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COENZYME Q10 SUPPLEMENTATION AS AN ADJUNCT TO NON-SURGICAL PERIODONTAL TREATMENT

Berkay Ali BİLGİN

Doctor of Philosophy

Supervisor

Prof. Dr. Şebnem DİRİKAN İPÇİ

Co-Supervisor

Asst. Prof. Dr. İlknur ÖZENCİ

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The dissertation titled COENZYME Q10 SUPPLEMENTATION AS AN ADJUNCT TO NON-SURGICAL PERIODONTAL TREATMENT prepared by BERKAY ALİ BİLGİN and submitted on 30/06/2025 has been **accepted unanimously** for the degree of PhD in Periodontology.

Asst. Prof. Dr. İlknur ÖZENCİ Co-Supervisor	Prof. Dr. Şebnem Dirikan İPÇİ Supervisor

Thesis Defence Commity Members:

Prof. Dr. Şebnem Dirikan İPÇİ	Department of Periodontology, Altınbaş University	
Prof. Dr. Gökser ÇAKAR	Department of Periodontology, Altınbaş University	
Asst. Prof. Dr. Mehmet Selim YILDIZ	Department of Periodontology, Altınbaş University	
Prof. Dr. Serdar ÇİNTAN	Department of Periodontology, İstanbul Kent University	
Assoc. Prof. Dr. Duygu YAMAN	Department of Periodontology, İstanbul University	

I hereby declare that this dissertation meets all format and submission requirements of a PhD dissertation.

I hereby declare that all information/data presented in this graduation project has been obtained in full accordance with academic rules and ethical conduct. I also declare all unoriginal materials and conclusions have been cited in the text and all references mentioned in the Reference List, have been cited in the text and vice versa as required by the above-mentioned rules and conduct.

Berkay Ali BİLGİN

Signature

DEDICATION

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to our beloved Antakya.

PREFACE

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ABSTRACT

COENZYME Q10 SUPPLEMENTATION AS AN ADJUNCT TO NON-SURGICAL PERIODONTAL TREATMENT

BİLGİN, Berkay Ali

PhD, Department of Periodontology, Altınbaş University

Supervisor: Prof. Dr. Şebnem Dirikan İPÇİ

Co-Supervisor: Asst. Prof. Dr. İlknur ÖZENCİ

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OBJECTIVE: The aim of this study was to clinically and biochemically evaluate the efficacy of coenzyme Q10 (CoQ10) to be used in addition to non-surgical periodontal treatment (NSPT) with full mouth disinfection (FMD) method in patients diagnosed with Stage I and II periodontitis.

MATERIALS AND METHODS: 28 patients, with periodontitis stage 1 or 2 were randomly assigned into two groups. FMD was applied to both groups. The test group received CoQ10 (Ocean® CoQ10, 100mg, Türkiye) supplement in addition to the FMD. Probing pocket depth (PPD), clinical attachment level (CAL), gingival index (GI), plaque index (PI) and bleeding on probing (BoP), were measured before the start of treatment and at the first, second and third month. For biochemical analysis, gingival crevicular fluid (GCF) samples were collected from two different teeth with the deepest pockets using special filter papers (Periopaper™). GCF samples were collected before the start and after the end of treatment. GCF samples were examined with ELISA to evaluate superoxide dismutase (SOD) levels.

RESULTS: Both groups have significant reductions in PI, GI, BoP, PPD and CAL from beginning to third month ($p<0.05$). According to intergroup comparisons, PPD reduction was significantly higher in test group than in control group ($p=0,001$; $p<0,01$). Also, CAL found significantly higher at control group than test group ($p=0,001$: $p<0,001$). BoP and GI scores found significantly higher at control group than test group ($p=0,001$: $p<0,01$). Also, PI scores are significantly higher at control group than in test group ($p=0,003$: $p<0,01$). No

significant difference was observed between the GCF volume, SOD concentration, and total SOD content of the groups when comparing baseline and endpoint values ($p>0,05$).

CONCLUSION: Within the limits of this study, adjunctive use of CoQ10 to NSPT revealed positively influenced periodontal outcomes in stage 1 and stage 2 periodontitis patients. These results suggest stage 1 and stage 2 periodontitis patients might benefit from CoQ10 usage. Further studies are warranted to define prolonged effect of CoQ10 in periodontitis patients.

Key Words: Full Mouth Disinfection, Coenzyme Q10, Periodontitis, Superoxide Dismutase, Micronutrients.

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ABBREVIATIONS

CAL	:	Clinical Attachment Level
CoQ10	:	Coenzyme Q10
CP	:	Chronic Periodontitis
FMD	:	Full Mouth Disinfection
GCF	:	Gingival Crevicular Fluid
GI	:	Gingival Index
IFN	:	Interferon
IL	:	Interleukin
LPS	:	Lipopolysaccharide
NSPT	:	Non-Surgical Periodontal Treatment
OS	:	Oxidative Stress
PI	:	Plaque Index
PMNL	:	Polymorphonuclear Leukocytes
PPD	:	Probing Pocket Depth
RANKL	:	Receptor Activator of Nuclear Factor KappaB Ligand
ROS	:	Reactive Oxygen Species
SOD	:	Superoxide Dismutase
SPT	:	Supportive Periodontal Therapy
SRP	:	Scaling and Root Planing
TGF	:	Transforming Growth Factor
Th	:	Thelper

TLR : Toll Like Receptors

TNF : Tumor Necrosis Factor

1. INTRODUCTION

Periodontitis is a chronic, complex inflammatory condition. Dysbiotic biofilm causes progressive breakdown of the tooth-supporting apparatus (Papapanou et al., 2018). *A. actinomycetemcomitans, T. forsythia, P. gingivalis* are the most common species in periodontal diseases. *P. intermedia, C. rectus, P. micros, F. nucleatum* were also identified as effective in periodontal diseases (Haffajee & Socransky, 1994).

Periodontal disease commences with dysbiosis of the oral microbiome, leading to inflammation. Untreated gingivitis results in the progression to periodontitis (Kinane et al., 2017). Colonization of microorganisms leads to inflammation of periodontal tissues and destruction of tissues due to the inflammatory process (Lamster & Novak, 1992). A critical role in the beginning and advancement of periodontal diseases is played by the host response (Lamont et al., 2018). Periodontitis is purportedly begun by pathogenic microbes, whereas the resultant loss of periodontal tissue to the host's immune response (Mark Bartold & Van Dyke, 2013). This establishes a complicated bi-directional series of host-microbial interactions that encompass cellular and humoral components. A disruption at the homeostatic equilibrium between proteolytic enzymes and their inhibitors, as well as between reactive oxygen species (ROS) and antioxidant defense mechanisms that safeguard and restore essential tissue, cellular, and molecular elements, is thought to be the underlying cause. The foundation for this dysregulation is partially hereditary and partially attributable to environmental influences (Chapple & Matthews, 2007; Michalowicz et al., 1991; Palmer et al., 2005).

Recently, periodontitis is classified using a stage and grade system (Papapanou et al., 2018). The stage of periodontitis is assessed based on its severity and complexity, while the grade is evaluated according to the pace of advancement. In assessing the stage of periodontitis, clinical attachment, radiographic bone loss, and any tooth loss are evaluated. Moreover, horizontal and vertical bone loss, together with potential pocket depth, are parameters considered in the diagnosis of stage. The advancement rate of periodontal disease is dictated by the grading methodology considering the presence of radiographic bone loss over a five-year period, contingent upon the availability of prior radiographs or the ratio of bone loss to age is utilized, categorized as grade A if it is below 0.25, grade B if it ranges from 0.25 to 1,

and grade C if it exceeds. Factors for modification are also considered throughout the grading process. The variables include diabetes (HbA1C level) and smoking (cigarettes per day) (Nikalus P. Lang & Jan Lindhe, 2015). Approximately 11% of the global population may suffer from severe periodontitis, impacting 743 million individuals. A substantial body of studies has identified potential correlations between periodontitis and specific non-communicable chronic diseases. Consequently, it is crucial to manage the early stages of periodontitis to avoid afterwards damage and disease development (Frencken et al., 2017).

Different non-surgical and surgical periodontal therapy modalities have been established to inhibit the advancement of periodontal disease, hence enhancing the prognosis of the teeth and the patient's quality of life (Graziani et al., 2017). Periodontitis is linked to the existence of bacterial biofilm and calculus on root surfaces. The objective of pocket/root instrumentation in NSPT is to eliminate microbial deposits and calculus from the tooth root surface. NSPT is conducted via curettes and/or sonic or ultrasonic tools (Armitage, 1999). The conventional NSPT therapy method is scaling and root planing (SRP) conducted across several sessions, segmenting the jaw into quadrants or sextants based on the degree and extent of the disease (Armitage, 1999).

Standard therapy is conducted in several weeks, targeting a distinct region (or 'quadrant') of the mouth at each session. This procedure has conventionally been referred to as SRP. An alternate method involves addressing the entire oral cavity within 24 hours during one or two sessions, referred to as full-mouth scaling. The incorporation of an antiseptic agent, such as chlorhexidine, into full mouth scaling is referred to as FMD. The justification for applying these full-mouth methodologies is to diminish the probability of re-infection in previously treated areas (Jervøe-Storm et al., 2022).

Success in NSPT is contingent upon several aspects, including the unique host response and mechanical debridement (Silva et al., 2015). Therefore, the utilization of pharmacological medications as a complement to nonsurgical periodontal therapy is frequently examined to enhance treatment efficacy (Grellmann et al., 2016; Scopp et al., 1980). Antimicrobial medications, including antibiotics and antiseptics like chlorhexidine, are utilized to diminish biofilm presence (Hope & Wilson, 2004). The clinical efficacy of antimicrobial agents remains under examination due to minimal differences in outcomes, potential side effects, and the risk of antibiotic resistance (Merle et al., 2023).

Various dietary supportive agents are currently undergoing increased scientific investigation to improve patient's overall and periodontal health (Najeeb et al., 2016). Consuming dietary components is necessary for survival since they supply a crucial source of energy (macronutrients) and important cofactors that are necessary for the proper functioning of enzymes, structural components, and transport (micronutrients). Malnutrition can occur at either the macronutrient or the micronutrient level, depending on whether these nutrients are depleted or absent. They both pose a threat to periodontal health as well as the general health of the individual. One of these micronutrients is known as CoQ10 (Dommisch et al., 2018).

CoQ10 is a recognized antioxidant that aids in replenishing other antioxidants, promoting cellular proliferation, and preventing apoptosis (Hans et al., 2012). CoQ10 facilitates the dismutation of superoxide anion (O2) into hydrogen peroxide and molecular oxygen, hence rendering the potentially toxic superoxide anion less hazardous (Linnane et al., 2007). Its insufficiency may correlate with periodontal disease (Prakash et al., 2010). The systemic delivery of CoQ10 in periodontal disease therapy can decrease GCF flow, probing depths, and enhance clinical attachment (Barbari & Hussein, 2022). SOD in the GCF serves as a primary antioxidant defense enzyme and is a significant marker of periodontal disease activity. Research has indicated a reduction in SOD levels after initial periodontal therapy (Karim et al., 2012).

Likewise, another study attempted to assess the impact of CoQ10 dietary supplementation on the treatment outcomes of CP patients following phase 1 periodontal therapy. The authors determined that prolonged regular consumption of the nutritional supplement CoQ10 is more advantageous for nonsurgical treatment outcomes of periodontal disease (Saini, 2014).

A recent clinical trial assessed the efficacy of CoQ10 supplementation (120mg, twice for three months) as an adjunct to SRP in thirty subjects exhibiting plaque-induced gingival inflammation and possessing at least three nonadjacent interproximal sites with a probing pocket (PPD) depth of $\geq$ 5mm. This brief study with a limited sample size shown a substantial decrease in inflammation of the gingival tissue when CoQ10 oral supplements were utilized in conjunction with SRP, compared to SRP alone (Manthena et al., 2015).

Another recent study evaluated the effect of CoQ10 supplementation (30mg, twice daily for three months) as an adjunct to SRP in thirty-two individuals with Stage II Grade B

periodontitis. At the end of the study, both groups exhibited a notable enhancement in clinical parameters, evidenced by a reduction in PPD and an increase in CAL, with a statistically significant difference favoring the test group (Barbari & Hussein, 2022).

The effectiveness of CoQ10 gel (2Ml) as a adjunctive treatment to NSPT as well as its impact on SOD levels in GCF among periodontitis patients were assessed. The authors determined that the supplementary application of CoQ10 alongside SRP can enhance antioxidant levels, although it is not more effective than SRP in the management of CP (Pranam et al., 2020).

Another study compared CoQ10 efficacy with and without sub-antimicrobial dose doxycycline (CoQ10 30 mg, sub-antimicrobial dose doxycycline 20mg, twice a day for 3 months). 40 patients were involved in study, equally divided into 4 groups. First group received sub-antimicrobial dose doxycycline with NSPT, the second group used CoQ10 in addition to NSPT, third group received both CoQ10 and sub-antimicrobial dose doxycycline in addition to NSPT, and the fourth group received NSPT only. The study's findings indicates that the combination of sub-antimicrobial dose doxycycline and CoQ10 exhibited the most effective treatment outcome relative to other groups. Treatment with sub-antimicrobial dosage doxycycline or CoQ10 significantly enhanced clinical metrics compared to NSPT alone (Darweesh, 2015).

Another study assessed the efficacy of CoQ10 supplementation (100 mg, once daily for 30 days) alongside NSPT in individuals with chronic periodontitis (CP) and diabetes. The scientists determined that the supplementary usage of CoQ10 to NSPT promotes the therapeutic response in CP patients with controlled diabetes and considerably reduces pocket depths (Ghasemi et al., 2022).

Due to its antioxidant properties, CoQ10 has generated significant research interest in literature in recent years. CoQ10, once seen as an alternative treatment, is utilized both topically and systemically in periodontology. A deficit of CoQ10 has been observed in the gingiva of individuals with periodontal disease (Littarru et al., 1971; Nakamura et al., 1973). Gingival samples from patients with inflammatory periodontal tissues demonstrated a deficit of CoQ10, unlike those with normal periodontal tissues. A multitude of clinical trials administering CoQ10 orally to individuals with periodontal problems have been done

(Ghasemi et al., 2022; Pranam et al., 2020; Saini, 2014). The findings indicate that oral administration of CoQ10 elevates CoQ10 levels in unhealthy gingiva and successfully minimizes periodontal inflammation and microorganisms (Hanioka et al., 1994; Prakash et al., 2010).

The primary intracellular enzymes that preserve cells and tissues from oxygen-derived free radicals are SOD, glutathione peroxidase, and catalase. SOD represents the first line of antioxidant defense mechanisms. It facilitates the dismutation of two superoxide molecules (O2) into hydrogen peroxide and molecular oxygen, thereby diminishing potential threat of the superoxide anion (Ighodaro & Akinloye, 2018).

SOD, as the primary element of the antioxidant system, functions as a significant biological marker for evaluating treatment effectiveness, and these subjects warrants additional research. Previous studies conducted with CoQ10 by various authors did not use any biochemical parameter to assess its efficacy and the results were assessed by the clinical parameters alone (Prakash et al., 2010). Only one study evaluated the effect of CoQ10 in terms of SOD levels (Pranam et al., 2020). The subject warrants further investigation.

This research will clinically and biochemically examine the effectiveness of CoQ10 as an adjuvant to the FMD protocole in individuals with stage one and two periodontitis.

2. LITERATURE REVIEW

2.1 PERIODONTAL DISEASES

Periodontal disorders are pathological conditions affecting the periodontium, defined as the supporting structures around the tooth, which encompass the gingiva, alveolar bone, cementum, and periodontal ligament. Gingivitis represents the least severe kind of periodontal disease, affecting as much as 90% of the population. This word refers to the inflammation of the gingiva caused by dental plaque. Gingivitis is a reversible condition that responds well to enhanced oral hygiene practices. Periodontitis occurs when the periodontal condition advances beyond gingivitis into a chronic, damaging, and irreversible inflammatory disease state. Periodontitis represents the subsequent phase of gingivitis. When bacteria entrenched in the gingiva penetrate deeper tissues, the host reaction is initiated. The host's response to eliminate the invading bacteria simultaneously inflicts harm on the periodontium. Initially, there is detachment, succeeded by osseous loss, and in the advanced stages, the loss of the afflicted tooth occurs (Highfield, 2009; Pihlstrom et al., 2005).

2.1.1 Periodontitis

Periodontitis is characterized by the apical migration of the junctional epithelium and the presence of gingivitis in regions exhibiting radiographic evidence of bone loss (Dyke, 2008). Periodontal pathogens, particularly Gram-negative anaerobic bacteria referred to as the red complex, induce microbial infection within the subgingival dental biofilm, resulting in chronic inflammation (Socransky & Haffajee, 2005). The activation of defense cells is marked by the release of inflammatory mediators, including proteases, acidic metabolites, cytokines, interleukins (IL), and chemokines, which damage tissue and ultimately lead to bone resorption (Gasmi Benahmed et al., 2024).

Periodontitis is a common chronic inflammatory condition. This condition impacts about two thirds of the adult population, with severe periodontal disease affecting around 19%, equating to over one billion individuals globally (Botelho et al., 2022; Trindade et al., 2023). The World Health Organization has recognized severe periodontal disease as a significant public health concern due to its high prevalence, and its associations with

systemic conditions for instance diabetes mellitus and cardiovascular disease (Abbafati et al., 2020; Darveau, 2010; Hajishengallis, 2015). The progression of periodontal disease is generally influenced by microbial dysbiosis and an abnormal host cellular and immunological response in the gingival and subgingival areas, resulting in gradual destruction if untreated (Abusleme et al., 2021; Darveau, 2010; Hajishengallis, 2015). Recognizing how complicated host–microbe interactions in periodontal disease is important. This offers profound insights into the complicated relationship between the host and microbiome, essential for both periodontal and systemic health (Makkar & Sriram, 2025).

In periodontitis, infections stimulate innate immune leukocytes to generate pro-inflammatory mediators such as cytokines, which substantially facilitate the advancement of CP. While infection is necessary for periodontitis, it is insufficient on its own for disease progression. Pathogens activate the acquired immune system, worsening the evolution of inflammatory conditions and causing significant damage to both soft and hard periodontal tissues. Individual susceptibility, exclusively linked to immune and inflammatory responses of the organism, is considered vital, as the majority of signaling pathways and cellular processes associated with these diseases may be traced to shared molecular origins (Martínez-García & Hernández-Lemus, 2024).

2.2 2017 PERIODONTAL CLASSIFICATION

A classification scheme for periodontal and peri-implant diseases and conditions is essential for clinicians to accurately diagnose and treat patients, as well as for researchers to investigate etiology, pathogenesis, natural history, and treatment of these diseases and conditions (G. Caton et al., 2018). Since the 1999 workshop, substantial new insights have been acquired through evidence from population surveys, fundamental scientific research, and studies monitoring environmental and systemic risk variables. The analysis of this evidence has prompted researchers to establish a new classification for periodontal disease (Papapanou et al., 2018).

Consequently, the World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions was convened in 2017. The classification has undergone multiple revisions in the past 30 years to align with new scientific evidence, and it has been determined that the updated classification should be defined by a multidimensional staging

and grading system that can be adjusted as further evidence arises (Figure 2.1) (Tonetti et al., 2018).

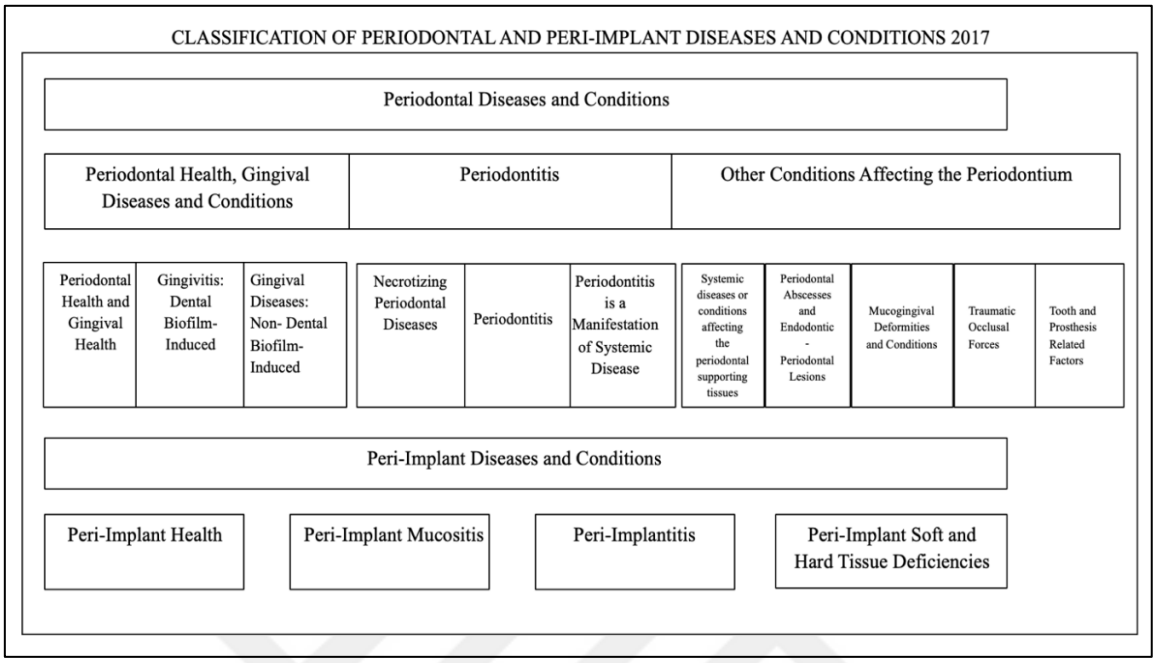


Figure 2.1: Classification of Periodontal and Peri-implant Diseases and Conditions 2017.

