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Anti-Inflammatory Potential of Origanum Vulgare Extract as an Adjunct Therapy in Periodontitis: A Narrative Review

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ABSTRACT

Periodontitis is a chronic inflammatory disease that affects the periodontium and leads to progressive loss of alveolar bone, with a global prevalence of approximately 20-50% of the population. Conventional treatment, such as scaling and root planing, often fails to fully reach deep periodontal pockets and furcation areas, leaving residual calculus and persistent inflammation. Adjunctive antimicrobial therapies can improve outcomes in the short term, but their use is limited by concerns over antimicrobial resistance, safety, and cost. This has led to growing interest in natural-product adjuncts with anti-inflammatory, antimicrobial, and antioxidant properties. Oregano (Origanum vulgare) is one of the most widely used and studied herbs for this purpose, containing bioactive compounds such as carvacrol, thymol, rosmarinic acid, and flavonoids. Carvacrol and thymol suppress inflammatory signalling pathways, including NF-κB, ERK1/2, and TLR4/ROS, reducing the production of pro-inflammatory mediators such as TNF-α, IL-6, and PGE2. These compounds also show antibacterial activity against key periodontopathogens and inhibit RANKL-induced osteoclast differentiation, thereby limiting alveolar bone resorption. A clinical study using a topical O. vulgare-based gel reported improvements in probing depth (PD), clinical attachment level (CAL), and periodontopathogen levels in patients with periodontitis. This review synthesises current preclinical and clinical findings to highlight the anti-inflammatory potential of Origanum vulgare, while pointing out the need for standardised formulations and larger controlled clinical trials before it can be recommended as an adjunctive periodontal therapy.

Keywords: Origanum vulgare; oregano; carvacrol; thymol; periodontitis; anti-inflammatory; adjunct therapy

INTRODUCTION

Periodontitis is a chronic inflammatory disease that degrades the periodontium, leading to progressive loss of alveolar bone [1, 2]. It has been reported that periodontal disease affects about 20-50% of the population globally, and its projected continued increase in the coming decades [3, 4]. The clinical manifestations of periodontitis include clinical attachment loss and gingival inflammation, which may present as erythema, swelling, and bleeding on probing (BOP). Other signs include periodontal pocket formation, gingival recession, furcation involvement, and alveolar bone loss visible on radiographs in advanced cases [5, 6]. The main principle of periodontal treatment is to reduce inflammation, prevent disease progression and restore periodontal supporting tissues. [2, 7].

Conventional periodontitis management, such as scaling and root planing (SRP) and surgery in advanced cases, remains the standard of therapy [8, 9]. However, SRP alone frequently fails to fully access deep periodontal pockets and furcation areas, resulting in residual calculus and persistent inflammation in susceptible individuals [10]. To overcome the limitations of SRP, adjunctive strategies are increasingly used in periodontal therapy [11]. Current clinical guidelines recommend several adjunctive modalities, including locally or systemically administered antimicrobials and host-modulation agents [12]. Although the use of adjunctive antimicrobials can improve clinical outcomes in the short term, their widespread application remains constrained by concerns regarding antimicrobial resistance, safety, patient compliance, and treatment costs [13].

This has driven interest in adjunctive natural-product and host-modulatory therapies, which are recognised for their anti-inflammatory, antimicrobial, antioxidant, and immunomodulatory properties [12, 14, 15].

Among various natural products, oregano (Origanum vulgare) is widely recognised as one of the most extensively utilised and therapeutically effective herbs [16, 17]. Oregano contains diverse bioactive compounds, including the phenolic monoterpenes carvacrol and thymol, as well as their precursors p-cymene and γ-terpinene, rosmarinic acid, flavonoids, and other phenolic acids [18, 19]. Carvacrol and thymol are the predominant compounds, comprising up to 85% of the essential oil composition, while p-cymene and γ-terpinene are present at lower concentrations [20]. These bioactive constituents contribute to the multiple biological activities of oregano, including antimicrobial, antioxidant, anti-inflammatory, antitumor, and immunomodulatory effects demonstrated in various preclinical models [21]. Recently, oregano-derived compounds have been suggested as potential candidates for periodontal therapy, demonstrating anti-inflammatory and antimicrobial activity against key periodontopathogens and favorable clinical and microbiological outcomes in patients with periodontitis [22, 23]. Therefore, this narrative review discusses the potential of O. vulgare extract as an adjunctive therapy for periodontitis, with particular emphasis on its antimicrobial and anti-inflammatory properties based on current evidence.

