Reveiw Article

Efficacy of Herbal Medicine for Treatment of Gingivitis and Periodontitis: A Review

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ABSTRACT

Background and Aim: The most common etiology of gingivitis is accumulation of bacterial plaque. Complete removal of microbial plaque by mechanical procedures is not possible in some cases; for example, aged and disabled patients might not be capable of removing the bacterial plaques properly. Also, chemical mouthwashes have some adverse effects. Therefore, finding a new treatment approach would be helpful. The global focus on the use of herbal medicine for treatment of different health conditions is on the rise. The present study aimed at searching and collecting scientific evidence regarding medicinal herbs to treat gingivitis and periodontitis.

Materials and Methods: In this review, an electronic search of the literature was conducted through PubMed, Scopus, Google Scholar, and Wiley online library databases. Studies were considered for inclusion if they evaluated medicinal herbs affecting gingival and periodontal inflammation or periodontal pathogens. Totally, 197 full-text articles were evaluated and finally, based on the inclusion criteria, 22 articles were selected.

Results: There are various medical herbs with antibacterial and anti-inflammatory properties, which can significantly decrease gingival and periodontal inflammation, bleeding on probing (BOP), plaque index (PI), probing depth (PD) and the count of major periodontal pathogens, and promote clinical attachment gain.

Conclusion: The introduced herbal products could be an efficient and safe alternative to chemical products.

Keywords: Anti-Inflammatory Agents; Gingivitis; Herbal; Mouthwashes; Periodontal Diseases

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Introduction

Periodontal diseases adversely affect the supporting tissue structures in the oral cavity. Gingivitis is the mildest type of such conditions. Gingivitis has a high prevalence in the general population, which reflects lack of adequate oral hygiene and plaque formation, particularly in certain areas of the mouth and teeth.[1, 2]

The significance of daily oral hygiene in oral health has long been acknowledged. Studies suggest that although the control of plaque through mechanical procedures is a necessary step, the level of mechanical oral hygiene practice is insufficient.[3-5]

The aged and disabled patients might not be capable of removing the bacterial plaque properly.[6] The mechanical plaque control methods are not sufficient to keep the gingiva healthy in some individuals; as a result, attention has been brought to medicinal treatments, including mouthwashes and different chemicals.

Chlorhexidine (CHX) is the gold standard for chemical plaque control. However, this substance cannot be used for long periods of time due to its adverse effects, such as unpleasant or unusual taste in the mouth, tooth or tongue staining, and calculus formation.[7,8] A few chemical agents used in toothpastes and mouth rinses have been shown to decrease dental plaque accumulation. Owing to enhanced awareness regarding indigenous medical practices in various parts of the world, application of "herbal" medicine has gained interest and paved the way for complementary and alternative therapies.[9,10]

In many countries, herbal remedies are used regardless of the lack of scientific evidence about their dosage, use, and effects since ancient times. Since people were not aware of the risks, allergenicity, or side effects of herbal medications, they used them without any caution. They believed that since herbal medicines are extracted from natural sources, they are completely safe. Therefore, it is crucial to examine the efficacy and safety of traditional alternative treatments as potential new adjuvants in periodontal therapy.[11] The present study aims to review the effective herbal products which have been studied in several different articles and also introduces potential sources for development of new drugs for periodontal diseases.

Materials and Methods

An electronic search of the literature was conducted primarily through PubMed, Scopus, Google Scholar and Wiley online library using "anti-inflammatory agents" and "gingivitis" OR "herbal" OR "mouthwashes" OR "periodontal diseases" as keywords. The search was limited to articles published from 2011 to 2021. The primary article selection was based on the titles and keywords. Next, a full-text assessment was done. Articles in English were included if they investigated medicinal herbs affecting gingival and periodontal inflammation or periodontal pathogens. We included meta-analysis, systematic reviews, human randomized clinical trials, and ex-vivo (animal), and in-vitro studies. Our search aimed to retrieve all articles in English published from 2002 to 2021 (n=197). Duplicates were excluded and eventually 22 articles were selected and reviewed.

Results and Discussion:

The effects of herbal medicine on periodontitis and its potential therapeutic advantages for periodontal disease were evaluated in several studies. Table 1 summarizes the results of the reviewed 22 articles.

Effects on gingivitis, plaque accumulation and bleeding:

Gingivitis does not have any destructive effect on the periodontium of teeth. It refers to chronic and local inflammation of the gingiva due to plaque accumulation.[12] The herbal products with significant anti-inflammatory and anti-plaque properties are discussed below.