2.2.1 Staging and Grading of Periodontitis

The staging process can be evaluated along two dimensions: severity and complexity. The severity score is predominantly determined by the degree of interdental clinical attachment, acknowledging the low specificity of both pocket and marginal bone loss, with marginal bone loss also included as an extra descriptor. This adheres to the established framework of prior severity-based indices and is predicated on the most adversely impacted tooth within the dentition. Only attachment loss resulting from periodontitis is utilized for the score.

Recently, it was observed that there is no evidence indicating that various forms of periodontitis possess a distinct pathophysiology; instead, the periodontitis phenotype in these patients may be elucidated by the intricate interplay of risk factors within a multifactorial disease model. In this context, it appears beneficial to provide a system for assessing the biological grade of periodontitis (risk or actual advancement). Periodontal grading is categorized into three levels: A, B, and C. Clinicians may initiate grading by presuming a moderate advancement rate (grade B), subsequently evaluating direct and indirect evidence or risk factors that could alter the prognosis and adjust the grade

accordingly. If the patient possesses risk characteristics linked to increased illness progression or diminished responsiveness to bacterial reduction therapy, this information can be utilized to adjust the forecast of the patient's future disease trajectory (Figure 2.2) (Tonetti et al., 2018).

	Periodontal Stage	**Stage I**	**Stage II**	**Stage III**	**Stage IV**
Severity	Greatest interdental clinical attachment loss	1-2 mm	3-4 mm	≥ 5 mm	
	Percent bone loss	Coronal third (>15%)	Coronal third (15% - 33%)	Middle third or apical third	
	Teeth lost to periodontitis	No tooth loss		≤ 4 teeth	≥ 5 teeth
Complexity		• Probing depths ≤ 4mm • Mostly horizontal bone loss	• Probing depths ≤ 5mm • Mostly horizontal bone loss	• Probing depths ≥ 6mm • Vertical bone loss ≥ 3 mm • Class II or Class III furcation	In addition to Stage III complexity: • Need for rehabilitation • Masticatory dysfunction • Tooth mobility ≥ 2 • < 20 remaining teeth
Extent	• Localized (<30% of teeth involved) • Generalized (>30% teeth involved) • Molar/incisor pattern				

Figure 2.2: Staging and Grading According to 2017 Periodontal Classification.

2.2.2 Pathogenesis of Periodontitis and Destruction of Periodontal Tissues

The connective epithelium establishes a distinct barrier between the root surface and the gingiva, primarily serving as a shield the underlying tissues from persistent exposure to oral microorganisms and their by-products. A variety of molecular variables associated with adhesion, cell-cell interactions, chemotaxis, proinflammatory cytokines, epithelial development, matrix metalloproteinase activation, and antimicrobial peptide generation influence the functionality of the junctional epithelium. This highly adapted defense mechanism, bacterial virulence factors, and chronic inflammation (clinically manifested as gingival hemorrhage and alterations in soft tissue morphology and pigmentation), result in

the apical migration of the attachment epithelium on the root surface and the activation of collagen degradation, ultimately culminating in the formation of periodontal pockets (Bosshardt & Lang, 2005).

Neutrophils, serving as the initial defense, traverse from blood vessels to tissue in response to chemokine stimulation. Neutrophils, macrophages, lymphocytes, plasma cells, and mast cells are present in the connective tissue, and complement proteins are activated. Clinical manifestations of gingival inflammation, including hemorrhage and elevated GCF, commence to manifest. Thereafter, the innate immune response transitions to an acquired immune response, commencing the established lesion phase. At this juncture, macrophages, plasma cells, and T and B lymphocytes emerge as the primary cell types. Collagenolytic activity escalates with an elevation in macrophage and tissue-derived matrix metalloproteinases. Nevertheless, there is a decline in tissue perfusion. This stage is clinically marked by significant gingivitis, exhibiting hemorrhaging gingiva along with alterations in color and texture. The subsequent phase is the established lesion stage, characterized histologically and clinically by irreversible attachment and bone loss, culminating in periodontitis (Newman et al., 2019). Antigens produced by bacteria, including lipopolysaccharides (LPS) and peptidoglycans, are detected by toll-like receptors (TLRs) on the surface of host cells, thereby initiating the inflammatory response (Mahanonda & Pichyangkul, 2007). Resident cells in the gingiva release pro-inflammatory cytokines, including TNF-α, IL-1, IL-6, and IL-8. Vasoactive amines and TNF-α released from mast cells enhance vascular permeability, leading to the accumulation of neutrophils in the affected area. Lysosomal enzymes released by neutrophils and matrix metalloproteinases activated by inflammatory mediators (Figure 2.3) contribute to the destruction of periodontal tissues (Ohlrich et al., 2009). In chronic inflammation, bacterial antigens are recognized by antigen-presenting dendritic cells, macrophages, and B lymphocytes. Thelper0 (Th) cells engage with antigen-presenting cells and differentiate into Th1, Th2, Th17, and regulatory Th cells. Th1 cells play a crucial role in cellular immunity by secreting interferon-γ (IFN-γ), transforming growth factor-beta (TGF-β), and IL-2. Th2 cells initiate humoral immunity through the secretion of cytokines IL-4, IL-5, IL-6, IL-10, and IL-13. Cytokines and prostaglandin e2 induce osteoclast formation and activation through modulation of RANKL and osteoprotegerin expression (Yucel-Lindberg & Båge, 2013).

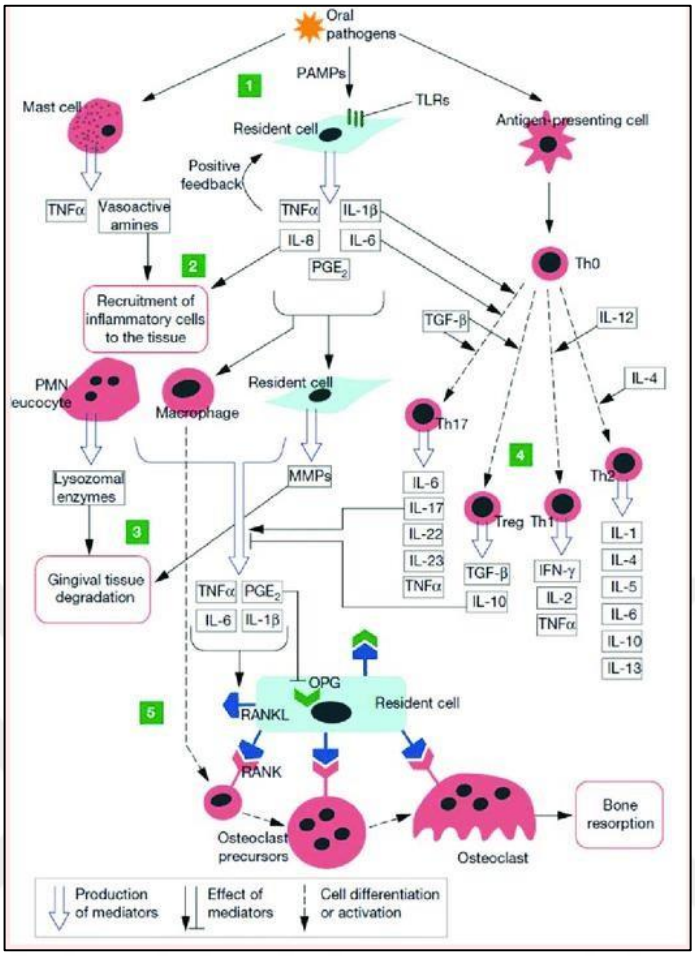


Figure 2.3: Inflammatory Mediators in Pathogenesis of Periodontitis (Tawfig, 2016).

2.3 THE CORRELATION BETWEEN OXIDATIVE STRESS AND PERIODONTITIS

During periodontal inflammation, periodontal infections induce the synthesis of proinflammatory cytokines that attract polymorphonuclear leukocytes (PMNL) to the affected region. PMNLs significantly contribute to the pathophysiology of periodontal disorders through the production of substantial quantities of proteolytic enzymes and ROS that facilitate tissue degradation (Graves, 1999).

Oral tissues, comprising the oral cavity and periodontal tissues, are physiologically sensitive to ROS. Alongside their physiological presence, the generation of ROS in tissues is augmented by pathogens infiltrating periodontal tissues (Vo et al., 2020).

ROS encompasses a category of oxygen-derived free radicals, including superoxide radical, hydroxyl radical, and nitric oxide, as well as oxygen-derived non-radical compounds such

as hydrogen peroxide and hypochlorous acid (Chapple, 1997; Waddington et al., 2000). ROS are physiologically generated inside the respiratory chain and during enzymatic reactions (Genestra, 2007). They are crucial for numerous biological functions, including cellular transduction signaling and regulation of gene expression. At elevated concentrations, ROS generation can induce tissue damage by many mechanisms, including protein and DNA impairment, lipid peroxidation, enzymatic oxidation, and the synthesis of proinflammatory cytokines (Chapple & Matthews, 2007).

The correlation between oxidative stress (OS) and periodontitis is attracting the attention of professionals (Qu, 2023). Elevated ROS levels or diminished antioxidant capability can disturb homeostasis and lead to OS (Battino et al., 1999). OS is an inflammatory phenomenon resulting from an imbalance between ROS and antioxidant mechanisms, leading to an oxidative condition that can harm cellular and extracellular structures. This has been linked to systemic disorders including cardiovascular disease, arthritis, and diabetes, indicating that OS may play a role in the etiology of periodontal disease (Chapple, 1997; Phull et al., 2018; Siti et al., 2015).

2.3.1 Free Radicals and Reactive Oxygen Species

An atom, ion, or molecule possessing an unpaired or absent electron in its outermost orbital is referred to as a free radical. Due to their instability, free radicals tend to react with other chemicals to achieve stability in biological systems, superoxide radicals, peroxyl radicals, lipid peroxyl radicals, alkoxyl radicals, and hydroxyl radicals are classified as ROS (Baltacıoğlu et al., 2014). Free radicals may arise from oxygen or nitrogen. Oxygen-derived free radicals are referred to as ROS, while nitrogen-derived free radicals are termed reactive nitrogen species (Valko et al., 2007).

Cellular metabolism encompasses the uptake of oxygen and its processing through glycolysis to generate pyruvate in the mitochondria. The amino acid cycle occurs, resulting in ATP production. Nonetheless, electrons migrate from their carriers at a steady rate, converting oxygen into the superoxide anion. The incomplete reduction of oxygen is believed to be 1–3% of absorbed oxygen, occurring at a pace that surpasses the capacity of mitochondrial antioxidants to eliminate superoxide (Cadenas, 1989; Nohl & Hegner, 1978). The inadequate reduction leads to mitochondrial DNA damage caused by ROS and reactive

nitrogen species, a process considered significant in specific chronic diseases and aging (Shigenaga et al., 1994). Mitochondria are a significant source of metabolism-derived ROS in vivo, and mitochondrial DNA seems to sustain damage more easily than nuclear DNA due to its proximity to the created ROS (Cuzzocrea et al., 2001).

2.3.2 Antioxidants

Antioxidants (Figure 2.4) are chemicals that inhibit oxidation caused by free radicals and traps, stabilize, and mitigate their effects. They also fulfill various critical functions, including the prevention, reduction, delay, or elimination of oxidative damage induced by ROS (Gutteridge & Halliwell, 2010; Wei et al., 2010).

Endogenous Antioxidants		Exogenous Antioxidants
Enzymatic	**Non-Enzymatic**	**Non-Enzymatic**
Catalase (CAT)	Myoglobin	**Vitamins**
Superoxide dismutase (SOD)	Ferritin	Vitamin C (ascorbic acid)
Glutathione peroxidases (GPxs)	Metallothioneins	Vitamin E (tocopherols)
Glutathione reductases (GRs)	Transferrin	Vitamin K
Glutathione-*S*-transferases (GSTs)	Lactoferrin	**Mineral elements**
Phospholipase A2	Albumin	Selenium
	Ceruloplasmin	Zinc
	Glutathione	Manganese
	Coenzyme Q10	Copper
\	Uric acid	**Nutritional**
	Bilirubin	Carotenoids
	Melatonin	Phytonutrients
	Vitamin A (retinol)	**Supplements**
		Lipoic acid
		Polyphenol
		D-Methionine
		Carnosine
		Omega-3 fatty acids
		Acetyl L-carnitine

Figure 2.4: Antioxidant List (Chakraborty, 2023).

2.3.3 Superoxide Dismutase

SOD is the enzyme that facilitates the transformation of the superoxide radical (O2-) into hydrogen peroxide (H2O2) (Halliwell et al., 2000; Nguyen et al., 2020). SOD is located in the periodontal ligament and functions as an essential barrier against superoxide production in gingival fibroblasts (Agnihotri et al., 2009).

SOD has anti-inflammatory properties by modulating OS, averting lipid peroxidation, and obstructing the adherence of inflammatory cells to endothelium monolayers, thereby facilitating less inflammation in diverse pathological processes (Islam et al., 2022).

SOD is regarded as a principal antioxidant, which accounts for its substantial research in periodontitis patients. SOD, found in all tissues and active in bodily fluids such as blood plasma, exhibits altered activity in many diseases (Fei et al., 2021; Reddy et al., 2004). SOD may serve as a crucial protective mechanism for gingiva against superoxide emission (Jacoby & Davis, 1991). Numerous research have investigated the correlation between SOD levels and periodontitis, SOD levels were assessed in serum, saliva, gingiva, and GCF in some instances (Na et al., 2006; Novakovic et al., 2014; Pranam et al., 2020; Ramesh et al., 2019; Sukhtankar et al., 2013; Wei et al., 2010).

In a research, the effect of NSPT on SOD levels in serum, saliva, and GCF samples collected from 48 patients with CP and 35 healthy control subjects were evaluated both before and 16 weeks after NSPT. Results show that NSPT appears to restore and regulate the antioxidant capacity of the patients by both local and systemic modifications of SOD levels (Wei et al., 2010).

In another study, A total of 26 individuals with CP and 18 control subjects were examined. In patients, teeth exhibiting moderate-to-severe periodontitis with pockets measuring ≥5 mm that necessitated full-thickness flap surgery in the right or left maxillary quadrant were examined, while in controls, teeth designated for extraction due to orthodontic considerations were analyzed. Following the clinical assessments (PD, CAL, GI, BoP, PI), GCF samples were obtained. Tissue samples were collected from the same teeth during flap surgery in patients and shortly following tooth extraction in controls. The activities of SOD were assessed using spectrophotometry. The gingival SOD activity was markedly elevated in the CP group compared to the control group ($p<0.05$). No substantial difference was observed in GCF SOD activity among the groups ($p>0.05$). The correlations between gingival and GCF SOD activity were not statistically significant in the CP and control groups ($p>0.05$). The researchers concluded that SOD activities in gingiva and GCF are independent, or that SOD activity in gingiva does not entirely transfer to GCF (Akalin et al., 2005).

A recent study included one hundred thirty-five people aged 20 to 55 years, consisting of 45 light smokers, 45 heavy smokers, and 45 nonsmokers. The documented clinical parameters were PI, PPD, and CAL. GCF and saliva samples were obtained, thereafter analyzed for SOD levels utilizing a spectrophotometric technique. The study results demonstrate that

smokers displayed markedly reduced mean SOD levels in both GCF and saliva relative to the control group. Analyses performed intra- and inter-group revealed that heavy smokers demonstrated markedly lower levels of SOD in GCF and saliva compared to light smokers and control participants. The authors highlighted a gradual decline in SOD levels from healthy nonsmokers to light smokers and then to heavy smokers in both saliva and GCF, indicating that a reduction in smoking exposure may enhance antioxidant levels (Ramesh et al., 2019).

Another study evaluated sixteen patients, aged 30 to 50 years, with mild to moderate CP of both sexes, exhibiting pocket depths of 5 to 7 mm in four nonadjacent interproximal sites. The sites were randomized and allocated into treatment and control groups. CoQ10 (PerioQ Gel) was administered at the treatment site, while a placebo gel was applied at the control site, both at baseline and following NSPT. The results indicated no statistically significant difference in clinical parameters between the two groups at any time interval; however, there was a significant increase in SOD levels in the test group compared to the control group at the end of 3-months. The study determined that the supplementary application of CoQ10 with SRP can enhance antioxidant levels; however, it does not surpass SRP in ameliorating clinical parameters after treatment of CP patients (Pranam et al., 2020).

These studies indicate that SOD levels can be assessed from samples obtained from blood serum, saliva, and GCF. These SOD values provide comprehensive insights about the condition of periodontitis (Akalin et al., 2005; Prakash et al., 2010; Pranam et al., 2020; Wei et al., 2010).

2.3.4 Gingival Crevicular Fluid (GCF)

GCF is a biological fluid derived from blood plasma, exhibiting varying compositions in the gingival groove, and possesses exudate characteristics that influence the ecology of the gingival groove. This fluid was initially reported to result from enhanced permeability of the arteries in the junctional and sulcular epithelium (Darveau et al., 1997; Page, 1992).
Desquamated epithelial cells, erythrocytes, migrating leukocytes, electrolytes like potassium, sodium, and calcium, bacterial metabolites like lactic acid, urea, endotoxins, and cytotoxic substances, carbohydrates, proteins, and host and bacterial enzymes like acid phosphatase, alkaline phosphatase, SOD, cytokines, and immunoglobulins are among the

cellular components found in GCF (Delima & Van Dyke, 2003). While the volume of GCF is minimal in healthy gingival tissue, it increases in response to inflammation and significantly decreases following periodontal treatment (Gomes et al., 2009).Several factors influencing GCF volume include systemic diseases, pharmacological treatments, hormonal fluctuations, circadian rhythms, psychological stress, smoking, periodontal therapy, and the severity of inflammation (Deinzer et al., 2000). To analyze the biochemical mediators in GCF, a variety of techniques have been used, including hybridization, flow cytometry, polymerase chain reaction, and enzyme-linked immunosorbent assay (Delima & Van Dyke, 2003).

The significance and diagnostic value of GCF in the pathophysiology of periodontal disease have been the subject of numerous investigations (Griffiths, 2003). At least 90 distinct components in GCF samples have been assessed as possible biomarkers for the identification and prognosis of periodontal disease (Buduneli, 2019).

From a conventional perspective, potential biomarkers can be assessed within three primary categories aligned with the three stages of periodontitis; inflammation, connective tissue deterioration, and bone resorption. Point-of-care diagnostics utilizing GCF biomarkers could offer immediate information into disease and susceptibility status, facilitating the monitoring of periodontal health (Buduneli et al., 2024).

A meta-analysis indicated that saliva and GCF concentrations of malondialdehyde, which is an indicator of OS, were considerably higher in GCF samples from periodontitis patients. The authors stated that the elevated GCF malonaldehyde levels may be attributed to superoxide anion generation, due to bacterial challenges or as a by-product of neutrophil interactions (M. Chen et al., 2019).

SOD is a crucial antioxidant present in mammalian tissues. The litreature presents inconsistent results concerning SOD levels in GCF samples (Buduneli et al., 2024).
A study evaluated SOD activity among GCF and gingival tissues of patients with CP and periodontally healthy individuals. The activity of gingival SOD was considerably elevated in patients with CP compared to healthy controls, but no variations in GCF SOD activity were seen across the research groups (Akalin et al., 2005).

Also, evaluation of biomarkers of GCF can be used to analyze and consolidate the effects of periodontal treatment. Furthermore, changes in the concentration of specific molecules derived from the host tissue response within GCF, including both increases and decreases, have been assessed as potential indicators of periodontal disease (Heasman et al., 1993).

2.4 TREATMENT OF PERIODONTITIS

The primary objective of periodontal treatment is to eradicate gingival inflammation, halt tissue deterioration, and avert disease recurrence (Lowenguth & Greenstein, 1995). Given that microbial dental plaque is the principal etiological factor in gingivitis and periodontitis, the management of plaque is essential for the prevention and treatment of these diseases. Bacteria within the periodontal pocket are structured in a biofilm layer that adheres to the root surface. Bacterial endotoxins and other antigenic substances provoke a tissue reaction that frequently results in inflammation and tissue damage. Consequently, the primary objective in the management of inflammatory periodontal disorders should be the elimination of subgingival plaque. Multiple studies indicate that plaque removal alleviates inflammation and halts tissue degradation (Brochut et al., 2005; Christgau et al., 2006; Kim et al., 2007). The primary approach to periodontal therapy is eliminating all local irritants that may induce gingival inflammation and educating the patient to enhance plaque control. The initial treatment constitutes the fundamental technique in all phases of periodontal therapy. Clinical studies indicate that the enduring efficacy of periodontal treatment is contingent upon the success of the first intervention (Nikalus P. Lang & Jan Lindhe, 2015). The management of periodontitis, resulting from a disparity between microbial aggression and host defenses, seeks to reestablish equilibrium by diminishing microbial assault. Maintaining low levels of microbial invasion by daily oral hygiene and consistent professional periodontal care can often stabilize the periodontal state (Van Der Weijden & Timmerman, 2002).