Pathogenesis of Periodontitis and The Role of Inflammation

The primary etiological agent in periodontitis is dental plaque, a biofilm composed of pathogenic bacteria that adhere to tooth surfaces [2]. Certain Gram-negative anaerobic bacteria, including Porphyromonas gingivalis, Fusobacterium nucleatum, and Prevotella intermedia, are strongly associated with the progression of periodontitis [24, 25]. These bacteria release toxins and virulence factors that induce the production of inflammatory cytokines and chemokines in periodontal tissues [26–28]. Although bacteria initiate the disease, tissue destruction is mainly driven by the host immune response, which releases inflammatory mediators [29]. The tissue destruction resulting from the immune-inflammatory response is clinically identified as periodontitis [30]. Polymorphonuclear leukocytes (PMNs) and macrophages, as key immune cells, release antimicrobial substances, phagocytose bacteria, and promote inflammation [31]. The stimulation of PMNs and macrophages by bacterial virulence factors leads to excessive production of pro-inflammatory cytokines such as TNF-α, IL-1β, IL-8, and PGE2, which contribute to bone resorption and tissue destruction by activating signalling pathways including nuclear factor kappa B (NF-κB), mitogen-activated protein kinase (MAPK), Phosphoinositide 3-kinase (PI3K)/Akt, and extracellular-regulated kinases (ERK) [32–34]. This inflammatory response also promotes the production of matrix metalloproteinases (MMPs), leading to the degradation of collagen fibres and further tissue destruction [35]. In parallel, excessive reactive oxygen species (ROS) released by activated immune cells overwhelm local antioxidant defences, and this oxidative imbalance further activates NF-κB and MAPK signalling and the NLRP3 inflammasome, amplifying pro-inflammatory cytokine release and accelerating periodontal tissue and bone destruction [31]. Taken together, it appears that dysregulation of immune cell function, depletion of antioxidant defence capacity, and the sustained release of virulence factors from periodontopathogenic bacteria are the most consistently implicated drivers of periodontitis pathogenesis; nevertheless, additional contributing factors are likely to be identified through further investigation.

Origanum Vulgare: Phytochemical Components and Biological Activities

O. vulgare, commonly known as oregano, is renowned for its rich essential oil content and diverse bioactive compounds [21]. The essential oil is primarily composed of monoterpenes and phenolic compounds, with carvacrol and thymol consistently identified as the major constituents [36, 37]. The proportion of these compounds can vary depending on the plant's origin and extraction method, but carvacrol often dominates, ranging from about 47% up to 78% in various studies, followed by thymol, p-cymene, and γ-terpinene as significant components [36, 38]. Beyond the essential oil, O. vulgare contains a variety of other bioactive substances such as phenolic acids and flavonoids, with rosmarinic acid consistently identified as the dominant phenolic compound across different accessions and growing conditions. In addition to rosmarinic acid, luteolin, chicoric acid, coumarin, and quercetin have been identified as major phenolic and flavonoid constituents, with their relative abundance varying considerably by subspecies and accession [39]. This complex chemical profile, and its close correlation with observed antioxidant capacity, underpins oregano's well-documented antioxidant, antibacterial, and anti-inflammatory properties, supported by findings that oregano extracts rich in rosmarinic acid also demonstrate meaningful anti-inflammatory activity [40].