Yaghini et al.[13] reported that aloe vera-green tea and matrica (containing chamomile extract) mouthwashes had positive effects on gingival indices. They concluded that the therapeutic effects of aloe vera-green tea mouthwash were close to those of CHX; however, the potency of matrica was reported to be lower than the other mouthwashes. Both herbal mouthwashes had a low impact on the stain index. Therefore, aloe vera-green tea mouthwash can be a proper alternative to CHX due to its anti-inflammatory and anti-plaque properties and absence of adverse effects; however, matrica was not a suitable option.[13]

Kamath et al.[14] reported that aloe vera and tea tree oil mouthwashes can decrease plaque, gingivitis, and oral Streptococcus mutans count in school-aged children between 8 to 14 years. The efficacy of aloe vera and tea tree oil mouthwashes was as high as that of CHX; however, CHX had better substantivity against salivary Streptococcus mutans count. Ripari et al.[15] showed that tea tree oil could be effective and nontoxic for gingivitis treatment. Also, tea tree oil in comparison with CHX resulted in greater improvement in plaque index (PI), bleeding on probing (BOP), and pocket depth (PD); furthermore, it did not cause tooth discoloration or taste alteration.

Deepak et al.[16] stated that use of Pomegranate extract mouth rinse twice a day was effective in reducing plaque accumulation, and gingival inflammation at 30, 60 and 90 days and can be considered as an efficient alternative to chemotherapeutics in treating gingivitis without any side effects. Bhadbhade et al. also conducted a trial to determine the amount of plaque accumulation, after five days of administration of pome-

granate, CHX and placebo mouth rinses. At the end of five days, the pomegranate group showed significantly lower plaque accumulation than the placebo group, and pomegranate mouthwash prevented plaque formation similar to CHX mouthwash.

Santi et al.[17] examined the efficacy of herbal mouth rinses such as Camelia sinensis, Azadirachta indica, Anacardium occidentale Linn, Schinustere binthifolius, and Curcuma longa as oral hygiene adjuvants. These products decreased gingival inflammation by 30% to 50%. They also caused plaque reduction and prevented gingivitis comparable to CHX. Even though some participants reported mild burning sensation by the utilization of the herbal mouth rinses, no other side effects were observed.

Mahyari et al.[18] showed that a polyherbal mouthwash that contained hydroalcoholic extracts of Zingiber officinale, Rosmarinus officinalis and Calendula officinalis (5%) was effective for treatment of gingivitis. Also, its performance was comparable to that of CHX. They stated that this mouthwash was harmless and there were no reports of adverse effects.

Bello et al.[19] studied the effect of a gluten-free spray containing an aqueous extract of Triticum vulgare, which belongs to the family of Graminaceae, on gingival inflammation and dental plaque in schoolchildren. According to their study, Triticum vulgare in spray formulation was harmless and effective in treating gingival inflammation. Thus, it could be a possible adjuvant for treatment of gingivitis together with mechanical plaque control, especially in young children who are unable to spit effectively.

Hashemi et al.[20] reported that the asafoetida mouthwash (Ferula assa-foetida oleo-gum resin) had a significant effect on reduction of PI and modified gingival index as compared to CHX mouthwash. There was no important harm or adverse effect in use of asafetida. Only few people complained of its smell.

Saliasi et al. [21] stated that the Carica papaya leaf extract dentifrice was as effective as sodium lauryl sulfate-free enzyme-containing dentifrice in reduction of gingival bleeding. Given the present concerns regarding the safety of many commercial types of dentifrices, the Carica papaya leaf extract dentifrice may serve as a natural alternative to decrease interdental bleeding in susceptible patients, particularly those in advanced stages of gingival bleeding.

Rayyan et al.[22] stated that subgingival application of a formulated 2% mucoadhesive grape seed extract gel improved the PI and gingival index, but there was no significant enhancement in PD.

Effects on periodontitis, clinical attachment level and bone loss:

Herbal products can also be used as an adjunctive therapy for periodontitis. These products can reduce clinical attachment loss and bone loss. [23] Kerdar et al.[24] reported that Scrophularia striata mouthwash was advantageous for treating chronic periodontitis and was more potent in comparison with Irsha mouthwash (Iranian form of Listerine). Scrophularia striata has short-term effects on PI, PD and BOP, and long-term antibacterial effects against Streptococcus mutans.

Kharaeva et al.[25] concluded that Chamomilla recutita leaves, Salvia officinalis leaves, Arnica montana flowers, and Echinacea purpurea flowers improved periodontal indices and diminished gingival bleeding, redness and swelling, dental plaque accumulation, and early symptoms of periodontitis, due to their anti-oxidant, anti-inflammatory, direct anti-septic, and indirect antibacterial properties.