CAL, PPD measurements, and GI, which signifies the occurrence of BoP, are frequently utilized to evaluate and track periodontal health. The objective of periodontal treatment is to decrease probing depth, sustain or enhance CAL, and minimize the occurrence of BoP. Periodontitis can be effectively managed with NSPT, then when necessary surgical treatment approach followed by supportive periodontal therapy (SPT) (Heitz-Mayfield et al., 2002). The crucial factor in successful periodontal treatment is NSPT and the patient's level of oral

hygiene. In this context, strong data supports that NSPT is a crucial and successful element in the treatment of inflammatory periodontal disease (Van Der Weijden & Timmerman, 2002).

2.4.1 Non-Surgical Periodontal Treatment

Periodontal treatment relies on a variety of treatment methods, including behavioral-change techniques such as personalized oral hygiene instructions, smoking cessation support, dietary modifications, subgingival instrumentation for plaque and calculus removal, local and systemic pharmacotherapy, and various surgical procedures. The management of persistent periodontal disease necessitates a variety of strategies and a lifelong dedication to periodontal self-care (Graziani et al., 2017).

NSPT is the crucial part and cornerstone of periodontal treatment. The primary aim of NSPT is to manage microbiological periodontal infection by eliminating bacterial biofilm, calculus, and toxins from periodontally compromised root surfaces both supra and subgingivally, without necessitating surgical excision of adjacent soft tissues (Adriaens & Adriaens, 2004; Aimetti, 2014).

The clinical guidelines issued by the EFP state that the therapy of periodontitis should advance stepwise. Consequently, the initial step in treatment is to augment the patient's motivation for oral hygiene, address their modifiable risk factors, and facilitate behavioral change. The subsequent step includes professional measures designed to remove supra- and subgingival calculus. After the re-evaluation phase, the next step is to start the periodontal treatments necessary to address subgingival infections that lead to pathological lesions in the supporting tissues of the teeth (Graziani et al., 2017).

During the 1970s and 1980s, manual instruments including dental curettes and scalers were considered the gold standard for periodontal care. Beginning in the 1990s, the utilization of sonic and ultrasonic scalers has emerged as a widely recognized alternative to manual instruments (Heitz-Mayfield & Lang, 2013). In most periodontitis cases, comparable outcomes were attained with both techniques, suggesting that either ultrasonics or hand instruments may be utilized based on the clinician's preference (Albeshri & Greenstein, 2022). Recent studies have shown that both manual tools and powered devices, as well as their combination, significantly enhance periodontal conditions and clinical parameters after

NSPT, with no indication that one type of instrument is preferable to the other (Suvan et al., 2020).

According to recent studies, the management of patients with stage 1 and stage 2 periodontitis is conducted in steps. The initial phase of therapy focuses on facilitating behavioral modification by encouraging the patient to effectively eliminate supragingival dental biofilm and manage risk factors. The second step of therapy focuses on managing the subgingival biofilm and calculus. Furthermore, subsequent interventions may be included. The third step of therapy focuses on focusing on the areas of the dentition that do not respond sufficiently to the second step, with the objective of facilitating subgingival instrumentation or targeting the regeneration or resection of lesions that complicate the management of periodontitis. In the end, SPT aims to preserve periodontal stability in treated periodontitis patients by combining the preventative and therapeutic interventions described in the initial two phases of therapy, depending upon the gingival and periodontal condition of the patient's dentition (Sanz et al., 2020).

2.4.2 Full Mouth Disinfection

FMD is another approach used in the management of patients with stage 1 and stage 2 periodontitis. The oral cavity provides many niches for the survival of periodontopathogens, including the mucosa, tongue, tonsils, saliva, and all oral hard surfaces such as teeth, dentures, and implants. Bacteria can migrate between different niches. Saliva is crucial for this transfer, as all species exist within it. This transmission may also occur via oral hygiene tools and/or dental instruments. If intraoral bacterial translocation transpires at an elevated rate, a deep pocket that has undergone SRP may be recolonized from residual untreated pockets or other intraoral niches prior to the establishment of a less pathogenic ecosystem, as it provides an optimal setting for the proliferation of pathogenic species. This may compromise the results of periodontal therapy (Quirynen et al., 1995; van Winkelhof et al., 1988). The FMD procedure entails SRP of all teeth and the cleaning of all oral niches with chlorhexidine throughout two sessions within a 24-hour period (Quirynen et al., 1995; Van Winkelhoff et al., 1988).

Chlorhexidine, utilized in the FMD approach, was invented by Löe in 1969. Chlorhexidine is a cationic agent derived from phenylguanidine. It is a broad-spectrum antiseptic effective

against gram-positive and gram-negative bacteria, dermatophytes, and certain lipophilic viruses (Quirynen et al., 2002). Its principal action is to compromise the cell membrane, exhibiting either bactericidal or bacteriostatic properties contingent upon the dose. Additionally, it is effective by suppressing proteolytic and glycosidic enzymes. It clings to the mouth mucosa and dental surfaces. This characteristic diminishes pellicle formation and enables prolonged environmental presence through controlled release from the surface. The objective of the FMD technique is to eliminate or at least diminish all periodontal infections not just from periodontal pockets but also from the entire oropharyngeal region (including mucous membranes, tongue, tonsils, and saliva) in a brief period using antimicrobial chlorhexidine. This inhibits bacterial translocation, known as cross-contamination, and provides time for periodontal repair prior to bacterial colonization (Loos et al., 1988; Mousquéegs et al., 1980).

The persistence of bacteria post-treatment in the junctional epithelium, pocket epithelium, and/or dentinal tubules is regarded as the primary factor for subgingival recolonization (Adriaens et al., 1988; Giuliana et al., 1997; Lamont & Yilmaz, 2002; Petersilka et al., 2002). Similarly, microorganisms in the oropharyngeal region may affect the subgingival recolonization of pockets following periodontal therapy. The recolonization is contingent upon the standard of oral hygiene, the efficacy of subgingival debridement, and the residual probing depth (Magnusson et al., 1984; Pedrazzoli et al., 1991; Petersilka et al., 2002; Sbordone et al., 1990; van Winkelhof et al., 1988). Two investigations have demonstrated that the microbial load in saliva is markedly decreased following therapy in patients with periodontitis (Dahlén et al., 1992; Rowshani et al., 2004).

In 1995, Quirynen et al. conducted a comparison between FMD and conventional therapy. Ten patients with advanced CP were randomly assigned to experimental and control groups. The experimental group participated in FMD. In the experimental group, subgingival irrigation utilizing 1% chlorhexidine gel was conducted twice in each pocket with 6 to 8 mm calibrated syringes for three sessions, each lasting 10 minutes per visit. The gel application was reiterated in all pockets on the eighth day post-treatment. Oral rinsing was conducted twice for one minute each with 10 ml of 0.2% chlorhexidine mouthwash, with the final 10 seconds targeting the tonsil region. The tongue was coated with 1% chlorhexidine gel for 1 minute. The patient was instructed to gargle with 10 ml of CHX 0.2% for 1 minute twice

daily at home for over 2 weeks. The patient received instruction on oral hygiene. Patients in the control group receive conventional therapy. Patients in the test group had a notable reduction in PPD relative to those in the control group. The culture results indicated a markedly reduced presence of harmful microorganisms in the research group throughout the initial month. In the following month, beneficial bacteria were observed to be significantly more prevalent in the identical regions. The findings indicated that microbiologically and clinically significant enhancements in treatment outcomes can be attained with FMD (Quirynen et al., 1995).

The FMD offers numerous economic benefits for both clinicians and patients. It entails fewer sessions (two rather than four appointments), necessitates reduced travel, and is more comprehensible for the patient. The operator may engage with the same patient for two hours while minimizing the pauses between patients. This enhances the efficiency of chair time and reduces the frequency of instrument replacement (Teughels et al., 2009).

Vandekerckhove conducted 8-month follow-up research in the group of patients published by Quirynen et al. Pockets measuring 7 mm or greater showed a statistically significant reduction with FMD (4 mm) compared to normal therapy (3 mm). The GI and bleeding propensity exhibited comparable enhancement. After 8 months, FMD exhibited a lesser amount of gingival recession and a greater gain in attachment level (3.7 mm vs to 1.9 mm). This study indicates that a FMD yields superior clinical results in CP vs to quadrant treatment (Vandekerckhove et al., 1996).

In a study, the authors evaluated 25 patients with generalized CP, categorizing them into three groups: quadrant-by-quadrant scaling at one-week intervals, a FMD group with chlorhexidine, and a FMD-only group. Initially, the FMD demonstrated a greater reduction in PPD and BoP after one and two months; however, all three treatment modalities provided improvements in clinical and microbiological indicators without significant intergroup differences after eight months (Sagar, 2014).

According to another study, FMD, full mouth scaling, and quadrant SRP are all efficacious treatments for adult CP, and they do not result in significant discomfort for patients. The comparison of FMD to quadrant SRP indicated that FMD provided moderate additional clinical advantages in PPD reduction and CAL gain. Moreover, from a realistic standpoint,

a single visit necessitated less time to complete treatment than multiple encounters. Nonetheless, due to the restricted number of studies available for comparison, additional research is required (Fang et al., 2016).

Alongside its benefits, review of literature indicates no distinction between FMD and intermittent treatment. A 2008 Cochrane analysis indicates that there is no substantial difference in periodontal clinical outcome measures between conventional standard treatment and a full mouth approach. The limited number of studies renders the evidence in this domain unclear, necessitating further research to establish the optimal treatment for CP (Sagar, 2014).

2.4.3 The Role of Antioxidants in Periodontitis

Research indicates that oral bacteria and their byproducts diminish the antioxidant defenses of the gingiva (Tsai et al., 2005). Numerous studies indicate that localized antioxidant application can modify the periodontal microenvironment and mitigate the pathological progression of periodontal inflammation. Oxidative modulation has emerged in recent years as a promising approach for treating severe periodontitis (E. Chen et al., 2023). It has been asserted that organisms can maintain consistent OS levels irrespective of supplementation, and that the efficacy of antioxidant supplementation has been demonstrated in instances where initial OS exceeds typical levels or beyond the individual's stabilization capacity (Pisoschi & Pop, 2015).

The importance of ROS in the genesis of numerous diseases has fostered the belief that their elimination would be advantageous in all such cases. This perspective posits that reestablishing equilibrium between ROS and antioxidants would substantially impact OS. To examine the advantageous effects of antioxidants, test tube experiments assessing their reactivity against ROS were deemed elucidative. Animal and cell culture studies have proven that antioxidant therapy can mitigate oxidative damage. Consequently, antioxidant supplements have been integrated into several health-related and advantageous applications (Lamprecht, 2014).

Host modulation therapy with antioxidant compounds helps to regulate excessive activity of the immune system, and numerous research has explored the advantages of antioxidant-targeted supplements in the context of periodontitis (Sulijaya et al., 2019). Antioxidants used

during periodontal care have been demonstrated to markedly reduce periodontal disease indicators in individuals with type 2 diabetes (Mizutani et al., 2021). Recent research demonstrates substantial positive impacts of antioxidants in the management of periodontitis (Castro et al., 2019; Chapple & Matthews, 2007).

A recent systematic analysis, informed by clinical studies, indicated that antioxidants such as CoQ10, lycopene, and green tea serve as effective adjuvants in periodontal therapy, reducing OS, in the periodontium during periodontitis (Castro et al., 2019). Consequently, antioxidant therapy may facilitate the preservation of periodontal health and reduction of inflammatory markers, including enhancements in PI, GI, BOP, and CAL. Additional longitudinal investigations to elucidate the processes underlying the reduction of inflammation are strongly advised (Castro et al., 2019).

2.4.4 Coenzyme Q10

CoQ10 (2,3-dimethoxy-5-methyl-6-decaprenyl benzoquinone) was initially extracted from bovine heart mitochondria during oxidation-reduction reactions (Crane et al., 1957). CoQ10 is a lipid-soluble micronutrient that is synthesized in both mammals and plants. The structure comprises two functional groups: a benzoquinone, referred to as the head group, and an isoprene side chain, designated as the tail group. The lipid-soluble side chain comprises ten isoprene units, totaling 50 carbon atoms (Acosta et al., 2016). CoQ10 can be synthesized endogenously or sourced from dietary options, including fish and meat, with the highest concentrations found in tissues characterized by elevated energy turnover, such as the heart, brain, liver, and kidneys (Tran et al., 2001). Its lipophilic nature results in infrequent absorption in the intestine. After it is partially absorbed from the intestine, it transports through the lymphatic system before entering the bloodstream (Palamakula et al., 2005). CoQ10, present in both oxidized (ubiquinone) and reduced (ubiquinol) forms, serves as a significant antioxidant and is crucial for mitochondrial adenosine triphosphate production, acting as a primary carrier for electron transfer in aerobic respiration (Åberg et al., 1992; Crane, 2001; Ernster & Dallner, 1995; Okamoto et al., 1989). Besides its intercellular antioxidant capabilities, it is acknowledged to influence gene expression, thereby affecting overall tissue metabolism (Groneberg et al., 2005; Schmelzer et al., 2008). For more than twenty years, CoQ10 has been extensively utilized as a dietary supplement to promote bodily health. Numerous disorders have been linked to CoQ10 deficiency and demonstrated

improvement with CoQ10 treatment. Primary and secondary CoQ10 deficiencies have been recognized in individuals with mitochondrial disorders, fibromyalgia, cardiovascular conditions, neurological disorders, cancer, diabetes mellitus, and male infertility (Garrido-Maraver et al., 2014). There is little evidence supporting a potential correlation between periodontal disease and CoQ10 deficiency (Prakash et al., 2010). During periodontitis, periodontal infections can trigger excessive formation of ROS; antioxidants such as CoQ10 can reduce this ROS generation and diminish the degeneration of periodontal tissues. Inadequate CoQ10 levels were identified in approximately 80% of gingival biopsies from patients with periodontitis (Soni et al., 2012).

In a rat model of aging, systemic CoQ10 treatment was found to mitigate age-related alveolar bone loss linked to a prolonged n-6 polyunsaturated fatty acid diet deficient in CoQ10. Moreover, genetic studies revealed that CoQ10 supplementation restored biogenesis and reduced age-related elevations in some mitochondrial components in gingival cells, possibly due to improved oxidative and respiratory balance (Varela-Lopez et al., 2016).

The antioxidant effects of CoQ10 in nicotine use were examined in vitro in periosteal fibroblasts and osteoblasts from patients with periodontal disease. The incubation phase of periosteal fibroblasts and osteoblasts with CoQ10, pycnogenol, or phytoestrogens significantly enhanced the production of physiologically active steroid metabolites, even in the presence of nicotine, unlike incubation with the toxin alone. Consequently, CoQ10, pycnogenol, or phytoestrogens seem to provide protective cellular antioxidative actions by counteracting the degenerative effects of nicotine (Figuero et al., 2006).

The precise optimal dosage of CoQ10 remains undetermined, yet it might vary based on the severity of the issue being managed (Gaby, 1996). CoQ10 is offered as a dietary supplement in dosages typically between 15 and 100 mg. CoQ10 demonstrates a commendable safety profile. The safety of high dosages of orally administered CoQ10 for extended durations is well established in individuals and verified by chronic toxicity investigations in animals. The side effects documented in human trials are predominantly limited to moderate gastrointestinal symptoms, including nausea and stomach discomfort, observed in a restricted proportion of participants. No adverse effects were noted with daily dosages between 600 and 1200 mg in two studies concerning Huntington's and Parkinson's disorders. Recent studies demonstrate the safety and tolerability of CoQ10 at doses up to

3000 mg per day in individuals with Parkinson's disease and amyotrophic lateral sclerosis (Bhagavan & Chopra, 2006).

The therapeutic impact of CoQ10 on periodontal healing has primarily been examined within the framework of non-surgical management of CP. The subgingival application of CoQ10, in conjunction with SRP, demonstrated substantial improvements in the BoP, PI, PPD, and CAL gains at 3 and 6 months post-treatment, relative to SRP alone (Barakat & Attia, 2019; Chatterjee et al., 2012; Hanioka et al., 1994; Hans et al., 2012; Raut et al., 2019; Raut & Sethi, 2016; Sale et al., 2014; Shaheen et al., 2020). The discrepancies in results can be attributed to variations in trial designs, including split-mouth and parallel group studies, patient numbers, statistical power, sample size, carrier type, treatment duration, and concentrations of CoQ10 evaluated. Systemic administration of CoQ10 demonstrated enhancements in periodontal clinical parameters in periodontitis patients at dosages of 30 mg twice a day for 3 months or 120 mg daily for 3 months (ElBarbary et al., 2022; Manthena et al., 2015). Studies assessing the impact of systemic CoQ10 at a dosage of 30 mg twice a day for three months or 100 mg daily for one month in type 2 diabetic individuals with moderate to severe CP demonstrated significant enhancements in clinical parameters and reduced levels of inflammatory cytokines (Ghasemi et al., 2022; Youssef et al., 2019).

CoQ10 aids in preserving cell membrane integrity by regulating elevated levels of ROS. Moreover, it extracts electrons from radicalized vitamins and stabilizes them, so averting cellular harm. The cell membranes, DNA, and LPS generated by periodontal infections elicit the recruitment of PMNLs to the area. Concurrently, pro-inflammatory cytokines are released by periodontal ligament cells and epithelial tissue. All these occurrences induce OS in the area. OS causes damage to periodontal tissues. CoQ10, owing to its antioxidant characteristics, mitigates OS by altering the free radical/antioxidant ratio in favor of antioxidants, hence it is believed to diminish periodontal damage (Gumus et al., 2016).

A new systematic review, including only randomized controlled trials of SRP with or without adjunct use of the antioxidant CoQ10 in adults with periodontitis, claims that, based on low-quality evidence, that the topical and localized application of CoQ10 in conjunction with NSPT does not provide any further clinical benefit in reducing periodontal disease or improving CAL. Conversely, although relying on low-quality evidence, oral supplementation for 3 months with 120 mg of CoQ10 capsules in conjunction with SRP may

potentially diminish PD and enhance CAL in individuals suffering from periodontitis (Fernandez et al., 2025).

CoQ10 is a recognized antioxidant that aids in replenishing other antioxidants, promoting cell proliferation, and preventing cell apoptosis (Hans et al., 2012). Facilitates the breakdown of superoxide anion (O2) into hydrogen peroxide and molecular oxygen, hence rendering the potentially toxic superoxide anion less hazardous. A deficit may be linked to periodontal disease. The systemic delivery of CoQ10 in periodontal disease treatment can decrease GCF flow, probing depths, and enhance clinical attachment (Karim et al., 2012).

As the primary protective antioxidant enzyme, SOD in GCF serves as a significant predictor of periodontal disease activity. Research has indicated a reduction in SOD levels subsequent to first periodontal therapy (Karim et al., 2012).

SOD, as the first step of the antioxidant mechanism, can be considered as a useful biological indicator in evaluating the effectiveness of the treatment and this issue is open to research. When the relevant literature was evaluated, it was found that the clinical and biochemical efficacy of CoQ10 used in addition to the FMD protocol in stage I-II periodontitis patients had not been investigated before. In the light of this information, this study will clinically and biochemically evaluate the efficacy of CoQ10 used as an adjunct to the FMD protocol in stage I-II periodontitis patients.

3. MATERIALS AND METHODS

3.1 STUDY POPULATION

This research was structured as a single center, randomized controlled trial. The subjects involved in this study were individuals who sought treatment at the Department of Periodontology, Altınbaş University Faculty of Dentistry. All operations, including their associated hazards and benefits, were elucidated by the volunteers, who granted informed permission by signing the consent forms. The study received ethical approval from the ethics committee, designated by protocol number 2024-196.

The total sample size determined by using the G-POWER algorithm, with an effect size of 0.97, 80% power, and a 0.50% margin of error, is n=28. The sample size was established using the Independent Sample T-test method, as the study will involve two groups based on the calculation. This study ensured that each group had an identical sample size. In this study, the sample size for each group was n=14, resulting in a total sample size of n=28 (Manthena et al., 2015; Pranam et al., 2020).

The study involved participants diagnosed with stage I and stage II periodontitis. The sample size was determined to be 28. Fourteen of the chosen volunteers received treatment with FMD and placebo (Control Group). The remaining fourteen volunteers received CoQ10 alongside FMD (Test Group). Patients were allocated to treatment groups using random computer assignments.

3.2 PATIENT SELECTION

Inclusion criteria were:

a. Systemically healthy
b. Volunteer for participation in the study
c. Non-Smoker
d. Periodontitis Stage I-II according to 2018 Periodontal and Peri-implant Disease Classification
e. Patients who did not undergo periodontal therapy within the past six months

f. Patients who have not utilized antibiotics or anti-inflammatory medications and antioxidants for any purpose in the past three months
g. At least two non-adjacent interproximal pockets with a PPD of ≥ 4 mm

Exclusion criteria were:

a. Patients with systemical disease
b. Patients who are lactating
c. Pregnant individuals and those with suspected pregnancy
d. Patients who decline to participate in the research study will be excluded from research.

3.3 STUDY DESIGN

The periodontal diagnosis was established through clinical and radiographic evaluations performed during the patients' initial clinic appointment (Figure 3.1). PI, GI, BoP, PPD and CAL were recorded. Measurements were performed with a Hu Friedy ® UNC 15 probe. Periodontal pockets, designated for the collection of GCF, have been identified. GCF samples were collected. Intraoral clinical photographs were captured.