Anti-Inflammatory Effects of Origanum vulgare and Their Potential Relevance to Periodontitis

It has been demonstrated that the anti-inflammatory properties of O. vulgare are mainly attributed to its phenolic monoterpenes, particularly carvacrol and thymol, together with other phenolic constituents such as rosmarinic acid and flavonoids [16, 41]. Carvacrol, one of the major bioactive compounds of O. vulgare, has been shown to exert anti-inflammatory effects by modulating key signalling pathways involved in inflammatory responses [42]. Carvacrol can suppress the NF-κB and ERK1/2 signalling pathways, consequently reducing the production of pro-inflammatory cytokines and inflammatory mediators [43, 44]. The suppression of NF-κB activation correlated with inhibition of inhibitor of kappaB (IκB) kinase (IKK) activation and attenuation of inhibitor of NF-κB (IκBa) degradation.

Carvacrol also promotes apoptosis in mature osteoclasts through caspase-3 activation and DNA fragmentation [45]. It also inhibits the production of nitric oxide (NO) and prostaglandin E2 (PGE2) by downregulating inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), while reducing the expression of MMPs, particularly MMP-3 and MMP-13 [46].

Similarly, thymol, a structural isomer of carvacrol also abundant in oregano, can effectively inhibit NF-κB activation through modulation of the Toll-like receptor 4 (TLR4) and ROS-mediated pathway, while also affecting p38 MAPK, signal transducer and activator of transcription 3 (STAT3), and activator protein-1 (AP-1) signalling [47, 48]. Through these mechanisms, thymol may reduce the expression of various pro-inflammatory mediators and limit the progression of inflammatory responses. In summary, these findings indicate that oregano components contribute to anti-inflammatory and therapeutic effects by modulating inflammatory factors and related agents.

Current Evidence of Origanum Vulgare in Periodontal Therapy

Preclinical Evidence

Several studies have demonstrated the therapeutic potential of O. vulgare and its principal bioactive constituents, carvacrol and thymol, against periodontitis, either directly or through closely related bone-inflammation models. Antibacterial effects of O. vulgare essential oil and ethanolic extracts have been confirmed against key anaerobic periodontopathogens implicated in disease pathogenesis, including P. gingivalis, F. nucleatum, P. intermedia, and A. actinomycetemcomitans [49]. In an in vitro and in vivo study performed by Deepak et al., it was demonstrated that carvacrol suppresses RANKL-induced formation of tartrate-resistant acid phosphatase (TRAP) positive osteoclasts, disrupts the actin ring formation necessary for osteoclastic bone resorption, and downregulates RANKL-induced NF-κB activation via inhibition of IκB kinase (IKK) and reduced IκBα degradation. Carvacrol further induced apoptosis in mature osteoclasts through caspase-3 activation, while sparing the viability of osteoblast-like MC3T3-E1 cells [45]. Osteoclasts are specialised multinucleated cells responsible for bone resorption, formed when monocyte or macrophage precursors are exposed to macrophage colony-stimulating factor (M-CSF) and RANKL; M-CSF drives precursor proliferation and survival via ERK/Akt activation, while RANKL binding to RANK recruits TRAF6 to activate NF-κB, MAPK, and downstream NFATc1. NFATc1 is the master transcription factor required for terminal osteoclast differentiation [50]. Mature osteoclasts additionally form a specialised actin-rich podosome belt (actin ring) that is essential for their attachment to bone and subsequent resorptive activity, the same structure disrupted by carvacrol in the study above [45, 51].

Additionally, thymol, a structural isomer of carvacrol, was shown by another research group to significantly reduce RANKL-induced osteoclast differentiation in RAW264.7 and bone marrow-derived macrophage (BMM) cultures. This effect occurs through inhibition of ERK, JNK, and AKT signalling, and downregulation of osteoclast marker genes such as NFATc1, c-Fos, MMP-9, and cathepsin K. Importantly, thymol also significantly reduced LPS-induced inflammatory bone loss in vivo in a mouse model, directly linking its in vitro anti-osteoclastogenic activity to a protective effect against inflammatory bone destruction [52]. Given that unchecked osteoclast activity underlies alveolar bone destruction in periodontitis, agents capable of interrupting this signalling cascade represent a rational anti-resorptive strategy. Interestingly, Potra et al. evaluated a topical hydrogel containing carvacrol combined with magnolol in a Wistar rat model of diabetes-associated periodontitis. The hydrogel showed dose-dependent free radical scavenging activity and reduced malondialdehyde (MDA), a marker of lipid peroxidation. This supports a localised antioxidant and anti-inflammatory effect in an inflamed periodontal environment [53]. Collectively, this preclinical evidence indicates that O. vulgare-derived compounds may improve periodontitis outcomes through antibacterial, antioxidant, and anti-osteoclastogenic mechanisms. However, most evidence comes from isolated constituents (carvacrol, thymol) rather than the whole plant extract, and standardised O. vulgare formulations in ligature-induced periodontitis models remain scarce.