Malekzadeh et al.[26] concluded that the oral capsules of nano-curcumin (turmeric) (80 mg) can be used as an adjunct treatment for gingivitis and mild cases of periodontal disease because of its anti-inflammatory actions. Previous studies showed that the anti-inflammatory effect of curcumin mouthwash was similar to that of 0.2% CHA, while topical application of curcumin gel decreased the amount of inflammation caused by periodontal disease and decreased disease severity.

Ivanaga et al.[27] discussed that in patients with type 2 diabetes mellitus, the treatment of residual pockets (with PD ≥5 mm and BOP) with antimicrobial photodynamic therapy with 100 mg/L curcumin solution and LED irradiation as adjunctive therapy to scaling and root planing, may yield short-term (three months) clinical benefits regarding clinical attachment gain.

Table 1. Summary of the results of reviewed studies

Authors\Year	Type of study	Herbal medication	Main effects	Reference number
Yaghini et al 2019	double-blind placebo-controlled clinical trial (n=60)	Aloe Vera-green Tea	Reduction of PI, GI, BOP, and stain index	13
Kamath et al 2019	A double-blind, placebo-controlled prospective interventional study (n=152)	aloe vera and tea tree oil	Reduction of plaque, gingivitis and oral S. mutans count in children	14
Ripari et al 2019	A pilot randomized, double blind clinical trial (n=42)	Tea tree oil	improvement in PI, BOP, and PD	15
Deepak et al 2013	Double-blind randomized trial (n=40)	Pomegranate	Reduction of plaque accumulation, gingival inflammation and total salivary protein count	16
Santi e al 2019	systematic review (n=20)	Five herbal products (Camelia sinensis, Azadirachta indica, Anacardium occidentale Linn, Schinus terebinthifolius and Curcuma longa)	Reduction of dental plaque and gingival inflammation	17
Mahyati et al 2015	randomized double-blind placebo-controlled trial (n=60)	Polyherbal mouthwash containing Zingiber officinale, Rosmarinus officinalis and Calendula officinalis	improvements of MGI, GBI and MQH	18
Paduano et al 2018	Randomized controlled trial (n=57)	Triticum vulgare	Improvement of GI and PI	19
Hashemi et al 2019	Randomized double-blind controlled trial (n=126)	Asafoetida (Ferula assa-foetida oleo-gum resin)	Improving PI and MGI	20
Saliasi et al 2018	Randomized clinical trial (n=100)	Carica papaya leaf	Reduction of gingival bleeding and inflammation	21
Rayyan et al 2017	Randomized clinical study (n=86)	Grape seed extract	improvement of PI and GI in subgingival application	22
Kerdar et al 2019	In vitro (n=50)	Scrophularia striata	Treatment of chronic periodontitis	24

f.kharaeva et al 2020	Randomized clinical trial (n=50)	Chamomilla recutita leaves, Salvia officinalis leaves, Arnica montana flowers and Echinacea purpurea flowers	Reduction of gingival inflammation (bleeding and redness), plaque, and initial symptoms of periodontitis	25
Malekzadeh et al 2020	Double blind randomized clinical trial (n=48)	Curcumin	Reduction of inflammation and gingival bleeding in patients with gingivitis and mild periodontitis	26
Ivanaga et al 2019	Randomized clinical trial (n=25)	Curcumin (and LED)	CAL gain at 3 months	27
Sparabombe et al 2019	Randomized clinical trial (n=34)	Polyherbal mouthwash (propolis resin extract, Plantago lanceolata, Salvia officinalis leaves extract, and 1.75% of essential oils)	Reduction of full mouth bleeding score, full mouth plaque score, PD, and CAL	28
Kuo et al 2019	In vitro	Hesperidin	Reduction of gingival inflammation, connective tissue loss, alveolar bone loss and mRNA expression levels of IL-6, IL-1 β, and iNOS	29
Celiksoy et al 2020	In vitro	Pomegranate (Punica granatum)	Anti-inflammatory and oral wound healing	30
Mekhemar et al 2020	Review	Nigella sativa and Thymoquinone	Significant improvement in PI, GI, BOP, and CAL Antibacterial effect against subgingival bacteria Significant reduction of alveolar bone loss and inflammatory cell infiltration Maintenance of osteoblastic activity	31
Sidhu et al 2018	Review	Licorice	Anti-adhesive and inhibitory effect on growth, biofilm formation, host immune response, volatile sulfur compound production and protease activity against Porphyromons gingivalis	32
Lagha et al 2018	In vitro	Green tea polyphenols	Enhancement of the integrity of a protective gingival keratinocyte monolayer against the deleterious effects (barrier integrity breakdown, invasion) caused by Porphyromonas gingivalis	33
Livada et al 2017	Review	Curcumin	Reduction of levels of Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum, Aggregatibacter actinomycetemcomitans and Capnocytophaga species Reduction of gingival inflammation and edema	34
Ben Lagha et al 2020	In vitro	Cinnamon	Reduction of lipopolysaccharide binding in monocytes and IL-6, IL-8, and TNF-α secretion in macrophage model stimulated with lipopolysaccharide from either Aggregatibacter actinomycetemcomitans or Escherichia coli	35