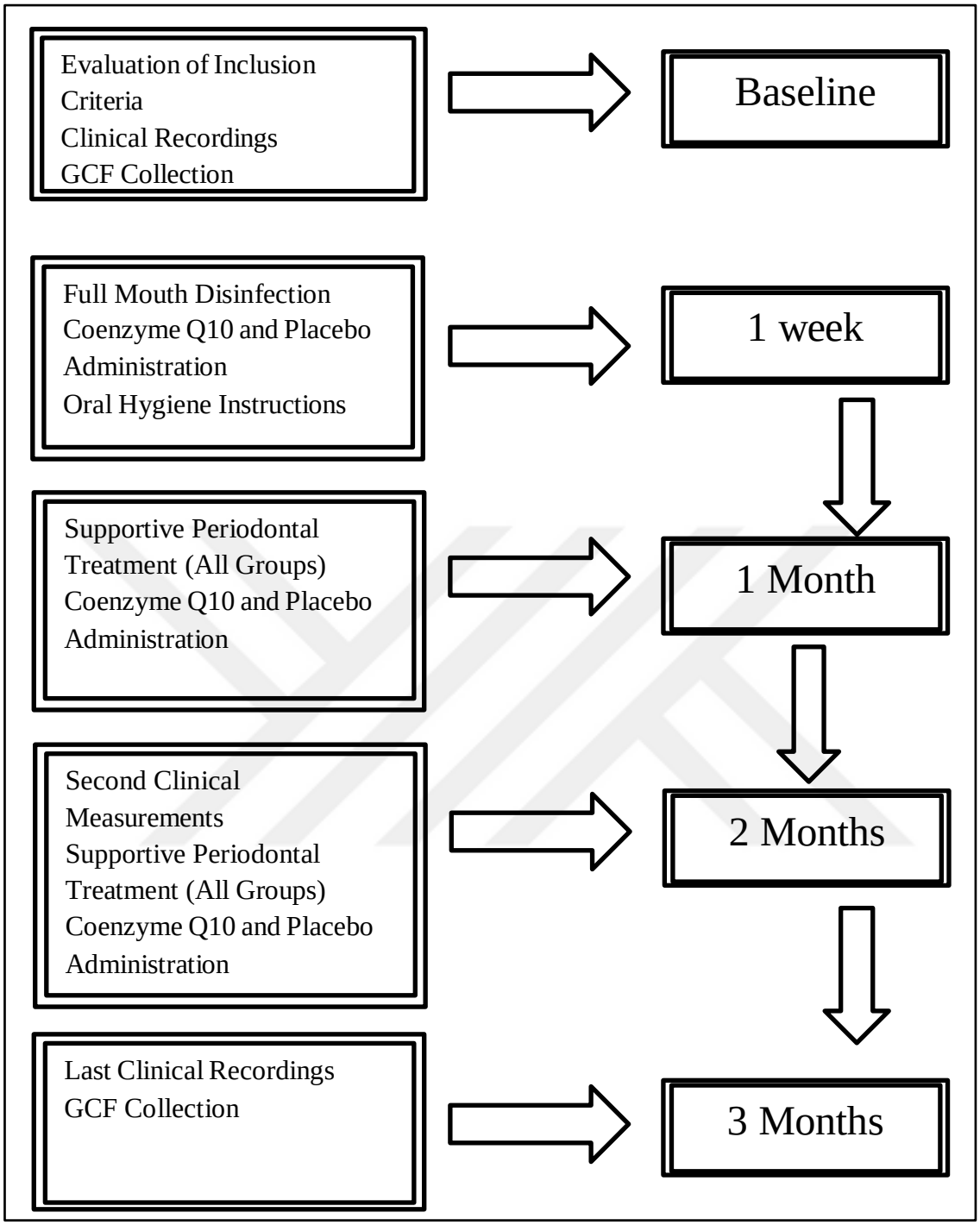


Figure 3.1: Study Design Schema.

In the second session, SRP, and polishing were performed over two consecutive days with ultrasonic instruments and Gracey curettes, in compliance with FMD (Figure 3.2).

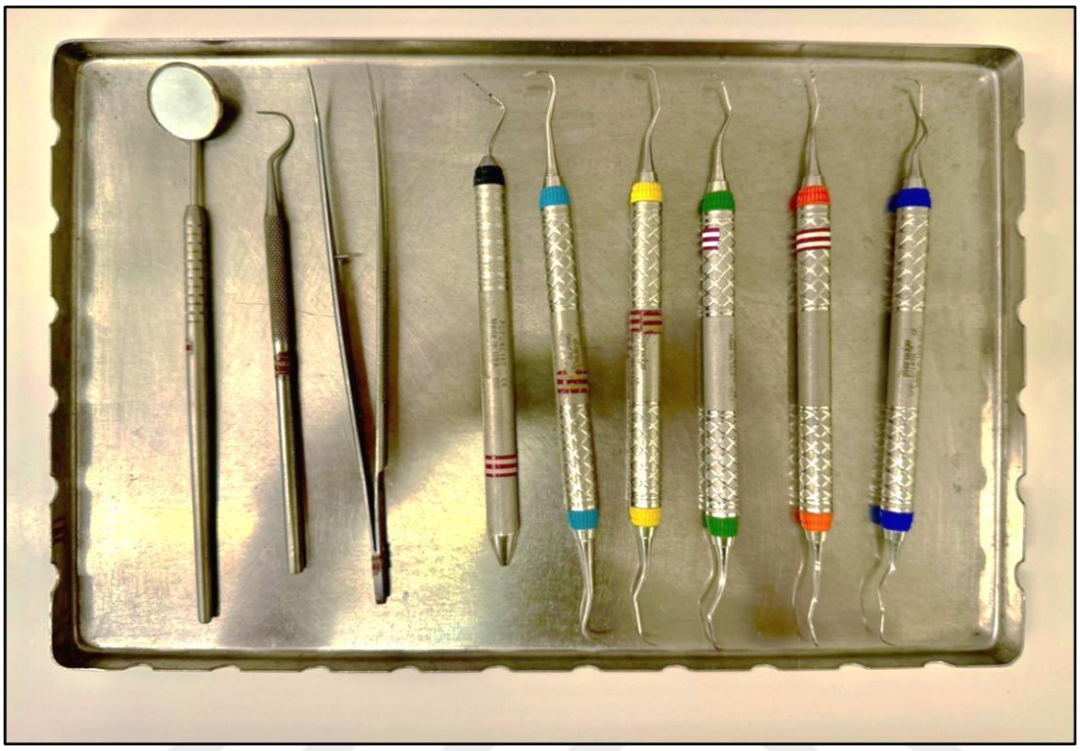


Figure 3.2: Instruments for SRP.

Periodontal pockets were irrigated with a solution of 0.12% chlorhexidine and 0.05% cetylpyridinium chloride (CPC) (PERIO-AID® Intensive Care, Spain) (Figure 3.3). The surface of the tongue was cleansed with a sponge saturated in the identical solution. The patient was also directed to gargle with the 0.12% chlorhexidine and 0.05% CPC (PERIO-AID® Intensive Care, Spain) solution for one minute. Patients received a prescription for 0.12% chlorhexidine and 0.05% CPC (PERIO-AID® Intensive Care, Spain) for a duration of 14 days. Patients were provided with comprehensive oral hygiene instructions, encompassing the non-traumatic modified Bass approach. It is advised to brush teeth twice a day with a medium toothbrush and to utilize an interdental brush. Patients were scheduled for visits one month later.

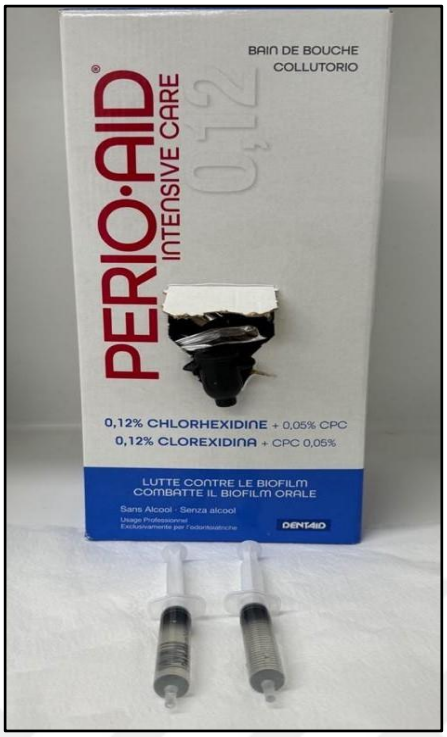


Figure 3.3: PERIO-AID® Intensive Care (CHX 0.12% + CPC 0.05%), Spain.

After one month, a comprehensive examination of the entire oral cavity is conducted. An evaluation is conducted to determine the necessity of SPT. SRP is administered to the patient if required. Clinical assessments of the patient are conducted. The test group is allocated an additional box of CoQ10. The control group is administered a placebo.
During the second monthly examination, the identical procedures are repeated as in the initial month.

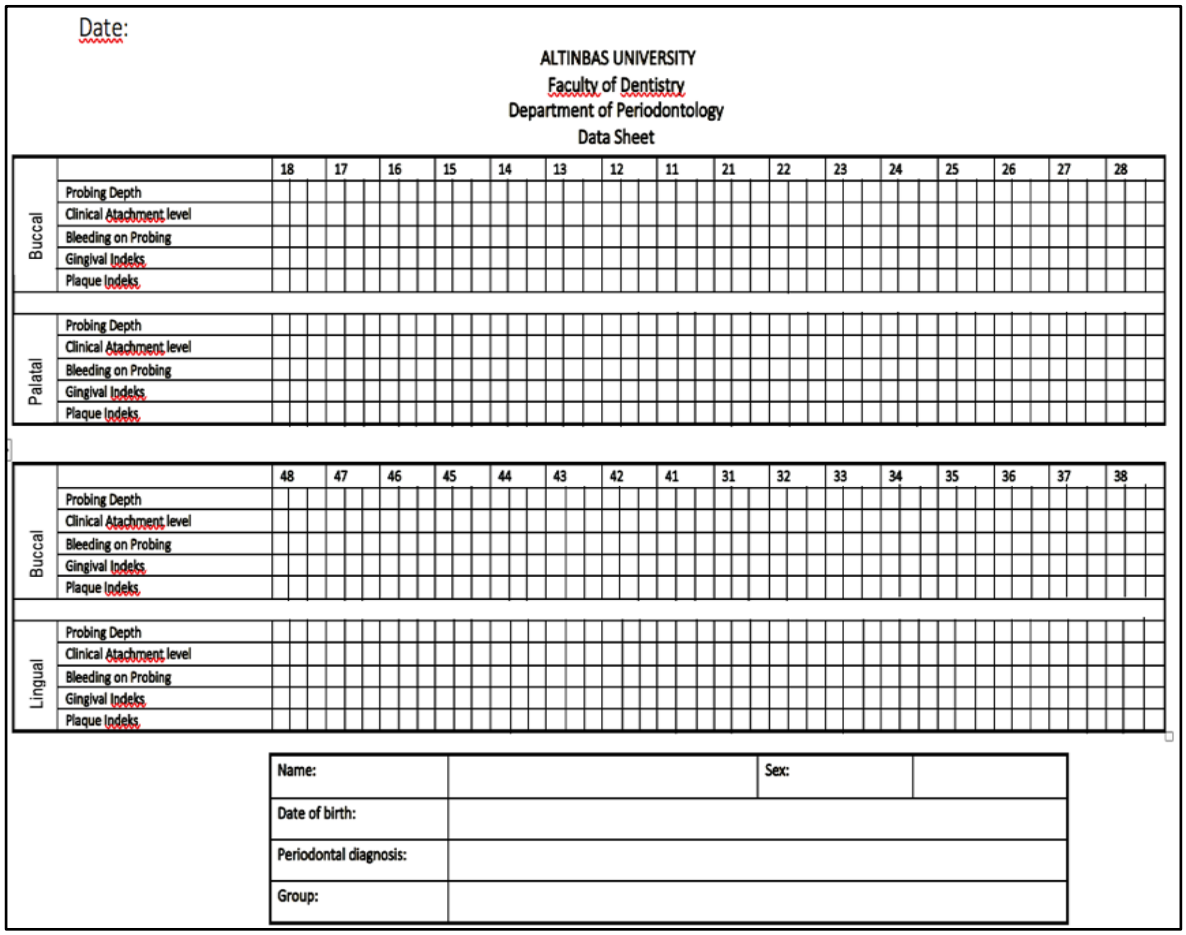
Clinical measurements were conducted again in the third month. GCF was reobtained from the pockets of the previously collected teeth. For biochemical examination, paper strips were placed in tubes and stored at -80 degrees. Intraoral photos were captured. The final visit was conducted in this manner.

3.4 CLINICAL PARAMETERS AND MEASUREMENTS

All clinical measurements were conducted by the same investigator at baseline, as well as throughout the first, second, and third months. Measurements from six locations (distobuccal, midbuccal, mesiobuccal, mesiopalatinal, midpalatinal, and distopalatinal) of all teeth. All measurements were conducted with a 15 mm periodontal probe (UNC 15, Hu-

Friedy®, United States) and documented on personal data sheets (Figure 3.4). The recorded measurements have been listed below:

Figure 3.4: Data Sheet.


Date:

ALTINBAS UNIVERSITY
Faculty of Dentistry
Department of Periodontology
Data Sheet

		18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
Buccal	Probing Depth																
	Clinical Atachment level																
	Bleeding on Probing																
	Gingival Indeks																
	Plaque Indeks																
Palatal	Probing Depth																
	Clinical Atachment level																
	Bleeding on Probing																
	Gingival Indeks																
	Plaque Indeks																

		48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38
Buccal	Probing Depth																
	Clinical Atachment level																
	Bleeding on Probing																
	Gingival Indeks																
	Plaque Indeks																
Lingual	Probing Depth																
	Clinical Atachment level																
	Bleeding on Probing																
	Gingival Indeks																
	Plaque Indeks																

Name:		Sex:	
Date of birth:			
Periodontal diagnosis:			
Group:			

3.4.1 Plaque Index

The Löe and Sillness PI was used to determine the extent of plaque formation and accumulation in the oral cavity. The periodontal probe was positioned parallel to the tooth surface within the gingival crevice adjacent to the gingival margin, and the quantity of accumulated plaque was assessed and graded.

0: Absence of plaque in the gingival margin.
1: Exclusively plaque adhering to the free gingival margin and the adjacent tooth region. The presence of plaque on the surface is identifiable with a probe.
2: Visible plaque in the gingival margin, along the gingival margin, and/or on the adjacent tooth surface, indicating a substantial deposit of soft plaque.

3: Significant plaque accumulation in the gingival pocket and/or on the gingival margin and neighboring tooth surface, characterized by the presence of soft plaque.

3.4.2 Gingival Index

The periodontal probe was positioned perpendicular to the tooth's long axis and maneuvered along the gingival margin, with scoring conducted on a scale of 0-3 based on bleeding and gingival surface characteristics:
0: Healthy gingiva.
1: Gingiva exhibiting minor irritation, slight redness, minimal edema, and no BoP.

2: Moderate inflammation; gingiva is bright red and edematous. Bleeding is observed upon probing.

3: There is significant inflammation, pronounced erythema, and edema. Susceptible to ulcerations and spontaneous bleeding.

3.4.3 Bleeding on Probing

The detection of blood in the gingival sulcus upon probing with the probe's weight was classified as positive (+), whilst negative (-) values were assessed for six locations of each tooth. The percentage of bleeding during comprehensive oral probing was determined using the data.

3.4.4 Probing Pocket Depth

All teeth were assessed using a periodontal probe (UNC 15, Hu-Friedy®, United States) across six surfaces: mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and disto-lingual. During the measurement, the probe was aligned parallel to the long axis of the tooth, based just on its weight without generating pressure. Measurements were documented in millimeters. The average PPD values for each patient were determined by dividing the entire sum of the PPD values across all teeth by the product of the total number of teeth and the number of indexed tooth surfaces (6).

3.4.5 Clinical Attachment Level

The CAL was defined as the distance between the cementoenamel junction and the bottom of the gingival pocket, measured with a periodontal probe. CAL measurements were taken in designated research locations. The periodontal probe was utilized for measurements. CAL was measured in millimeters from the base of the pocket to the edge of the gingiva.

3.4.6 Gingival Crevicular Fluid Collection

GCF was collected from pockets above 4 mm identified during the initial session. Collection of GCF was performed using specialized papers (Periopaper strips, OraFlow, Amityville, NY). Before the collection of GCF, supragingival plaque were eliminated from the tooth surfaces, which were subsequently air-dried and isolated using cotton pellets. GCF samples were collected using paper strips. The GCF collection is a non-invasive method that does not require anesthesia. Specialized paper strips were delicately applied to the gingiva and maintained for 30 seconds. Paper strips contaminated with blood or saliva were excluded. For biochemical examination, paper strips were placed in eppendorf tubes and stored at -80 degrees celcius

3.5 BIOCHEMICAL ANALYSES

GCF obtained from patients using periostrips were tested with the sandwich ELISA method at the biochemistry laboratory at Altinbas University. The samples were stored at 80 ^{o}C until the day of analysis. On the day of analysis, the samples were kept in the room temperature for 30 minutes according to the manufacturer's manual. Phosphate buffered saline solution with the volume of 200 µL was added into the eppendorf tubes and vortexed for the dissolution of the GCF.

3.5.1 Assessment of Superoxide Dismutase Levels in Gingival Crevicular Fluid

The Bioscience (SOD-1) ELISA kit was used to analyze the SOD biomarker (Figure 3.5). 50µL of standards and 50µL of Streptavidin-HRP were added to the control wells of 96-well pre-coated plate. GCF samples of 40µL, 10µL of SOD antibody, and 50µL of Streptavidin-HRP were added to the test wells. No solution was introduced to the blank wells. The wells were incubated at 37^{o}C for 60 minutes. Subsequently, the plate was washed five times.

Following the washing procedure, chromogen solution-A and chromogen solution-B were added to each well. The plate was thereafter incubated at 37ºC for 10 minutes in the absence of light. Following incubation, the stop solution was added to all wells. The absorbance at 450 nm was measured spectrophotometrically with the ELISA reader (BioTek Synergy H1 Microplate Reader, Winusky, VT, USA) (Figure 3.6). The results were expressed as nanograms, and concentrations as ng/µL.

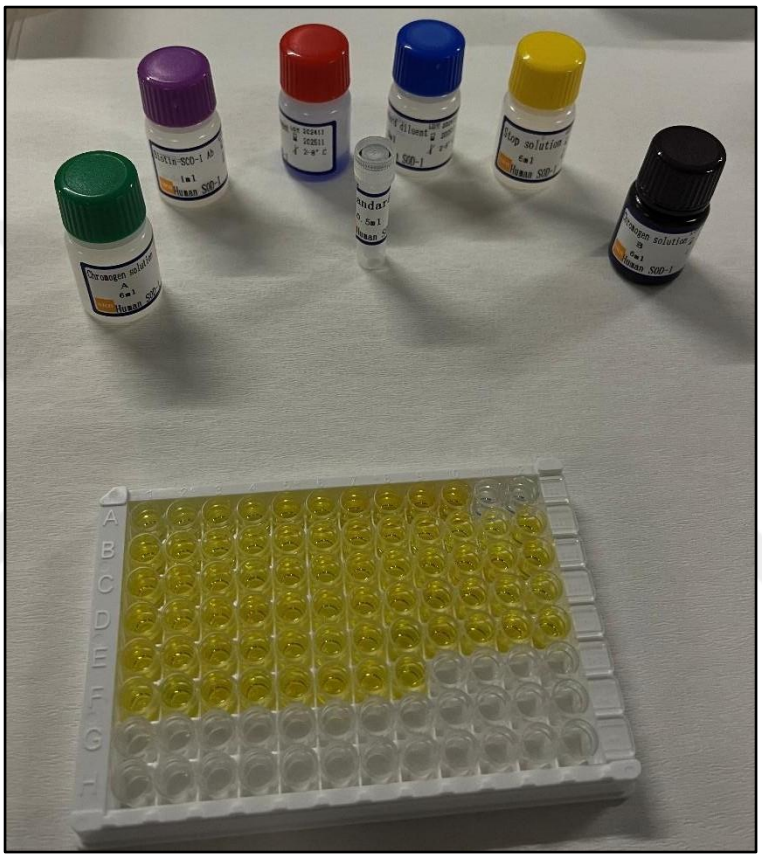


Figure 3.5: Elisa Kit.

Figure 3.6: Spectrophotometry with Elisa Reader.

3.6 NON-SURGICAL PERIODONTAL THERAPHY

3.6.1 Full Mouth Disinfection

NSPT constitutes the initial phase of gingival treatment. The objective is to eradicate the etiological factors of periodontal disease and minimize the depth of periodontal pockets to the maximum extent achievable. Following the removal of calculus and plaque, the practitioner administers oral hygiene instruction to the patient and recommends regular check-ups, which substantially enhances the patient's gingival health. In our research, FMD was favored and utilized as a technique for NSPT. Patients were randomly assigned to groups. FMD treatment was provided in two sessions within a 24-hour interval. The patient was informed about the treatment to be provided in each session. Infiltrative anesthesia was administered utilizing a local anesthetic comprising articaine hydrochloride and epinephrine hydrochloride (Ultracain D-S Fort – 40 mg/Ml + 12 mcg/Ml). SRP were conducted utilizing ultrasonic equipment and region-specific Gracey curettes (No. 5-6, 11-12, 13-14), subsequently followed by polishing. The patient was directed to clean their teeth twice a

day with a medium-firm toothbrush, using the modified Bass technique, and to utilize an interdental brush of the specified dimensions. Following SRP, periodontal pockets were irrigated with a solution of 0.12% chlorhexidine and 0.05% cetylpyridinium chloride (PERIO-AID® Intensive Care (CHX 0.12% + CPC 0.05%), Spain). The surface of the tongue was cleansed with a toothbrush or sponge saturated with the identical solution. The patient was also directed to rinse with the 0.12% chlorhexidine and 0.05% CPC (PERIO AID® Intensive Care (CHX 0.12% + CPC 0.05%), Spain) solution for one minute. Patients received a prescription for 0.12% chlorhexidine and 0.05% CPC (PERIO-AID® Intensive Care (CHX 0.12% + CPC 0.05%), Spain) to be administered twice a day for a duration of 14 days.