Clinical Evidence

Although direct clinical evidence for O. vulgare in human periodontitis is substantially more limited than the available preclinical data, an initial clinical evaluation has recently been reported. Radu et al. conducted a 4-month observational cohort study assessing SmartGel OV, a topical gel containing 2.5% O. vulgare essential oil, administered twice daily via gingival massage as an adjunct following a single baseline scaling session, in 30 adults with moderate-to-severe periodontitis (17 females, 13 males; age 32-60 years) in Oradea, Romania. Of the 30 enrolled participants, 28 completed the full protocol, and no adverse effects were observed [23].

All clinical parameters showed significant improvement ($p < 0.05$) after 4 months of SmartGel OV use. Mean probing depth (PD) decreased from 3.6 ± 0.5 mm to 2.2 ± 0.3 mm, clinical attachment level (CAL) decreased from 4.8 ± 0.6 mm to 3.9 ± 0.5 mm, BoP decreased from 1.0 ± 0.2 to 0.2 ± 0.1, and plaque index (PI) decreased from 1.1 ± 0.3 to 0.3 ± 0.2. Real-time PCR analysis of gingival crevicular fluid revealed significant reductions (McNemar test) in the prevalence of major periodontopathogens, particularly F. nucleatum (42.9% to 10.7%) and Capnocytophaga spp. (35.7% to 7.1%), as well as reductions in red-complex species P. gingivalis (32.1% to 3.5%) and T. forsythia (28.6% to 7.1%) [23]. These findings suggest that O. vulgare-based topical formulations may substantially improve both clinical and microbiological outcomes when used as an adjunct to minimal mechanical debridement.

Taken together, the available clinical and preclinical evidence indicates that O. vulgare and its major bioactive constituents may influence several periodontitis-related outcomes, including periodontal inflammation, pathogenic bacterial activity, oxidative stress, and alveolar bone remodelling. The current evidence, including the study models, investigated interventions, observed effects, and proposed mechanisms, is summarised in Table 1.

TABLE 1: Current evidence of O. vulgare and its bioactive constituents in periodontitis-related outcomes.

Intervention	Effects/Mechanism	Study Model	Reference
O. *vulgare* EO	Antibacterial activity against *P. gingivalis, F. nucleatum, P. intermedia, A. actinomycetemcomitans*	In vitro	[49]
Carvacrol	Suppresses RANKL/LPS-induced osteoclastogenesis through inhibition of NF-κB activation and induces apoptosis in mature osteoclasts (caspase-3)	In vitro / In vivo	[45]
Thymol	Inhibits RANKL-induced osteoclast differentiation via suppression of ERK, JNK, and AKT signalling, and reduces LPS-induced inflammatory bone loss *in vivo*	In vitro / In vivo	[52]
Carvacrol and magnolol hydrogel	Exerts antioxidant activity through direct scavenging of free radicals, reducing MDA levels	In vivo	[53]
SmartGel OV (2.5% *O. vulgare* EO gel)	Improves clinical parameters (PD, CAL, BOP, PI) and reduces periodontopathogen prevalence in GCF	Clinical (human)	[23]

