjunct to non-surgical treatment of chronic periodontitis: a meta-analysis of randomized controlled clinical trials. *J Periodontal Res*. 2016, 51(3): 275-283.
- Sgolastra F, Petrucci A, Ciarrocchi I, Masci C, Spadaro A. Adjunctive systemic antimicrobials in the treatment of chronic periodontitis: A systematic review and network meta-analysis. *J Periodontal Res*. 2021, 56(2): 236-248.
- Pretzl B, Sälzer S, Ehmke B, Schlagenhauf U, Dannewitz B, Dommisch H, Eickholz P, Jockel-Schneider Y. Administration of systemic antibiotics duringnon-surgical periodontal therapy-a consensus report. *Clin Oral Investig*. 2019, 23(7): 3073-3085.
- Chen X, Wang L, He Z, Zhao H, Cai Y, Song S, Yu Q. Effects of xipayi mouth rinse combined with minocycline on localized aggressive periodontitis' therapeutic effect and the levels of CRP, TNF- α , IL-6 in serum. *Ann Palliat Med*. 2020, 9(5): 3410-3417.
- Yongjian Huang, Zili Huang, Yafei Sui, Pingbo Yang, Shu Wu. Clinical effectiveness of sipail solid gingival fluid combined with minocycline in periodontitis. *Chinese Journal of Clinical Rational Drug Use*, 2021, 14(26): 155-162.

- Abdulbaqi HR, Shaikh MS, Abdulkareem AA, Zafar MS, Gul SS, Sha AM. Efficacy of erythritol powder air-polishing in active and supportive periodontal therapy: A systematic review and meta-analysis. *Int J Dent Hyg*. 2021, 28: 1-21.
- CHENG Nan, SUN Xiaoyu, Wang Xiaowe, Zhang Lei, Hong Biao, WangYang. Subgingival erythritol powder air-polishing as an additional approach to scaling and root planning in treatment with untreated moderate to severe chronic periodontitis. *Anhui Medical Journal*. 2021, 42(07): 731-735.
- WU Yuhong, WU Shaohong, XIE Xuejun, ZHANG Hongmei, LYU Qian. Kangfuxin Liquid Combined with Minocycline Hydrochloride in Treating Periodontitis. *China Pharmaceuticals*. 2020, 29(20): 70-72.
- Bailly C. The implication of the PD-1/PD-L1 checkpoint in chronic periodontitis suggests novel therapeutic opportunities with natural products [J]. *JpnDentSci Rev*. 2020, 56(1): 90-96.
- WU Hao, ZHANG Bing, LIN Zhijian, ZHANG Xiaomeng. Comparison of International Pharmacovigilance of Traditional Chinese Medicine and Natural Medicines. *Chinese Journal of Pharmacovigilance*. 2021, 18(05): 406-421.
- Song Y, Zeng K, Jiang Y, Tu P. Cistanches Herba, from an endangered species to a big brand of Chinese medicine. *Med Res Rev*, 2021, 41(3): 1539-1577.
- Fu Z, Fan X, Wang X, Gao X. Cistanches Herba: An overview of its chemistry, pharmacology, and pharmacokinetics property. *J Ethnopharmacol*, 2018, 219: 233-247.
- Liao PL, Li CH, Tse LS, Kang JJ, Cheng YW. Safety assessment of the Cistanche tubulosa health food product Memoregain®: Genotoxicity and 28-day repeated dose toxicity test. *Food Chem Toxicol*, 2018, 118: 581-588.
- Zhang B, Yang LL, Ding SQ, Liu JJ, Dong YH, Li YT, Li N, Zhao XJ, Hu CL, Jiang Y, Ma XQ. Anti-Osteoporotic Activity of an Edible Traditional Chinese Medicine Cistanche deserticola on Bone Metabolism of Ovariectomized Rats Through RANKL/RANK/TRAF6-Mediated Signaling Pathways. *Front Pharmacol*, 2019, 10: 1412-1412.
- Li TM, Huang HC, Su CM, Ho TY, Wu CM, Chen WC, Fong YC, Tang CH. Cistanche deserticola extract increases bone formation in osteoblasts. *J Pharm Pharmacol*, 2012, 64(6): 897-907.
- Wang F, Tu P, Zeng K, Jiang Y. Total glycosides and polysaccharides of Cistanche deserticola prevent osteoporosis by activating Wnt/ β -catenin signaling pathway in SAMP6 mice. *J Ethnopharmacol*, 2021, 10: 271-280.

- ZHANG Yu, ZHANG Hongbing, GUO Hong, CHEN Chang-qing, ZHANG Tie-jun, LIU Changxiao. Research progress on Curcuma Longae Rhizoma and predictive analysis of its quality markers. Chinese Traditional and Herbal Drugs, 2021, 52(15): 4700-4710.
- Zielińska A, Alves H, Marques V, Durazzo A, Lucarini M, Alves TF, Morsink M, Willemen N, Eder P, Chaud MV, Severino P, Santini A, Souto EB. Properties, Extraction Methods, and Delivery Systems for Curcumin as a Natural Source of Beneficial Health Effects. Medicina (Kaunas), 2020, 56(7): 336-351.
- Zhang Y, Huang L, Mazurel D, Zheng H, Yang J, Deng D. Clinical efficacy of curcumin versus chlorhexidine as an adjunct to scaling and root planing for the treatment of periodontitis: A systematic review and meta-analysis. Phytother Res, 2021, 35(11): 5980-5991.
- Sha AM, Garib BT, Azeez SH, Gul SS. Effects of curcumin gel on osteoclastogenic bone markers in experimental periodontitis and alveolar bone loss in wistar rats. J Dent Sci, 2021, 16(3): 905-914. [28] Xiong Y, Zhao B, Zhang W, Jia L, Zhang Y, Xu X. Curcumin promotes osteogenic differentiation of periodontal ligament stem cells through the PI3K/AKT/Nrf2 signaling pathway. Iran J Basic Med Sci, 2020, 23(7): 954-960.