3.6.2 Supportive Periodontal Therapy

SPT is an essential element in the management of chronic periodontal disorders, emphasizing the sustained preservation of periodontal health after active treatment. It underscores the necessity of routine follow-up appointments to oversee and regulate the condition, thereby diminishing the likelihood of disease recurrence and tooth loss. The combination of both active and supportive therapy is crucial for optimal outcomes, as it facilitates the ongoing evaluation and reinforcement of oral hygiene routines (OJHA et al., 2024; Sharma, 2023).

SPT aids in preserving CAL and averting the recurrence of periodontal disease. Early diagnosis using SPT can avert reinfection of previously treated regions and the advancement of periodontal degradation (Lang & Tonetti, 2003).

After therapies, all patients were arranged for monthly follow-up sessions over a period of 3 months to assess their periodontal condition. During each appointment, supragingival plaque was eliminated, polishing was conducted, and dental hygiene education was repeated.

3.6.3 Clinical Cases

3.6.3.1 Test group clinical case

One representative case from Test Group (Figure 3.7- 3.12).

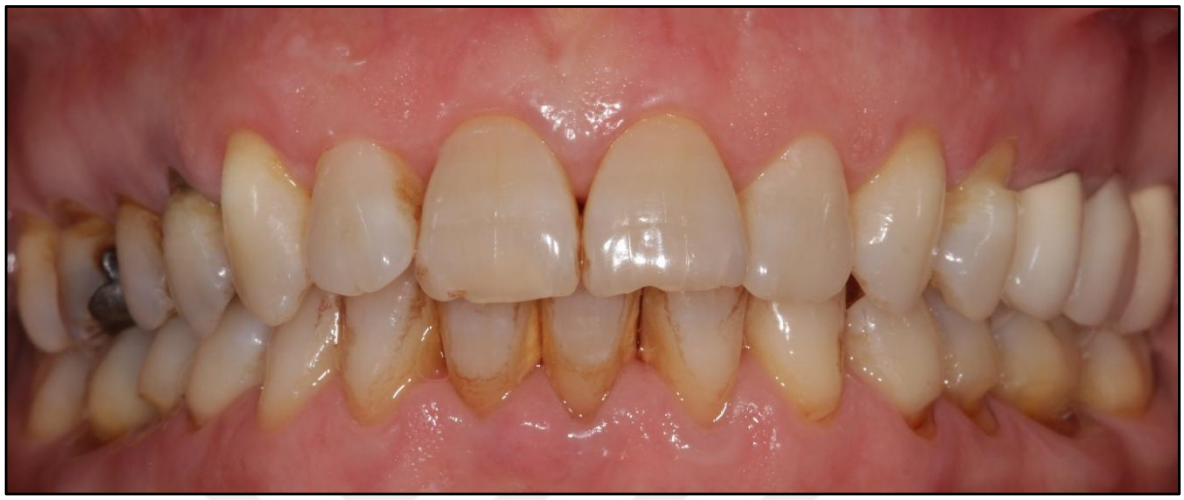


Figure 3.7: Test Group Baseline Clinical View.

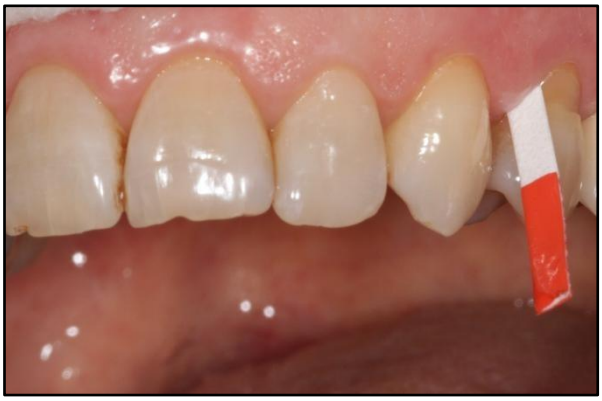


Figure 3.8: Test Group Baseline GCF Sample Collecting.

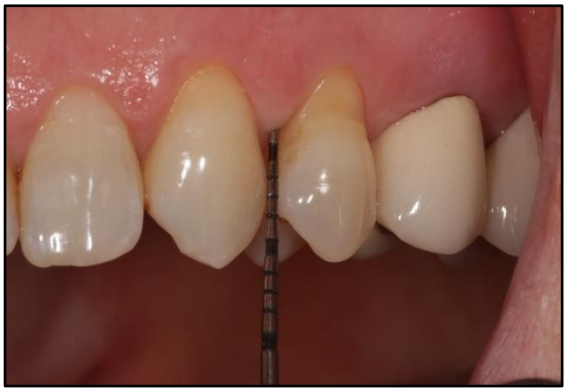


Figure 3.9: Test Group Baseline PPD Measurement.

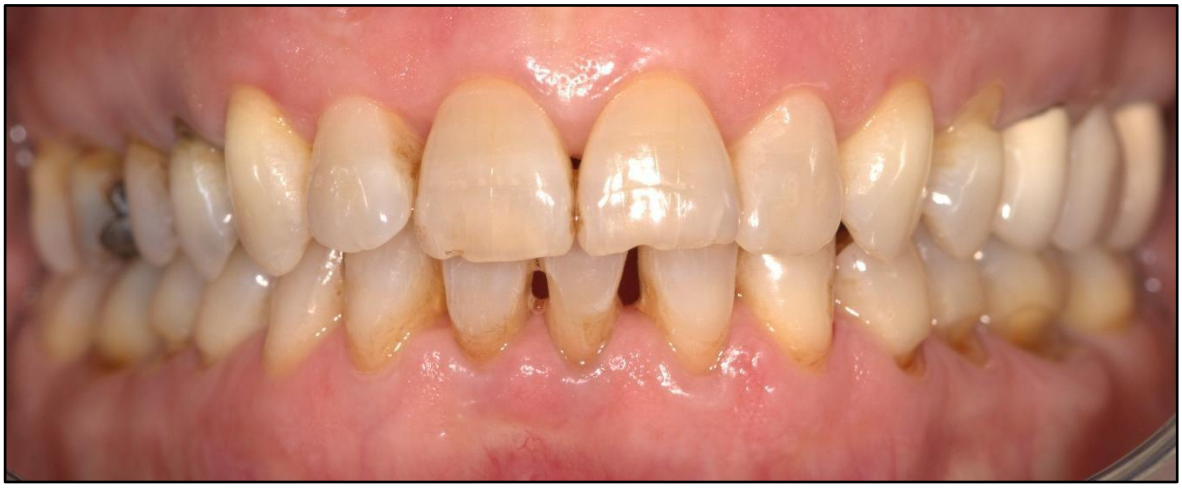


Figure 3.10: Test Group Final Clinical View.

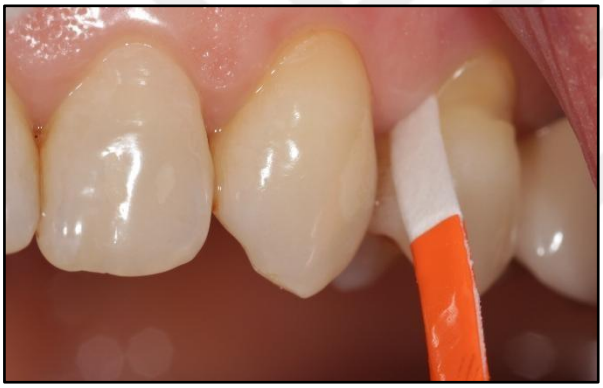


Figure 3.11: Test Group Final GCF Sample Collecting.

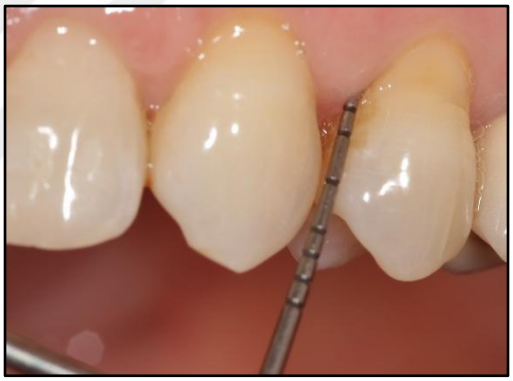


Figure 3.12: Test Group Final PPD Measurement.

3.6.3.2 Control Group Clinical Cases

One representative case from Control Group (Figure 3.13-3.18).

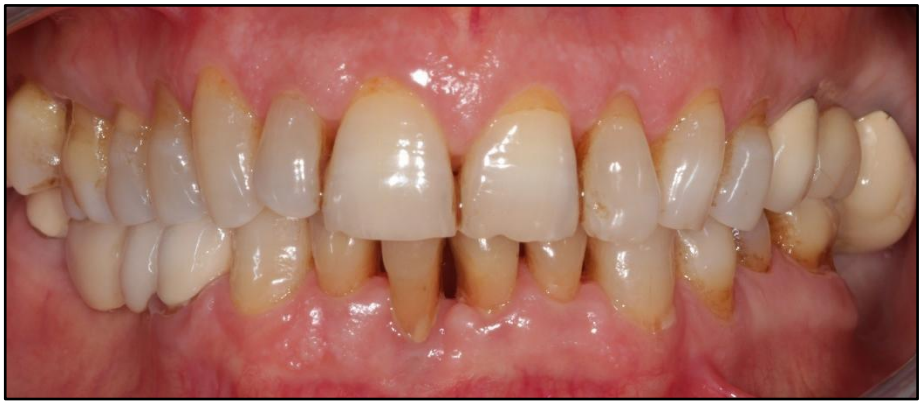


Figure 3.13: Control Group Baseline Clinical View.

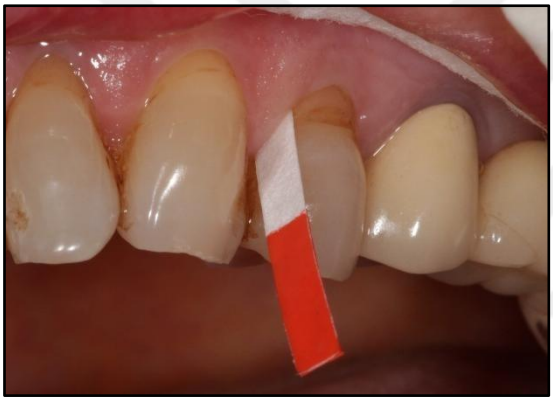


Figure 3.14: Control Group Baseline GCF Sample Collecting.

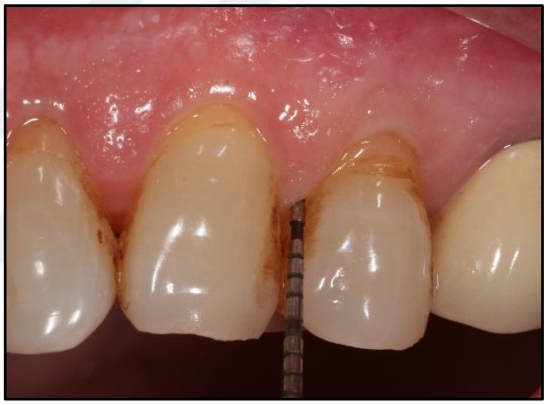


Figure 3.15: Control Group Baseline PPD Measurement.

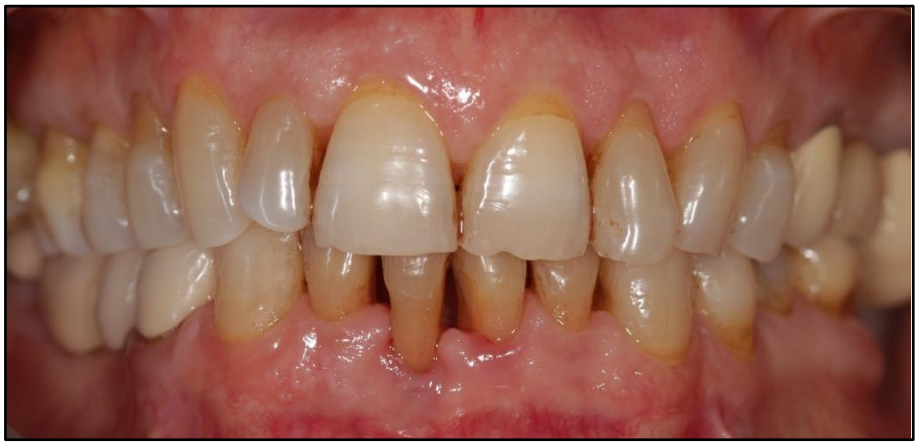


Figure 3.16: Control Group Final Clinical View.

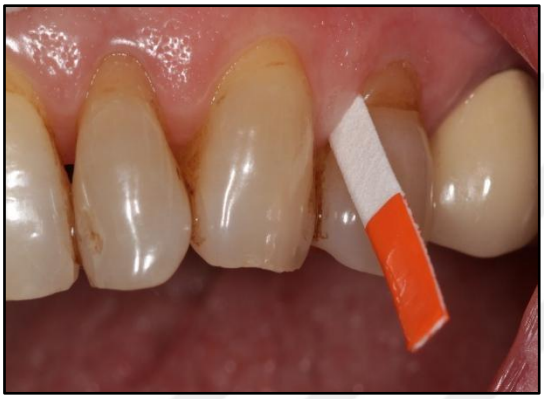


Figure 3.17: Control Group Final GCF Sample Collecting.

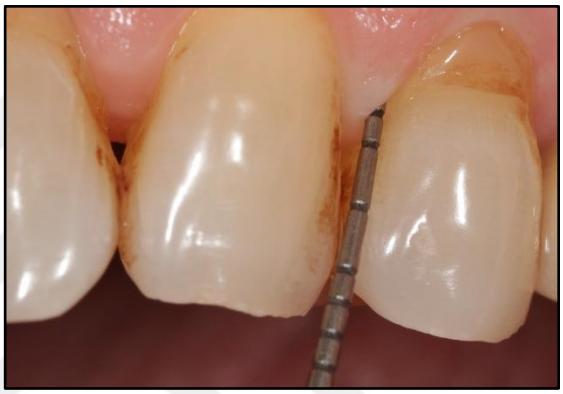


Figure 3.18: Control Group Final PPD Measurement.

3.6.4 Statistical Analysis

The statistical analyses were conducted using SPSS (Statistical Package Social Sciences) version 24.0. Descriptive statistical techniques (Mean, Standard Deviation, Median, Minimum, Maximum, Percentage) were employed to analyze the study data. The Independent Samples T-Test was employed for group comparisons. The Repeated Measures Test was employed to assess follow-up measurements. Significance was assessed at $p<0.01$ and $p<0.05$ thresholds.

4. RESULTS

4.1 STUDY POPULATION, DEMOGRAPHIC DATA

A total of 28 patients, comprising 20 women (71.4%) and 8 men (28.6%) aged between 19 and 79 years were included. The patients were randomly allocated to either test group (Coenzyme Q10 (120mg 1x1, 90 days) + NSPT) (n=14, test group), or control group (placebo + NSPT) (n=14, control group). All participants completed the study. There was no statistical difference observed in mean age and gender between test and control group (Table 4.1).

Table 4.1 Demographic Data.

	Test Group	**Control Group**	
	Mean±Sd	**Mean±Sd**	**p**
Age	50.93±12.39	46.64±13.77	[1]0.394
Gender; n (%)			
Female	11 (78.6)	9 (64.3)	[2]0.403
Male	3 (21.4)	5 (35.7)	

[1]Independent Sample T Test [2]Pearson Chi-Square Test **p<0.01, *p<0.05

4.2 INTRA-GROUP AND INTER-GROUP COMPARISONS OF PROBING POCKET DEPTH

No statistical difference was observed in the mean PPD between groups at baseline (p>0,05). At first (p=0,020; p<0,01), second (p=0,003; p<0,01) and third month (p=0,001; p<0,01) significant difference observed in the mean PPD between groups. Deeper periodontal pockets measured in Control Group than Test Group (Table 4.2).

Table 4.2 Intra-Group and Inter-Group Comparisons of PPD.

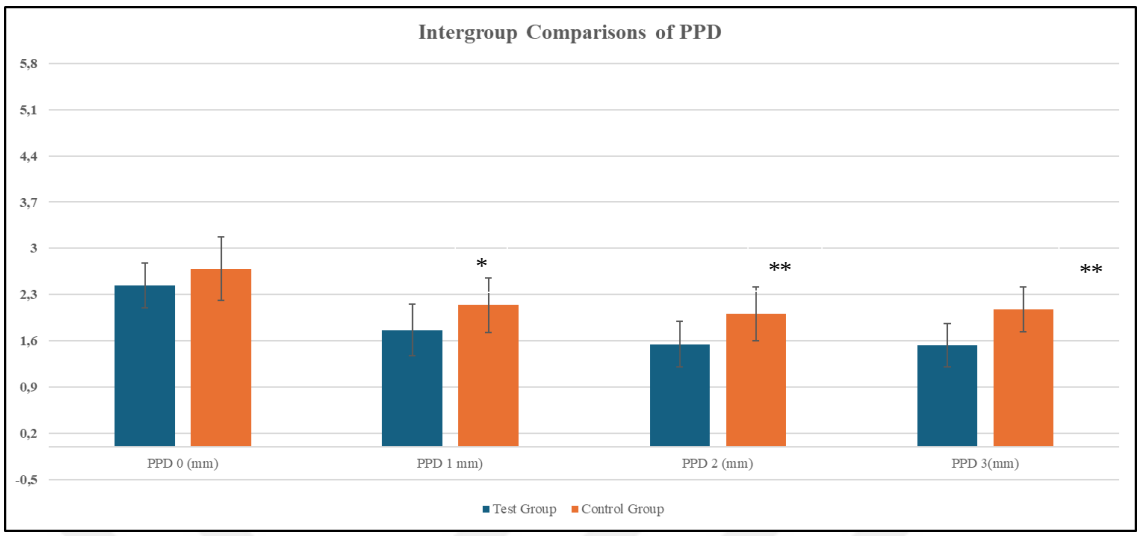
	Test Group	**Control Group**	
PPD (mm)	**Mean±Sd (median)**	**Mean±Sd (median)**	**[1]p**
Baseline (T0)	2.44±0.34 (2.42)	2.69±0.48 (2.59)	0.136
1st month (T1)	1.76±0.39 (1.67)	2.14±0.41 (2.21)	0.020*
2nd months (T2)	1.55±0.34 (1.46)	2.01±0.41 (1.87)	0.003**
3rd months (T3)	1.53±0.33 (1.4)	2.08±0.34 (2.11)	0.001**
[2]p	0.001*	0.001*	
T0-T1 [2]p	p=0.001**	p=0.001**	
T0-T2 [2]p	p=0.001**	p=0.001**	
T0-T3 [2]p	p=0.001**	p=0.001**	
T1-T2 [2]p	p>0.05	p>0.05	
T1-T3 [2]p	p>0.05	p>0.05	
T2-T3 [2]p	p>0.05	p>0.05	

[1]Independent Sample T Test [2]Repeated Measures Test **p<0.01, *p<0.05

The reduction in the PPD measurement in Test Group during the third month, relative to the baseline PPD measurement, was statistically significant (p=0.001; p<0.01). The pairwise comparisons indicate that the reductions in PPD during the 1st month (p=0.001), 2nd month (p=0.001), and 3rd month (p=0.001) relative to the baseline were statistically significant (p<0.01). The alterations observed in the other months were considered insignificant (p>0.05).

The reduction in the PPD measurement in Control Group the third month relative to the baseline was statistically significant (p=0.001; p<0.01). The pairwise comparisons indicate that the reductions in PPD measurements during the 1st month (p=0.001), 2nd month (p=0.001), and 3rd month (p=0.001) relative to baseline were statistically significant (p<0.01). The changes observed in the other months were not statistically significant (p>0.05) (Chart 4.1).

Chart 4.1: Intergroup Comparisons of PPD.



4.3 INTRA-GROUP AND INTER-GROUP COMPARISONS OF CLINICAL ATTACHMENT LEVEL

No statistical difference was observed in the mean CAL between groups at baseline ($p>0.05$). At first ($p=0.029$; $p<0.05$), second ($p=0.012$; $p<0.05$) and third month ($p=0.001$; $p<0.01$) significant difference observed in the mean CAL between groups. More clinical attachment loss observed in Control Group than Test Group (Table 4.3).

Table 4.3 Intra-Group and Inter-Group Comparisons of CAL.