Limitations and Future Perspectives of Origanum Vulgare

Interest in Origanum vulgare has grown substantially in recent years, driven by increasing public awareness of its long history of culinary use alongside emerging evidence of its pharmacological versatility [21]. Based on the preclinical and clinical evidence discussed above, one of the most promising therapeutic applications of O. vulgare is its potential to ameliorate periodontitis [54]. Current evidence indicates that O. *vulgare*, through its principal bioactive constituents carvacrol, thymol, and other constituents, can act on periodontitis by suppressing NF-κB and MAPK-mediated inflammatory signalling, disrupting periodontopathogen membranes and biofilm formation, and interrupting RANKL-driven osteoclast differentiation [45, 49, 52]. Experimental data emphasize that these constituents possess a meaningful capacity to reduce alveolar bone resorption, attenuate osteoclastogenesis and associated ROS generation, and act directly against the Gram-negative anaerobic bacteria implicated in disease pathogenesis. Preliminary clinical evidence also supports these findings: a topical O. vulgare-based gel not only reduced the prevalence of major periodontopathogens but also improved clinical parameters, probing depth (PD), clinical attachment level (CAL), bleeding on probing (BOP), and plaque index (PI) in patients with periodontitis [23].

Nonetheless, safety and dosing considerations warrant attention before broader clinical use. Regulatory toxicological review has established thymol as safe at doses up to 1000 mg/kg body weight, with toxicity emerging only at substantially higher exposures, while carvacrol is considered non-toxic at low doses but has been associated with toxicity above approximately 2480 mg/kg body weight [55]. At the local mucosal level, thymol has shown acceptable cytocompatibility in human gingival fibroblasts and produced no acute irritation in a chorioallantoic membrane irritation assay even at concentrations exceeding typical oral care use, though the authors noted that the margin between its biological activity and cytocompatibility is relatively narrow, such that repeated short-contact exposure, as occurs in real oral hygiene routines, may still generate local peak concentrations not captured in single-exposure laboratory models [56].

From a pharmaceutical standpoint, further challenges limit the extensive clinical use of O. vulgare essential oil, most notably its inherent volatility, poor water solubility, and susceptibility to degradation from light, oxygen, and temperature all of which restrict its dispersion and sustained bioavailability within the moist oral environment [57]. Therefore, identifying effective strategies to harness the therapeutic potential of this natural agent while overcoming its physicochemical limitations has become a critical research priority. In recent years, drug delivery systems including nanoemulsions, liposomes, and nanoemulgels have shown considerable promise in improving the stability, solubility, and controlled local release of volatile phytochemicals such as essential oils [58]. Such systems function as carriers that regulate the rate, timing, and site of active compound release, thereby enhancing both safety and efficacy. Accordingly, further research into nanoparticle-based or nanoemulgel formulations of O. vulgare is strongly warranted to enable its effective and sustained application in the adjunctive treatment of periodontitis.

CONCLUSIONS

In summary, experimental and preliminary clinical findings suggest that Origanum vulgare, particularly its principal constituents, carvacrol, thymol, and other phenolic acids, represents a promising candidate for adjunctive periodontitis management. Preclinical data consistently demonstrate that these compounds inhibit key periodontopathogens, including P. *gingivalis*, F. *nucleatum*, and *A. actinomycetemcomitans*. They also disrupt biofilm formation and bacterial adhesion and interfere with intracellular signalling cascades such as NF-κB, ERK1/2, TLR4/ROS, and p38 MAPK, which drive the release of pro-inflammatory mediators including IL-6, TNF-α, and PGE2 in gingival tissue. Additional evidence indicates that carvacrol and thymol act at the bone level by suppressing RANKL-induced osteoclast differentiation and downregulating MMPs responsible for collagen degradation. This activity limits alveolar bone resorption, a central process in periodontal tissue destruction. Furthermore, a single clinical evaluation of a topical O. *vulgare*-based gel has reported measurable improvements in probing depth (PD), clinical attachment level (CAL), bleeding on probing (BOP), and plaque index (PI), as well as a reduction in periodontopathogen prevalence in patients with periodontitis. However, the evidence base remains at an early and largely uncontrolled stage, and larger, randomised, placebo-controlled trials are needed before O. *vulgare* can be recommended as a validated adjunct to conventional periodontal therapy.

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