Sparabombe et al.[28] reported that the use of a polyherbal mouthwash (Propolis resin extract, Plantago lanceolata, Salvia officinalis leaves extract, and 1.75% essential oil) in patients with moderate or severe periodontitis was safe and effective for BOP and PI after 3 months, in comparison with the control group; however, there was no significant difference between the two groups regarding PD and clinical attachment level.

Kuo et al.[29] reported that oral administration of Hesperidin prevented ligation-induced alveolar bone loss and attachment loss in rats, which might be mediated by its inhibitory effects on the expression of pro-inflammatory cytokines. These findings could further support the investigations regarding the use of hesperidin as an adjuvant to periodontal therapy.

Celiksoy et al. [30] reported that pomegranate (Punica granatum) extract and its bioactive constituents, such as punicalagin, had strong anti-oxidant properties, and punicalagin, together with the Zn (II), improved the migration of gingival fibroblasts and wound healing but had minimum effectiveness for fibroblast proliferation. Therefore, purified punicalagin in combination with Zn (II) may aid in oral soft tissue wound healing.

Antibacterial effects:

Gingival inflammation occurs following bacterial biofilm formation, ecological alterations in the microbiome, formation of inflammatory mediators, and immune responses. It will lead to activation of several key molecular pathways which promote destruction of supporting tissues. Therefore, it is reasonable to use herbal medicine which can reduce high-risk periodontal pathogens and/or the destruction caused by them.[31] According to Sidhu et al.[32] polysaccharides in licorice can prevent the adhesion of Porphyromonas gingivalis in children and inhibit the early stages of infection. Thus, it can be a potential prophylactic tool in alternative treatment regimens against bacterial infection. The licorice extract showed great anti-inflammatory properties by inhibiting the periodontopathogen lipopolysaccharide-induced IL-1beta, IL-6, and IL-8 and tumor necrosis factor-alpha responses of macrophages stimulated by Aggregatibacter actinomycetemcomitans and Porphyromonas gingivalis.

Lagha et al.[33] stated that the green tea extract and epigallocatechin-3-gallate, the most important component of green tea, could promote the epithelial barrier against the Porphyromonas gingivalis-mediated damage and prevent the penetration of bacteria through a keratinocyte monolayer.

Livada et al.[34] reported that curcumin significantly decreased the levels of Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum and Capnocytophaga species in several clinical trials and animal studies.

Lagha et al.[35] reported that cinnamon extract had antibacterial and anti-biofilm properties against major periodontal pathogens, including Actinobacillus actinomycetemcomitans. The anti-inflammatory activity of the cinnamon extract resulted in decreased secretion of IL-6, IL-8, and tumor necrosis factor-alpha and promoted a healthy periodontium.

Mekhemar et al.[31] studied the effectiveness of Nigella sativa and Thymoquinone as possible adjuncts for periodontal treatment. In this animal study on rats, researchers applied 0.2% Thymoquinone systemically or as oral gel on subgingival bacteria causing gingivitis and periodontitis. On microbiological evaluation, Thymoquinone administration was shown to have medicinal effects on Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans, Prevotella intermedia and other subgingival bacteria.

Effects on saliva and gingival circular fluid:

A 90-day use of Pomegranate mouth rinse significantly reduced total salivary proteins compared with the placebo. Periodontal pathogens are considered to trigger the inflammatory process and thereby increase the total salivary protein levels. Microbial control in turn reduces the inflammatory response, which in turn decreases the plasma leakage in saliva through gingival crevicular fluid; this statement could be supported by the overall reduction in total salivary protein levels.[16]

Further investigations:

Several studies have reported anti-inflammatory effects of cocoa flavonoids,(36) thyme,[37] Artemisia annua,[38] Inonotus obliquus (chaga mushroom),[39] leaf extract of Ananas comosus,[40] Thykamine extracts from spinach [41] and White Willow Bark (Salix alba) [42] on different parts of the body. An analysis

evaluating the influence of these products would be beneficial in order to elucidate their effects on periodontal disease.

Conclusion:

According to the findings of the reviewed studies, the following conclusions can be made:

1.Herbal products mentioned earlier can significantly reduce gingival and periodontal inflammation, BOP, PI, clinical attachment loss and count of major periodontal pathogens.

2.These herbal products could be an efficient and safe alternative to CHX and other chemical products.

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