	Test Group	**Control Group**	
CAL (mm)	**Mean±Sd (median)**	**Mean±Sd (median)**	**[1]p**
Baseline (T0)	2.62±0.4 (2.58)	2.83±0.45 (2.75)	0.221
1st month (T1)	1.97±0.42 (1.76)	2.31±0.37 (2.37)	0.029*
2nd months (T2)	1.8±0.38 (1.68)	2.21±0.41 (2.15)	0,012*
3rd months (T3)	1.75±0.39 (1.77)	2.27±0.36 (2.34)	0.001**
[2]p	0.001*	0.001*	
T0-T1 [2]p	p=0.001**	p=0.001**	
T0-T2 [2]p	p=0.001**	p=0.001**	
T0-T3 [2]p	p=0.001**	p=0.001**	
T1-T2 [2]p	p>0.05	p>0.05	
T1-T3 [2]p	p>0.05	p>0.05	
T2-T3 [2]p	p>0.05	p>0.05	

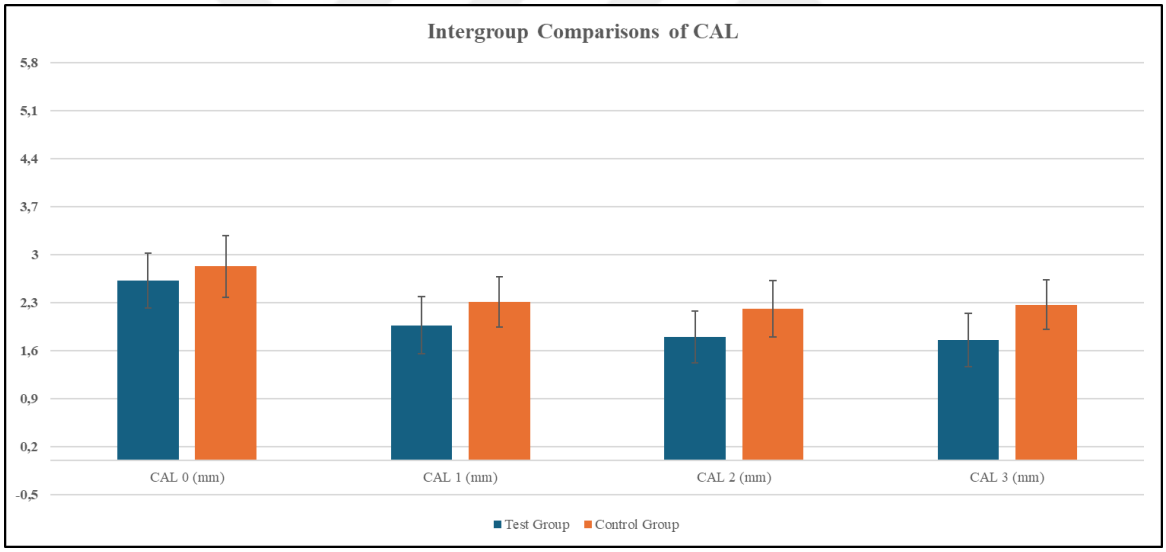
[1]Independent Sample T Test [2]Repeated Measures Test **p<0.01, *p<0.05

The reduction observed in Test Group the third month CAL measurement compared to the baseline CAL measurement was statistically significant (p=0.001; p<0.01). The pairwise comparisons indicated that the reductions in CAL measures during the 1st month (p=0.001), 2nd month (p=0.001), and 3rd month (p=0.001) relative to the baseline were statistically significant (p<0.01). The alterations seen in the other months were deemed statistically insignificant (p>0.05).

The reduction observed in Control Group the third month CAL measurement relative to the baseline CAL measurement was statistically significant (p=0.001; p<0.01). The pairwise comparisons indicate that the reductions in CAL measurements during the 1st month (p=0.001), 2nd month (p=0.001), and 3rd month (p=0.001) relative to baseline were statistically significant (p<0.01). The variation observed in the other months was not statistically significant (p>0.05) (Chart 4.2).

* * **

Chart 4.2: Intergroup Comparisons of CAL.



4.4 INTRA-GROUP AND INTER-GROUP COMPARISONS OF PLAQUE INDEX

No statistical difference was observed in the mean PI between groups at baseline (p>0,05). At first (p=0.038; p<0.05) second (p=0.001; p<0.01) and third month (p=0.003; p<0.01) significant difference observed in the mean PI between groups. Mean PI measured more at Control Group than Test Group at these months (Table 4.4).

Table 4.4 Intra-Group and Inter-Group Comparisons of PI.

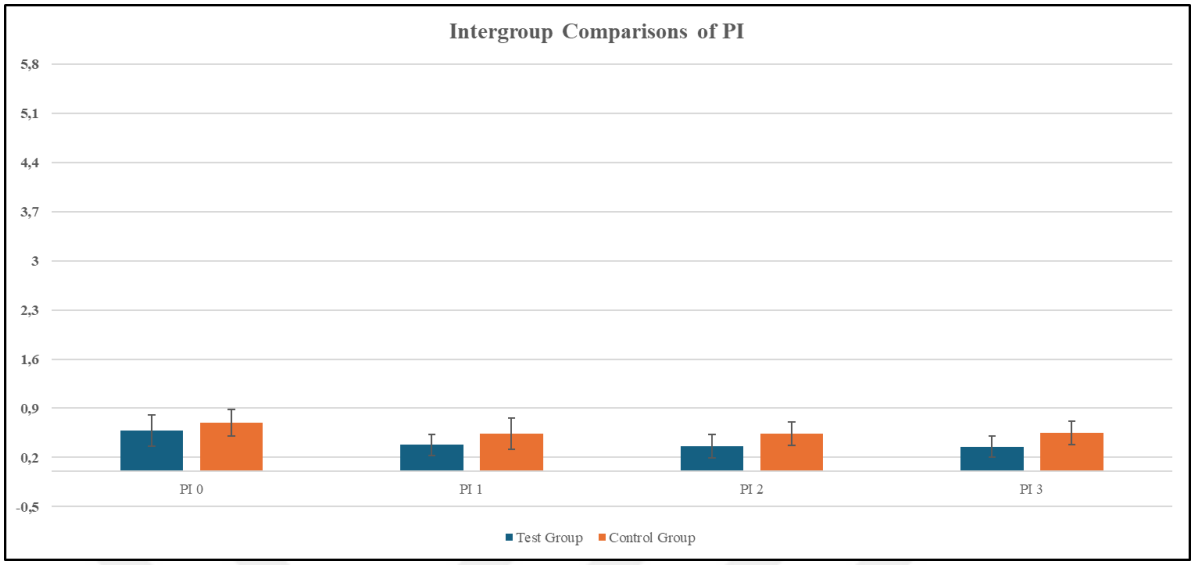
	Test Group	**Control Group**	
PI	**Mean±Sd (median)**	**Mean±Sd (median)**	**[1]p**
Baseline (T0)	0.58±0.22 (0.5)	0.69±0.19 (0.7)	0.177
1st month (T1)	0.38±0.15 (0.33)	0.54±0.22 (0.49)	0.038*
2nd months (T2)	0.36±0.17 (0.31)	0.54±0.17 (0.46)	0.001**
3rd months (T3)	0.35±0.15 (0.36)	0.55±0.17 (0.51)	0.003**
[2]p	0.001*	0.001*	
T0-T1 [2]p	p=0.001**	p=0.001**	
T0-T2 [2]p	p=0.001**	p=0.001**	
T0-T3 [2]p	p=0.001**	p=0.001**	
T1-T2 [2]p	p>0.05	p>0.05	
T1-T3 [2]p	p>0.05	p>0.05	
T2-T3 [2]p	p>0.05	p>0.05	

[1]Independent Sample T Test [2]Repeated Measures Test **p<0.01, *p<0.05

The alteration seen in Test Group the third-month PI measurement relative to the baseline measurement was statistically significant (p=0.001; p<0.01). The pairwise comparisons indicate that the alterations observed in the 1st month (p=0.001), 2nd month (p=0.001), and 3rd month (p=0.001) readings relative to the baseline PI measurement were statistically significant (p<0.01). The alterations observed in the subsequent months have been considered statistically insignificant (p>0.05).

The reduction in Control Group the third month PI measurement relative to the baseline PI measurement was statistically significant (p=0.001; p<0.01). The pairwise comparisons indicate that the reductions in PI measurements during the 1st month (p=0.001), 2nd month (p=0.001), and 3rd month (p=0.001) relative to baseline were statistically significant (p<0.01). The changes observed in the other months were not statistically significant (p>0.05) (Chart 4.3).

Chart 4.3: Intergroup Comparisons of PI.



4.5 INTRA-GROUP AND INTER-GROUP COMPARISONS OF BLEEDING ON PROBING

No statistical difference was observed in the mean BoP between groups at baseline. At first (p=0.001; p<0.01), second (p=0.001; p<0.01) and third month (p=0.001; p<0.01) significant difference observed in the mean BoP between groups. Mean BoP measured more at Control Group than Test Group in these months (Table 4.5).

Table 4.5 Intra-Group and Inter-Group Comparisons of BoP.

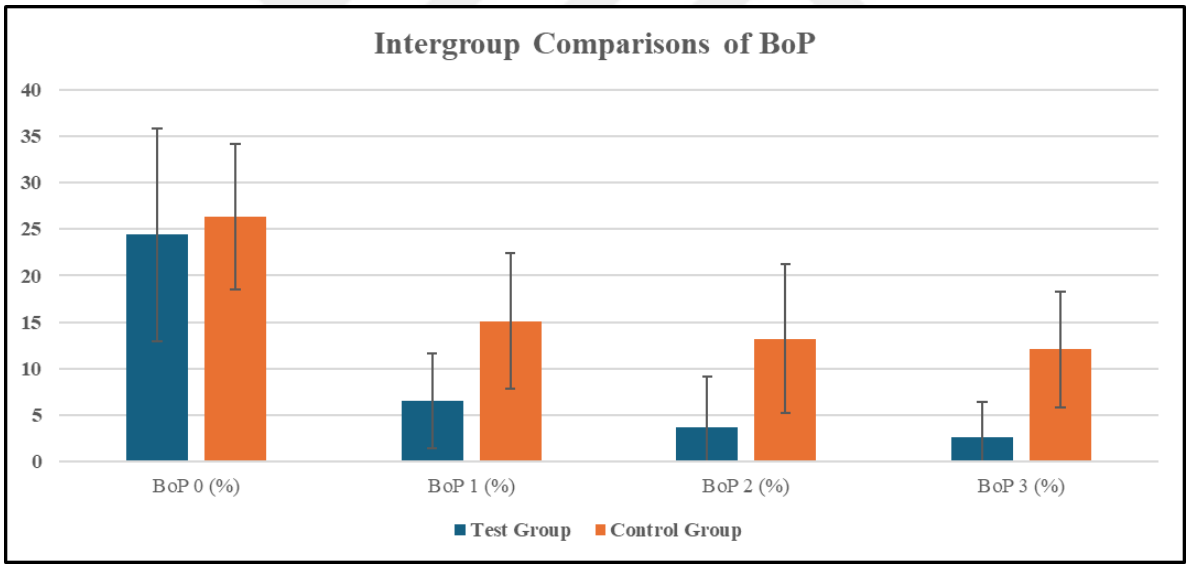
	Test Group	**Control Group**	
BoP	**Mean±Sd (median)**	**Mean±Sd (median)**	**[1]p**
Baseline (T0)	24.39±11.49 (25.11)	26.34±7.87 (26.36)	0.606
1st month (T1)	6.53±5.14 (6.03)	15.12±7.25 (12.66)	0.001**
2nd months (T2)	3.66±5.48 (1.24)	13.21±8 (11.63)	0,001**
3rd months (T3)	2.64±3.79 (0)	12.05±6.17 (11.43)	0.001**
[2]p	0.001*	0.001*	
T0-T1 [2]p	p=0.001**	p=0.001**	
T0-T2 [2]p	p=0.001**	p=0.001**	
T0-T3 [2]p	p=0.001**	p=0.001**	
T1-T2 [2]p	p>0.05	p>0.05	
T1-T3 [2]p	p>0.05	p>0.05	
T2-T3 [2]p	p>0.05	p>0.05	

[1]Independent Sample T Test [2]Repeated Measures Test **p<0.01, *p<0.05

The alteration seen in Test Group the third month BoP measurement relative to the baseline BoP measurement was statistically significant (p=0.001; p<0.01). The pairwise comparisons indicated that the alterations observed in the 1st month (p=0.001), 2nd month (p=0.001), and 3rd month (p=0.001) readings relative to the baseline BoP assessment were statistically significant (p<0.01). The alterations noted in the subsequent months were not statistically significant(p>0.05).

The alteration in Control Group the third month BoP measurement relative to the baseline BOP measurement was statistically significant (p=0.001; p<0.01). The pairwise comparisons indicate that the reductions in BoP measurements during the 1st month (p=0.001), 2nd month (p=0.001), and 3rd month (p=0.001) relative to baseline were statistically significant (p<0.01). The changes noted in the other months were not statistically significant (p>0.05) (Chart 4.4).

Chart 4.4: Intergroup Comparisons of BoP.



4.6 INTRA-GROUP AND INTER-GROUP COMPARISONS OF GINGIVAL INDEX

No statistical difference was observed in the mean GI between groups at baseline. At first (p=0.001; p<0.01), second (p=0.001; p<0.01) and third month (p=0.001; p<0.01) significant difference observed in the mean GI between groups. Except baseline, at all control points, GI scores of Control Group is, significantly higher than Test Group (Table 4.6).

Table 4.6 Intra-Group and Inter-Group Comparisons of GI.

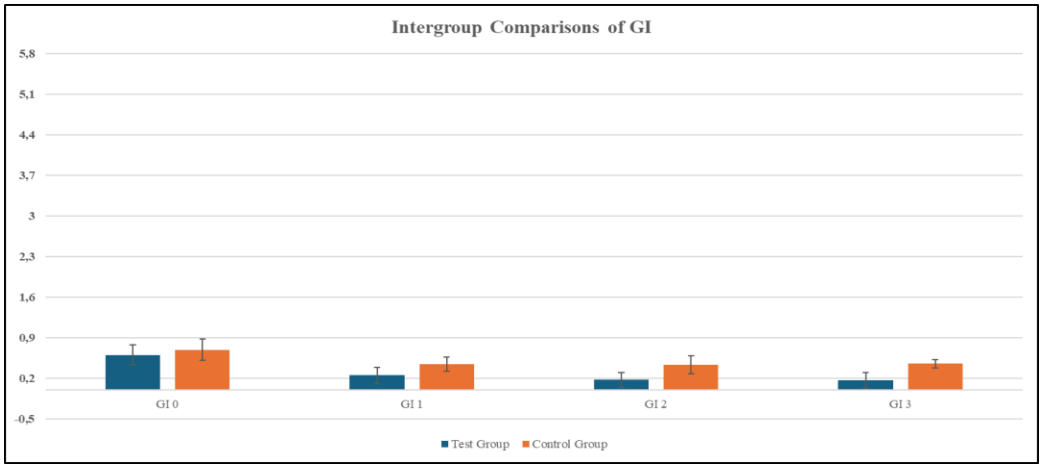
GI	Test Group	Control Group	
	Mean±Sd (median)	**Mean±Sd (median)**	**[1]p**
Baseline (T0)	0.6±0.17 (0.58)	0.69±0.18 (0.67)	0.182
1st month (T1)	0.25±0.14 (0.22)	0.44±0.12 (0.41)	0.001**
2nd months (T2)	0.17±0.13 (0.11)	0.43±0.16 (0.45)	0,001**
3rd months (T3)	0.16±0.14 (0.12)	0.45±0.07 (0.44)	0.001**
[2]p	0.001*	0.001*	
T0-T1 [2]p	p=0.001**	p=0.001**	
T0-T2 [2]p	p=0.001**	p=0.001**	
T0-T3 [2]p	p=0.001**	p=0.001**	
T1-T2 [2]p	p>0.05	p>0.05	
T1-T3 [2]p	p>0.05	p>0.05	
T2-T3 [2]p	p>0.05	p>0.05	

[1]Independent Sample T Test [2]Repeated Measures Test **p<0.01, *p<0.05

The reduction in Test Group the third month GI measurement relative to the baseline GI measurement was statistically significant (p=0.001; p<0.01). The pairwise comparisons indicated that the reductions in measures during the 1st month (p=0.001), 2nd month (p=0.001), and 3rd month (p=0.001) relative to the baseline GI measurement were statistically significant (p<0.01). The alterations observed in the subsequent months were determined to be statistically insignificant (p>0.05).

The reduction in Control Group the GI measurement during the third month relative to the baseline was statistically significant (p=0.001; p<0.01). The pairwise comparisons indicate that the reductions in measurements during the 1st month (p=0.001), 2nd month (p=0.001), and 3rd month (p=0.001) relative to the baseline GI measurement were statistically significant (p<0.01). The changes observed in the other months were not statistically significant (p>0.05) (Chart 4.5).

Chart 4.5: Intergroup Comparisons of GI.



4.7 INTER-GROUP COMPARISONS OF SITE LEVEL PROBING DEPTH (PPDS)

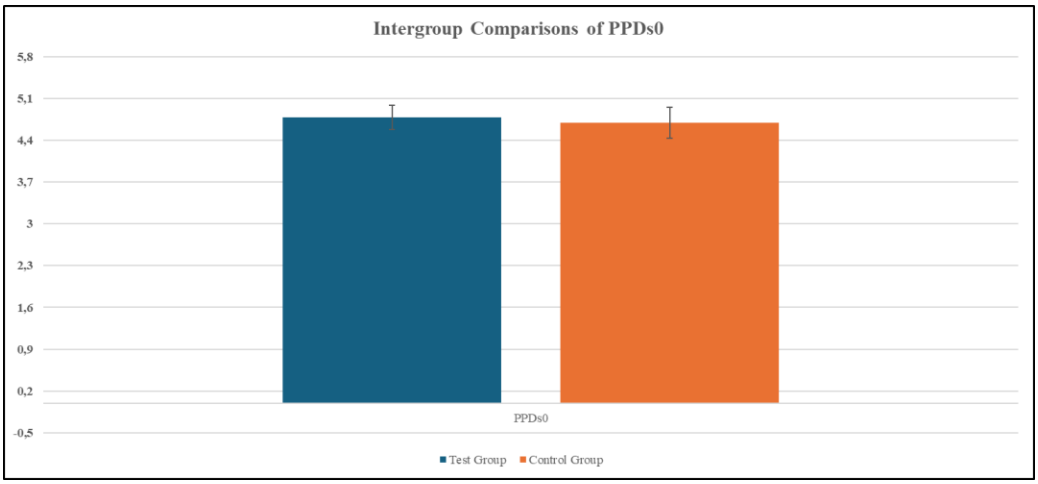
Regional measurements were conducted and compared between the groups in pockets with a depth equal and above 4 millimeters. No significant difference was discovered as a result of these comparisons. (p>0.05) (Table 4.7) (Chart 4.6).

Table 4.7 Inter-Group Comparisons of PPDs0.

	Test Group	**Control Group**	
PPDs	**Mean±Sd (median)**	**Mean±Sd (median)**	**[1]p**
Baseline (T0)	4.78±0.2 (4.78)	4.69±0.26 (4.72)	0.338

[1]Independent Sample T Test **p<0.01, *p<0.05

Chart 4.6: Intergroup Comparisons of PPDs0.



4.8 INTER-GROUP COMPARISONS OF SITE LEVEL CLINICAL ATTACHMENT LEVEL (CALS)

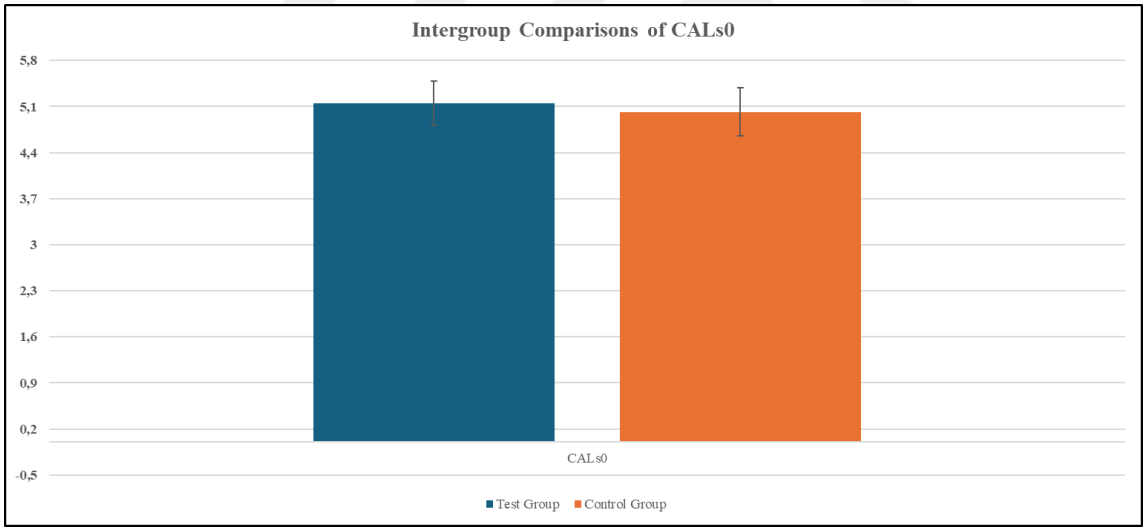
Regional CAL measurements were conducted and compared between the groups in pockets with a depth equal and above 4 millimeters. No statistical difference found between mean CALs0 at baseline (p>0.05) (Table 4.8) (Chart 4.7).

Table 4.8 Inter-Group Comparisons of CALs0.

	Test Group	**Control Group**	
CALs0	**Mean±Sd (median)**	**Mean±Sd (median)**	**[1]p**
Baseline (T0)	5.15±0.34 (5.13)	5.02±0.37 (4.97)	0.347

[1]Independent Sample T Test **p<0.01, *p<0.05

Chart 4.7: Intergroup Comparisons of CALs0.



4.9 INTRA-GROUP AND INTER-GROUP COMPARISONS OF GINGIVAL CREVICULAR FLUID VOLUME

No statistical difference is found between mean GCF volume at baseline and third month (p>0.05) (Table 4.9).

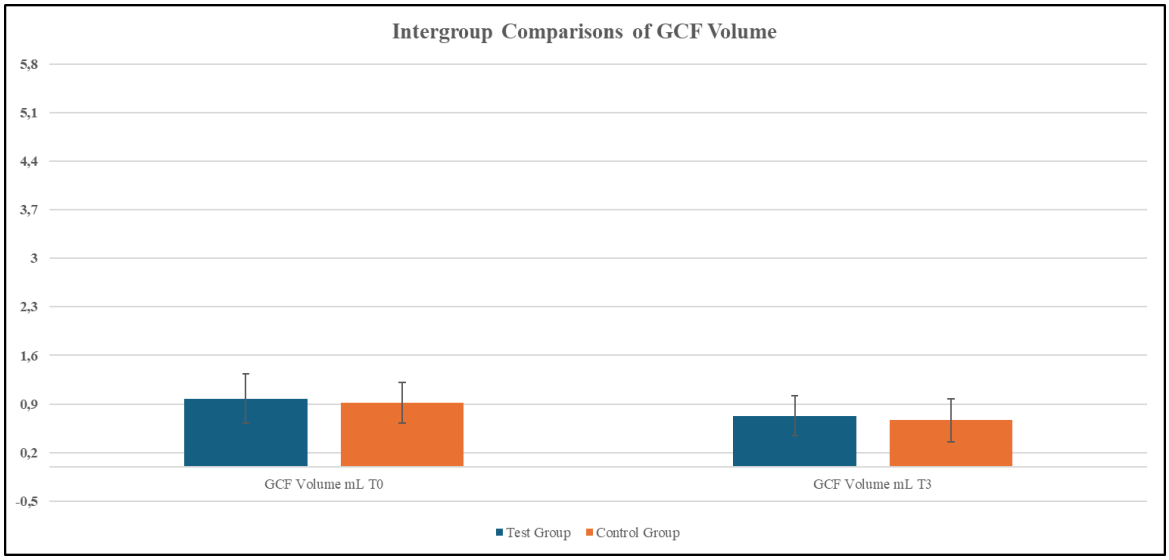
Table 4.9 Intra-Group and Inter-Group Comparisons of GCF Volume.

	Test Group	**Control Group**	
GCF Volume	**Mean±Sd (median)**	**Mean±Sd (median)**	**[1]p**
Baseline (T0)	0.98±0.35 (0.93)	0.92±0.29 (0.89)	0.619
3rd months (T3)	0.73±0.29 (0.63)	0.67±0.31 (0.57)	0.584
[2]p	0.001*	0.001*	
T0-T3 [2]p	p=0.048*	p=0.023*	

[1]Independent Sample T Test [2]Repeated Measures Test **p<0.01, *p<0.05

The decrease in, GCF volume at Test Group the third month compared to baseline GCF volume was statistically significant (p=0.048; p<0.05). The decrease in GCF volume at Control Group, the third month compared to baseline GCF volume was statistically significant (p=0.023; p<0.05) (Chart 4.8).

Chart 4.8: Intergroup Comparisons of GCF Volume.



4.10 INTRA-GROUP AND INTER-GROUP COMPARISONS OF SOD CONCENTRATION

No statistical difference was found between mean SOD concentration at baseline and third month (p>0.05) (Table 4.10).

Table 4.10 Intra-Group and Inter-Group Comparisons of SOD Concentration.

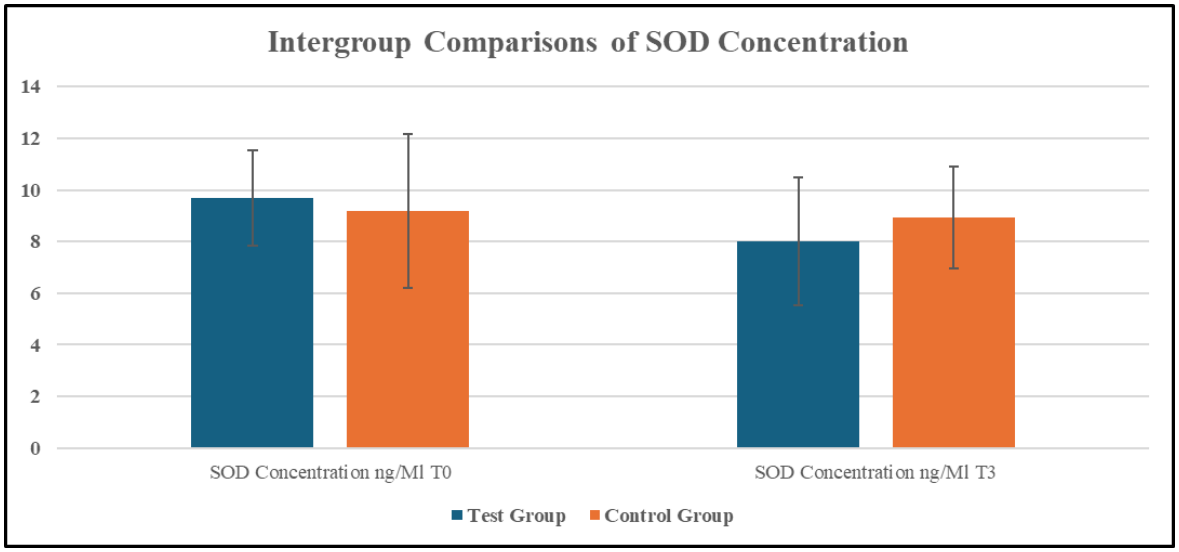
	Test Group	**Control Group**	
SOD Concentration	**Mean±Sd (median)**	**Mean±Sd (median)**	**[1]p**
Baseline (T0)	9.68±1.84 (9.95)	9.19±2.99 (8.97)	0.607
3rd months (T3)	8.01±2.47 (8.56)	8.93±1.97 (8.76)	0.281
[2]p	0.001*	0.001*	
T0-T3 [2]p	p=0.101	p=0.805	

[1]Independent Sample T Test [2]Repeated Measures Test **p<0.01, *p<0.05

The change in SOD concentration in Test Group the third month according to baseline SOD concentration measurement was not statistically significant (p>0.05).

The change in SOD concentration in Control Group the third month according to the baseline SOD concentration measurement was not statistically significant (p>0.05) (Chart 4.9).

Chart 4.9: Intergroup Comparisons of SOD Concentration.



4.11 INTRA-GROUP AND INTER-GROUP COMPARISONS OF TOTAL SOD AMOUNT

No statistical difference is found between the mean total SOD amount at baseline and third month (p>0.05) (Table 4.11).

Table 4.11 Intra-Group and Inter-Group Comparisons of SOD Total Amount.

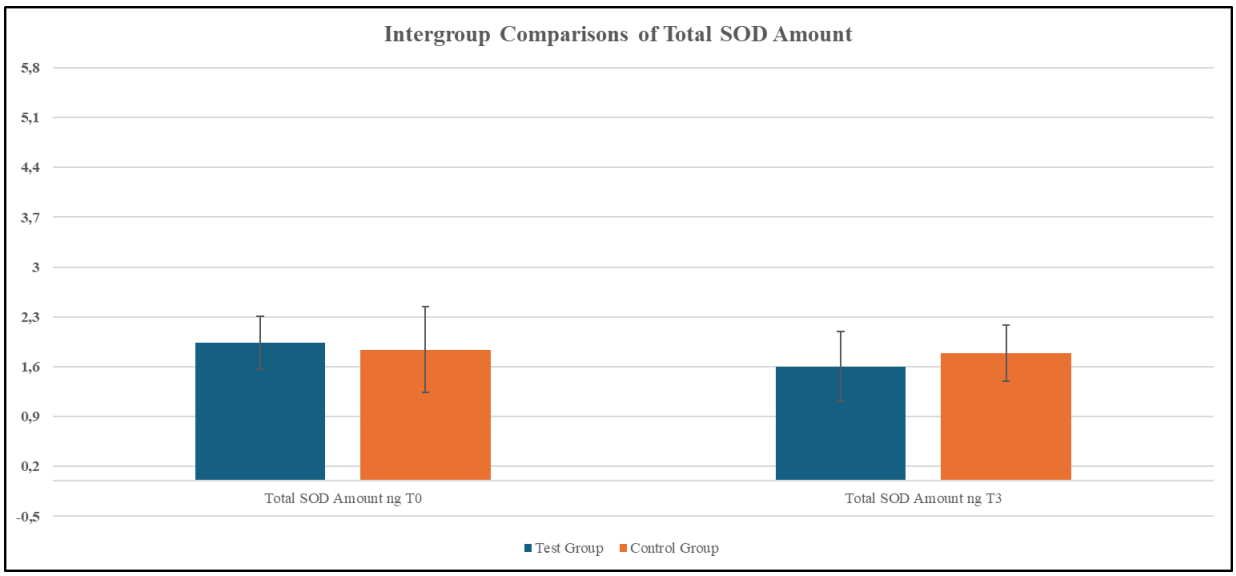
	Test Group	**Control Group**	
SOD Total Amount	**Mean±Sd (median)**	**Mean±Sd (median)**	**[1]p**
Baseline (T0)	1.94±0.37 (1.99)	1.84±0.6 (1.79)	0.607
3rd months (T3)	1.6±0.49 (1.71)	1.79±0.39 (1.75)	0.281
[2]p	0.001*	0.001*	
T0-T3 [2]p	p=0.108	p=0.800	

[1]Independent Sample T Test [2]Repeated Measures Test **p<0.01, *p<0.05

The change seen in the Test Group, third month SOD total amount according to the baseline SOD total amount was not statistically significant (p>0.05).

The change seen in the Control Group, third month SOD total amount according to the baseline SOD total amount was not statistically significant (p>0.05) (Chart 4.10).

Chart 4.10: Intergroup Comparisons of Total SOD Amount.



5. DISCUSSION AND CONCLUSION

Periodontitis is a chronic infectious disease marked by alternating active and inactive phases, during which the supporting tissues of the teeth are compromised, leading to alveolar bone destruction, the formation of periodontal pockets, and tooth loss due to destructive inflammatory processes (Chapple et al., 2007). The principal etiological factor in the pathophysiology of periodontitis is biofilm. The onset and progression of periodontitis are influenced by systemic immune response, genetic predispositions, and environmental variables (Genco, 1996; Kinane et al., 2017). NSPT is essential for establishing and maintaining periodontal health. The historical significance of NSPT has been extensively highlighted, with many procedures created and assessed to improve treatment results. Studies demonstrate that NSPT, in conjunction with oral hygiene instruction, significantly diminishes PPD, reduces biofilm accumulation and BoP, and improves overall periodontal health (Badersten et al., 1984; Van der Weijden et al., 2019). Changes in PPD, CAL, PI, and BoP have been recognized as critical parameters for assessing therapy efficacy in patients with periodontitis (Van Der Weijden & Timmerman, 2002). Therefore, in this study, we aimed to evaluate the efficacy of CoQ10 supplementation to NSPT in terms of PPD, CAL, PI, GI and BoP.

The recruitment of neutrophils to the gingival region and the secretion of proteolytic enzymes and ROS are the two primary elements of the host response to bacterial stimulation (D'Aiuto et al., 2010). OS is caused by an imbalance between the production of free oxygen radicals and their neutralization by the antioxidant defense system, leading to damage to various cellular and extracellular components (Sies, 1991). The harmful consequences of elevated OS, known as oxidative damage, arise from increased levels of ROS and/or diminished antioxidant defenses against ROS. OS is an important risk factor to the onset of more than one hundred illnesses, including periodontitis (Çanakçi et al., 2005). The destruction of tissue in periodontal disease is directly associated with the host's immuno-inflammatory response, and research aimed at understanding the disease's pathophysiology is becoming increasingly important. GCF, salivary, and serum complement are elements of the host defense system. The utilization of GCF samples aims to establish a precise, sensitive, and reproducible technique for detecting periodontal disease and predicting the possibility of subsequent periodontal destruction. GCF samples can be obtained by many

methods. Methods include micropipettes, crevicular washing, and paper points. Among these methods, the most suitable and precise for collecting GCF is the utilization of paper points (Majeed et al., 2016).

Clinical inspections are used to determine periodontal condition, and the combination of clinical and radiographic evaluations is regarded as the benchmark for diagnosing periodontitis. Clinical measurements used in the diagnosis of periodontal diseases reveal insights into the severity of the circumstances, although they are inadequate for assessing disease activity. To determine the activation of periodontal disease, it is essential to evaluate the host tissue response (Champagne et al., 2003; Chatzopoulos et al., 2019; Ertugrul et al., 2013).

The excess abundance of free radicals due to OS or a lack of antioxidants has been associated with periodontal disease, as explained above (Tóthová & Celec, 2017). The antioxidant defense system may decrease and/or diminish the damage inflicted by the harmful effects of free radicals or nonradical reactive species. The antioxidant defense system can mitigate and/or diminish the damage inflicted by harmful free radicals or nonradical reactive species. Antioxidants are presently utilized in several adjunctive therapies for cardiovascular diseases, respiratory disorders, aging, and atherosclerosis. These medical conditions have physiological connections to periodontal diseases, suggesting that possible benefits may also be detected with these therapy (Castro et al., 2019).

The administration of non-enzymatic or enzymatic antioxidants may enhance clinical outcomes in periodontal patients (Gomes Muniz et al., 2015). CoQ10 warrants special attention. CoQ10 serves a crucial physiological function in the electron transport chain, preserving cells from damage caused by free radicals and ROS (Arenas-Jal et al., 2020). Additionally, CoQ10 may serve as an essential cofactor in the mitochondrial electron transport chain, functioning as an antioxidant in lipid membranes and affecting gene expression modulation (Groneberg et al., 2005). Its application also entails the promotion of cellular proliferation and the suppression of apoptosis (Papucci et al., 2003).

CoQ10 facilitates the breakdown of superoxide anion (O2) into hydrogen peroxide and molecular oxygen, hence rendering the potentially toxic superoxide anion less hazardous. A deficit may be linked to periodontal disease. The systemic delivery of CoQ10 in periodontal

disease treatment can decrease GCF flow, probing depths, and enhance clinical attachment (Karim et al., 2012).

In our study, adjunctive CoQ10 (100 mg/day for 3 months) with NSPT led to significantly greater PPD reduction and CAL gain compared to therapy alone. This outcome aligns with ElBarbary et al. (2022), who treated 32 periodontitis patients with NSPT plus systemic CoQ10 (60 mg/day for 3 months) versus NSPT alone. They reported significant additional PPD reduction and attachment gain in the CoQ10 group, affirming that CoQ10 may provide an added benefit to periodontal healing (Barbari & Hussein, 2022). Similarly, Darweesh et al. (2015) found that CP patients receiving NSPT with CoQ10 (60 mg/day for 3 months) showed greater improvements in PPD reduction and CAL gain than those with NSPT alone. Notably, Darweesh's study also tested CoQ10 combined with doxycycline and observed the greatest PPD reduction/CAL gain improvements with the combination, but CoQ10 alone still produced significant gains over control (Darweesh, 2015). In contrast, one study by Manthena et al. (15 patients per group, 120 mg/day CoQ10, for 3 months) reported no significant inter-group difference in PPD reduction despite marked intra-group improvements (Manthena et al., 2015) . This discrepancy may stem from their sample size or study design, as both groups in that study had substantial NSPT-induced PPD reductions, potentially masking CoQ10's effect. Importantly, our findings are supported by a recent systematic review and meta-analysis (Fernandez et al., 2025), which concluded that daily oral CoQ10 (~120 mg for ~12 weeks) yields an additional mean PPD reduction of ~0.4 mm and a CAL gain of ~0.5 mm compared to NSPT alone (Fernandez et al., 2025). This modest but significant improvement in soft-tissue outcomes with CoQ10 is consistent with the ~0.5 mm greater CAL gain we observed in our test group. On the other hand, some studies have reported minimal clinical benefit. For example, Chug and Shukla (2020) observed no additional PPD improvement with CoQ10 supplementation, concluding that CoQ10 had no appreciable role in further reducing deep pockets (Chug & Shukla, 2020). Such divergent results underscore that CoQ10's impact on pocket depth may depend on patient factors and study protocols. In systemic conditions that exacerbate periodontal breakdown, CoQ10 seems more impactful: Youssef et al. (2019) studied periodontitis in type II diabetics and found the CoQ10 (60 mg/day) group had significantly greater PPD reduction at 3 and 6 months, whereas the control group's initial improvements plateaued or even regressed by 6 months (Youssef et al., 2019). This sustained PPD reduction with CoQ10 in diabetics

suggests that the antioxidant adjunct can counteract the chronic inflammatory stress in such high-risk patients, helping maintain pocket reduction over time. Overall, the literature concurs with our thesis that systemic CoQ10 adjunctive therapy leads to greater pocket depth reduction and attachment level gains, though the magnitude can vary. Differences in dosage (typically 60–120 mg/day), duration, and population (healthy vs. diabetic) may explain some conflicting outcomes, but the trend favors CoQ10 as a beneficial adjunct for improving PPD and CAL.

Our study demonstrated a pronounced reduction in gingival inflammation and bleeding (GI and BoP) in the CoQ10 group compared to control group by 3 months. At the end of our study, the mean GI and BoP percentages were significantly lower with CoQ10, indicating superior resolution of gingival inflammation. This finding is strongly emphasized by multiple studies. Manthena et al. (15 patients per group, 120 mg/day CoQ10, for 3 months) specifically found that while PI and PPD outcomes were similar between groups, GI scores were significantly better in the CoQ10 adjunct group at 1 and 3 months. They concluded that oral CoQ10 yielded a notable reduction in gingival inflammation beyond NSPT alone (Manthena et al., 2015). ElBarbary et al. also indirectly support this; although they only measured PPD/CAL and biochemical markers, their CoQ10 group had greater improvement in those parameters alongside reduced crevicular MMP-9 levels (Barbari & Hussein, 2022). Given MMP-9 associated with gingival inflammation, its suppression with CoQ10 corresponds to an anti-inflammatory effect that likely manifested as lower GI and BoP in the test group. Darweesh et al. (2015) explicitly measured bleeding index and reported significantly lower bleeding scores in the CoQ10-treated group than control group. In their study, mean bleeding index at 3 months was 0.10 with CoQ10 versus 0.26 in controls, a significant difference (Darweesh, 2015) . This aligns closely with our observations that CoQ10 adjunct markedly reduces bleeding tendency, reflecting improved gingival health. Moreover, Youssef et al. found persistent gingival inflammation in diabetic periodontitis was better controlled with CoQ10: by 6 months the test group had significantly lower scores of GI and BoP than the control group, which had worsened after initial improvement. They noted that the CoQ10-supplemented patients sustained continuous reduction in inflammation up to 6 months, whereas controls experienced a rebound in gingival indices after 3 months. This divergence was attributed to CoQ10's antioxidant action helping to stabilize periodontal inflammation in a high OS (Youssef et al., 2019) . On the other hand, a few studies did not

observe significant adjunctive effects on gingival indices. Chug & Shukla reported no meaningful difference in clinical bleeding outcomes with CoQ10 usage, corroborating findings from a similar study by Pranam et al. (2020) that CoQ10 was not superior to NSPT in improving GI or bleeding despite boosting antioxidant levels (Chug & Shukla, 2020; Pranam et al., 2020). Such results may be related to short follow-up or split-mouth designs that are less sensitive to mild inflammation differences. Nevertheless, the superiority of evidence, including our study, indicates that CoQ10 adjunctively yields greater reductions in gingival inflammation and BoP.

All patients in our study received thorough oral hygiene instruction and FMD, resulting in significant PI reductions in both groups. However, by 3 months the test group showed lower mean PI score than control group, and this difference was statistically significant. This suggests CoQ10 might have indirectly supported plaque control, possibly by improving patient comfort or gingival condition (less bleeding/pain can facilitate better brushing). The literature on PI outcomes with CoQ10 is mixed. Manthena et al. observed no significant difference in PI between CoQ10 and placebo groups at 1 or 3 months – both groups' PI dropped from ~2.5 at baseline to ~0.5 at 3 months due to NSPT and improved oral hygiene, with virtually identical results (Manthena et al., 2015). This indicates that NSPT and oral hygiene education were the dominant factors in plaque reduction, and any adjunct antioxidant effect on plaque accumulation was minimal. Darweesh et al. reported a little bit lower final PI in their CoQ10 group than control group. After 3 months, the mean PI was 0.22 in the CoQ10-only group compared to 0.46 in the NSPT-only (control) group, suggesting a significant adjunctive improvement. Their combination therapy group (CoQ10 + doxycycline) had an even lower PI (~0.27) than either alone, hinting that host modulation might positively influence plaque scores by altering the gingival condition (Darweesh, 2015). Overall, most studies, including ours, found substantial plaque reduction in both test and control groups due to the efficacy of NSPT and patient compliance with oral hygiene instructions. CoQ10 by itself is not antiplaque, so it is expected that PI improvements will come primarily due to increased oral hygiene of patients. The slight improvements in plaque scores observed in some CoQ10 groups could be secondary effects of reduced gingival inflammation – healthier, less sensitive gingiva enable patients to brush more effectively, resulting in marginally lower plaque levels. Indeed, no study reported CoQ10 worsening plaque indices; at worst it has no effect on plaque, and at best it may aid patients in

maintaining plaque control by improving periodontal well-being. Therefore, our finding of a marginally lower PI with CoQ10 is in line with the notion that while CoQ10 does not replace mechanical cleaning, it can support the periodontal environment conducive to better oral hygiene maintenance.

Review of literature reveals that dose and duration of CoQ10 application also varied (Barbari & Hussein, 2022; Chug & Shukla, 2020; Darweesh, 2015; Manthena et al., 2015; Pranam et al., 2020; Youssef et al., 2019). Most studies administered 60 mg/day (often as 30 mg twice daily) for 3 months, however in our study the dose was defined as 100 mg/day for 3 months (Barbari & Hussein, 2022; Darweesh, 2015; Youssef et al., 2019). Manthena et al. used a higher dose (120 mg/day) yet saw limited group differences in some parameters. (Manthena et al., 2015). These findings suggest that prolonged administration (at least 3 months) may be necessary for CoQ10 to manifest clinically detectable benefits, and that doses in the 60–120 mg range are effective. Notably, the recent meta-analysis by Fernandez et al. restricted analysis to ~12-week outcomes and still found a significant advantage to daily ~120 mg CoQ10, supporting our 3-month regimen (Fernandez et al., 2025). Moreover, the application method is also important: our study and the cited studies all used systemic CoQ10 supplementation. By contrast, some research has investigated local CoQ10 delivery into periodontal pockets. For instance, Pranam et al. applied CoQ10 gel subgingivally in a split-mouth design and observed improved SOD levels but no superior clinical improvement compared to NSPT alone (Chug & Shukla, 2020; Pranam et al., 2020). In line with that, a systematic review concluded that locally delivered CoQ10 (topical or intra-pocket) had no significant effect on PPD/CAL, whereas systemic CoQ10 did yield measurable clinical benefits (Fernandez et al., 2025). This suggests that systemic CoQ10 is likely more effective, perhaps because it improves the overall redox status and reaches the periodontal tissues via the bloodstream continuously, unlike a one-time local application (Fernandez et al., 2025). Our systemic administration approach is therefore validated by literature as the more reliable route to achieve adjunctive benefits.

It is also instructive to compare biomarker outcomes across these studies, as CoQ10's mechanism of action is largely attributed to its antioxidant and anti-inflammatory properties. Our study measured SOD levels in GCF and found decrease in SOD after treatment, alongside a significant decrease in GCF volume. GCF volume is known to rise in the

presence of inflammation (as an inflammatory exudate), so the reduction in GCF flow in our CoQ10 group is a positive indicator correlating with reduced periodontal inflammation. This finding is consistent with other studies that measured inflammatory mediators in GCF. ElBarbary et al. and Youssef et al. both focused on matrix metalloproteinases: ElBarbary's trial noted that GCF MMP-9 levels dropped significantly from baseline in both SRP-only and SRP + CoQ10 groups, but the CoQ10 group achieved a greater reduction by 3 months. Likewise, Youssef et al. analyzed GCF MMP-8 in diabetic patients and found a continual decrease in MMP-8 levels up to 3 months in the CoQ10-supplemented group, whereas the control group's MMP-8 levels showed a plateau or slight rebound after initial improvement. These MMP findings suggest that adjunctive CoQ10 can suppress tissue-destructive enzymes in the periodontal environment, likely by mitigating OS and inflammation (ElBarbary et al., 2022; Youssef et al., 2019). In another biochemical study, Mamdouh et al. evaluated cytokine profiles with local CoQ10 application (0.2 ml of 1% CoQ10 gel delivered into pockets after SRP). They observed that after therapy, the CoQ10 group had significantly lower GCF IL-1β and higher IL-10 compared to controls, indicating a shift toward a less inflammatory, more protective cytokine profile. Although Mamdouh et al.'s investigation was on local application of CoQ10, it reinforces the notion that CoQ10 adjuncts (whether systemic or local) can favorably modulate the biochemical environment of periodontal sites by downregulating pro-inflammatory mediators and upregulating anti-inflammatory mediators (Mamdouh et al., 2024). The decreased GCF volume in our study is harmonious with such anti-inflammatory effects.

Against this backdrop of anti-inflammatory benefits, our finding of decreased SOD levels post-treatment stands out. Typically, one might expect CoQ10's antioxidant action to increase antioxidant enzyme activity or levels. In fact, a study has reported that CoQ10 adjuncts lead to elevated SOD in GCF or serum as the body's oxidative balance improves. For example, a recent trial by Pranam et al. found that adjunctive CoQ10 (used in a gel form after SRP) led to a significant rise in crevicular SOD levels at 3 months relative to SRP alone (Pranam et al., 2020). That and similar reports imply CoQ10 can support the antioxidant defense system. In contrast, our patients showed a drop in GCF SOD concentration after 3 months of CoQ10. One hypothesis for this paradoxical result is that, at baseline, SOD was elevated in response to the high OS of active periodontitis – essentially a compensatory upregulation. As treatment reduced the bacterial load and inflammation (and CoQ10 directly

scavenged free radicals), the stimulus for SOD production may have diminished, leading to a normalization or reduction of SOD levels. In other words, SOD in GCF could be consumed or downregulated once the redox imbalance is corrected. Another possibility is a negative feedback mechanism: exogenous CoQ10 might fulfill some of the antioxidant needs, so the body produces less SOD during the healing phase. It is also important to consider the compartment of measurement – GCF SOD might behave differently than systemic SOD. Regardless of the exact cause, this finding underscores that antioxidant biomarkers can respond in complex ways to therapy. Our results diverge from most studies on this point, and thus prompt further investigation. It would be worthwhile in future studies to measure additional OS markers (e.g., malondialdehyde, total antioxidant capacity) alongside SOD to get a more complete picture of how CoQ10 influences the periodontal oxidative environment. Our observation does not contradict the clinical improvements seen – on the contrary, clinical outcomes were positive – but it suggests that SOD levels may not need to increase for periodontal healing to occur, so long as OS is overall reduced. This nuance could be mentioned as a novel insight of our work, especially since many previous studies simply assumed increased antioxidant enzyme levels equate to better outcomes.

Finally, it is useful to place our findings in context of the latest evidence syntheses. A recent systematic review by Fernandez et al. consolidated data from 10 RCTs of CoQ10 as an adjunct in periodontitis (6 systemic supplementation studies and 4 local delivery studies). The review concluded that locally delivered CoQ10 (gels or solutions placed in pockets) did not yield statistically significant improvements in PPD or CAL overall, whereas systemic CoQ10 supplementation (at ~120 mg/day for ~12 weeks in most trials) was associated with an additional mean PPD reduction of 0.4 mm and CAL gain of 0.5 mm compared to control. These effect sizes are modest but clinically meaningful when considering population averages (Fernandez et al., 2025). Our study's clinical improvements fall in line with this magnitude of benefit – we observed roughly half-millimeter greater PPD/CAL changes in the CoQ10 group versus control, reinforcing the review's findings. It should be noted that Fernandez et al. rated the evidence as *"very low certainty,"* citing the small sample sizes and heterogeneity across studies. Indeed, the CoQ10 studies to date vary in dosage (30 mg up to 150 mg daily), formulations (capsules, gels, topical rinses), and study populations (e.g. smokers, diabetics, various severity of periodontitis). Our study contributes to this body of evidence by adding a well-controlled trial with a 100 mg/day dose, a middle-ground regimen

that had not been as extensively studied as 60 mg or 120 mg in prior trials. The consistency between our results and the meta-analysis increases confidence that CoQ10's adjunctive effect on periodontal clinical parameters is real, even if not dramatic. However, the low certainty of evidence also implies that larger, multi-center trials are needed. Many authors have pointed out the need for larger sample sizes and longer follow-ups to validate the long-term benefits of CoQ10 and to determine optimal dosing strategies. Future research should also stratify outcomes by patient subsets – for instance, those with systemic conditions like diabetes or smokers with high OS might derive differing levels of benefit from CoQ10.

In summary, our discussion of results considering these studies indicates a broad agreement that systemic CoQ10 supplementation can positively influence periodontal therapy outcomes. CoQ10 at doses ranging from 60 mg to 120 mg daily for about 3 months has shown improvements in inflammation (reduced GI, BoP) and, in most studies including ours, modest yet significant gains in CAL and deeper PPD reduction beyond what mechanical therapy alone achieves. Key methodological differences (like use of placebos, sample health status, adjuncts combination) likely account for some variability in findings. Importantly, our study is one of the few to report a decrease in SOD after therapy, contrary to the increased SOD reported elsewhere – a finding that provides new insight into the complex OS dynamics during periodontal healing. Altogether, the evidence suggests that CoQ10's benefits are consistent with its role as a mitigator of oxidative tissue damage and inflammation in periodontitis.

This study strengthens the growing consensus that CoQ10 can be a valuable adjunct in periodontal therapy. Adjunctive systemic CoQ10 (100 mg daily for 3 months) combined with NSPT produced better clinical outcomes than NSPT alone, including greater PPD reduction, improved attachment levels, and reduced gingival inflammation. These improvements were accompanied by biochemical signs of reduced periodontal inflammation (lower GCF volume and inflammatory mediator levels), highlighting CoQ10's potential to modulate the host response. Notably, we observed a unique reduction in SOD levels post-treatment, suggesting that CoQ10's antioxidant effect may alleviate OS without necessitating an upregulation of endogenous SOD – an interesting finding that warrants further research. Clinically, the adjunctive use of CoQ10 appears safe and may enhance periodontal healing, which could be especially beneficial for patients with heightened OS

(such as those with diabetes or smoking history). The practical implications are that CoQ10, as an over-the-counter nutraceutical, could be integrated into periodontal maintenance regimens to possibly improve outcomes and stabilize disease. However, given the relatively modest improvements (on the order of a few tenths of a millimeter in PD/CAL) and the variability across studies, CoQ10 should be viewed as a supportive adjunct rather than a standalone therapy. The potential of CoQ10 in periodontal care is promising, but larger long-term studies and meta-analyses are needed to confirm optimal dosage, treatment duration, and specific patient populations that may benefit the most. In conclusion, our findings underscore the therapeutic promise of CoQ10 in periodontitis management and add impetus to the idea of host modulation therapy using antioxidants. Integrating CoQ10 supplementation into periodontal treatment could become a cost-effective strategy to augment clinical outcomes, provided future research continues to affirm its benefits and clarifies its role in the complex pathogenesis of periodontal disease.

REFERENCES

Abbafati, C., Machado, D. B., Cislaghi, B., Salman, O. M., Karanikolos, M., McKee, M., Abbas, K. M., Brady, O. J., Larson, H. J., Trias-Llimós, S., Cummins, S., Langan, S. M., Sartorius, B., Hafiz, A., Jenabi, E., Mohammad Gholi Mezerji, N., Borzouei, S., Azarian, G., Khazaei, S., … Zhu, C. (2020). Five insights from the Global Burden of Disease Study 2019. In *The Lancet* (Vol. 396, pp. 1135–1159). Elsevier B.V. https://doi.org/10.1016/S0140-6736(20)31404-5

Åberg, F., Appelkvist, E. L., Dallner, G., & Ernster, L. (1992). Distribution and redox state of ubiquinones in rat and human tissues. *Archives of Biochemistry and Biophysics*, *295*(2), 230–234. https://doi.org/10.1016/0003-9861(92)90511-T

Abusleme, L., Hoare, A., Hong, B. Y., & Diaz, P. I. (2021). Microbial signatures of health, gingivitis, and periodontitis. In *Periodontology 2000* (Vol. 86, pp. 57–78). Blackwell Munksgaard. https://doi.org/10.1111/prd.12362

Acosta, M. J., Vazquez Fonseca, L., Desbats, M. A., Cerqua, C., Zordan, R., Trevisson, E., & Salviati, L. (2016). Coenzyme Q biosynthesis in health and disease. *Biochimica et Biophysica Acta*, *1857*(8), 1079–1085. https://doi.org/10.1016/J.BBABIO.2016.03.036

Adriaens, P. A., & Adriaens, L. M. (2004). Effects of nonsurgical periodontal therapy on hard and soft tissues. *Periodontology 2000*, *36*, 121–145. https://doi.org/10.1111/J.1600-0757.2004.03676.X

Adriaens, P. A., De Boever, J. A., & Loesche, W. J. (1988). Bacterial invasion in root cementum and radicular dentin of periodontally diseased teeth in humans. A reservoir of periodontopathic bacteria. *Journal of Periodontology*, *59*(4), 222–230. https://doi.org/10.1902/JOP.1988.59.4.222

Agnihotri, R., Pandurang, P., Kamath, S. U., Goyal, R., Ballal, S., Shanbhogue, A. Y., Kamath, U., Bhat, G. S., & Bhat, K. M. (2009). Association of cigarette smoking with superoxide dismutase enzyme levels in subjects with chronic periodontitis. *Journal of Periodontology*, *80*(4), 657–662. https://doi.org/10.1902/JOP.2009.080545

Aimetti, M. (2014). Nonsurgical periodontal treatment. *The International Journal of Esthetic Dentistry*, *9*, 251–267.

Akalin, F. A., Toklu, E., & Renda, N. (2005). Analysis of superoxide dismutase activity levels in gingiva and gingival crevicular fluid in patients with chronic periodontitis and periodontally healthy controls. *Journal of Clinical Periodontology*, *32*, 238–243. https://doi.org/10.1111/j.1600-051X.2005.00669.x

Albeshri, S., & Greenstein, G. (2022). Efficacy of nonsurgical periodontal therapy for treatment of periodontitis: practical application of current knowledge. *General Dentistry*.

Arenas-Jal, M., Suñé-Negre, J. M., & García-Montoya, E. (2020). Coenzyme Q10 supplementation: Efficacy, safety, and formulation challenges. In *Comprehensive Reviews in Food Science and Food Safety* (Vol. 19, pp. 574–594). Blackwell Publishing Inc. https://doi.org/10.1111/1541-4337.12539

Armitage, G. C. (1999). Development of a classification system for periodontal diseases and conditions. *Annals of Periodontology*, *4*(1), 1–6. https://doi.org/10.1902/ANNALS.1999.4.1.1

Badersten, A., Nilveus, R., & Egelberg, J. (1984). Effect of nonsurgical periodontal therapy: II. Severely advanced periodontitis. *Journal of Clinical Periodontology*, *11*, 63–76. https://doi.org/10.1111/j.1600-051X.1984.tb01309.x

Baltacıoğlu, E., Yuva, P., Aydın, G., Alver, A., Kahraman, C., Karabulut, E., & Akalın, F. A. (2014). Lipid peroxidation levels and total oxidant/antioxidant status in serum and saliva from patients with chronic and aggressive periodontitis. Oxidative stress index: a new biomarker for periodontal disease? *Journal of Periodontology*, *85*(10), 1432–1441. https://doi.org/10.1902/JOP.2014.130654

Barakat, A. K., & Attia, A. (2019). Clinical Evaluation of Co-enzyme Q10 in Management of Chronic Periodontitis Patients: Mouth Split Study. *International Journal of Health Sciences & Research*, *9*(1), 69.

Barbari, A., & Hussein, H. (2022). The Effect of Using Coenzyme Q10 With Non-Surgical Periodontal Treatment on MMP9 Gingival Crevicular Fluid Level in Patients With Periodontitis: Randomized Controlled Trial. *Advanced Dental Journal*, *0*, 0–0. https://doi.org/10.21608/adjc.2022.98415.1113

Battino, M., Bullon, P., Wilson, M., & Newman, H. (1999). Oxidative injury and inflammatory periodontal diseases: the challenge of anti-oxidants to free radicals and reactive oxygen species. *Critical Reviews in Oral Biology and Medicine : An Official Publication of the American Association of Oral Biologists*, *10*(4), 458–476. https://doi.org/10.1177/10454411990100040301

Bhagavan, H. N., & Chopra, R. K. (2006). Coenzyme Q10: Absorption, tissue uptake, metabolism and pharmacokinetics. *Free Radical Research*, *40*, 445–453. https://doi.org/10.1080/10715760600617843

Bosshardt, D. D., & Lang, N. P. (2005). The junctional epithelium: from health to disease. *Journal of Dental Research*, *84*(1), 9–20. https://doi.org/10.1177/154405910508400102

Botelho, J., Machado, V., Leira, Y., Proença, L., Chambrone, L., & Mendes, J. J. (2022). Economic burden of periodontitis in the United States and Europe: An updated estimation. *Journal of Periodontology*, *93*, 373–379. https://doi.org/10.1002/JPER.21-0111

Brochut, P. F., Marin, I., Baehni, P., & Mombelli, A. (2005). Predictive value of clinical and microbiological parameters for the treatment outcome of scaling and root planing. *Journal of Clinical Periodontology*, *32*(7), 695–701. https://doi.org/10.1111/J.1600-051X.2005.00730.X

Buduneli, N. (2019). Biomarkers in periodontal health and disease: Rationale, benefits, and future directions. In *Biomarkers in Periodontal Health and Disease: Rationale, Benefits, and Future Directions*. Springer International Publishing. https://doi.org/10.1007/978-3-030-37317-7

Buduneli, N., Bıyıkoğlu, B., & Kinane, D. F. (2024). Utility of gingival crevicular fluid components for periodontal diagnosis. In *Periodontology 2000*. John Wiley and Sons Inc. https://doi.org/10.1111/prd.12595

Cadenas, E. (1989). Biochemistry of oxygen toxicity. In *Annual Review of Biochemistry* (Vol. 58, pp. 79–110). https://doi.org/10.1146/annurev.bi.58.070189.000455

Çanakçi, C. F., Çiçek, Y., & Çanakçi, V. (2005). Reactive oxygen species and human inflammatory periodontal diseases. In *Biochemistry (Moscow)* (Vol. 70, pp. 619–628). Maik Nauka-Interperiodica Publishing. https://doi.org/10.1007/s10541-005-0161-9

Castro, M. M. L., Duarte, N. N., Nascimento, P. C., Magno, M. B., Fagundes, N. C. F., Flores-Mir, C., Monteiro, M. C., Rösing, C. K., Maia, L. C., & Lima, R. R. (2019). Antioxidants as Adjuvants in Periodontitis Treatment: A Systematic Review and Meta-Analysis. In *Oxidative Medicine and Cellular Longevity* (Vol. 2019). Hindawi Limited. https://doi.org/10.1155/2019/9187978

Chakraborty, S. (2023). Antioxidants and Ageing. In *Evidence-based Functional Foods for Prevention of Age-related Diseases* (pp. 61–80). Springer Nature Singapore. https://doi.org/10.1007/978-981-99-0534-8_4

Champagne, C. M. E., Buchanan, W., Reddy, M. S., Preisser, J. S., Beck, J. D., & Offenbacher, S. (2003). Potential for gingival crevice fluid measures as predictors of risk for periodontal diseases. In *Periodontology 2000* (Vol. 31, pp. 167–180). https://doi.org/10.1034/j.1600-0757.2003.03110.x

Chapple, I. L. C. (1997). Reactive oxygen species and antioxidants in inflammatory diseases. *Journal of Clinical Periodontology*, *24*(5), 287–296. https://doi.org/10.1111/J.1600-051X.1997.TB00760.X

Chapple, I. L. C., Brock, G. R., Milward, M. R., Ling, N., & Matthews, J. B. (2007). Compromised GCF total antioxidant capacity in periodontitis: Cause or effect? *Journal of Clinical Periodontology*, *34*, 103–110. https://doi.org/10.1111/j.1600-051X.2006.01029.x

Chapple, I. L. C., & Matthews, J. B. (2007). The role of reactive oxygen and antioxidant species in periodontal tissue destruction. *Periodontology 2000*, *43*(1), 160–232. https://doi.org/10.1111/J.1600-0757.2006.00178.X

Chatterjee, A., Kandwal, A., Singh, N., & Singh, A. (2012). Evaluation of Co-Q10 anti-gingivitis effect on plaque induced gingivitis: A randomized controlled clinical trial. *Journal of Indian Society of Periodontology*, *16*(4), 539. https://doi.org/10.4103/0972-124X.106902

Chatzopoulos, G. S., Mansky, K. C., Lunos, S., Costalonga, M., & Wolff, L. F. (2019). Sclerostin and WNT-5a gingival protein levels in chronic periodontitis and health. *Journal of Periodontal Research*, *54*, 555–565. https://doi.org/10.1111/jre.12659

Chen, E., Wang, T., Tu, Y., Sun, Z. Y., Ding, Y., Gu, Z., & Xiao, S. (2023). ROS-scavenging biomaterials for periodontitis. *Journal of Materials Chemistry B*, *11*(3), 482–499. https://doi.org/10.1039/D2TB02319A

Chen, M., Cai, W., Zhao, S., Shi, L., Chen, Y., Li, X., Sun, X., Mao, Y., He, B., Hou, Y., Zhou, Y., Zhou, Q., Ma, J., & Huang, S. (2019). Oxidative stress-related biomarkers in saliva and gingival crevicular fluid associated with chronic periodontitis: A systematic review and meta-analysis. In *Journal of Clinical Periodontology* (Vol. 46, pp. 608–622). Blackwell Munksgaard. https://doi.org/10.1111/jcpe.13112

Christgau, M., Männer, T., Bauer, S., Hiller, K. A., & Schmalz, G. (2006). Periodontal healing after non-surgical therapy with a modified sonic scaler: a controlled clinical trial. *Journal of Clinical Periodontology*, *33*(10), 749–758. https://doi.org/10.1111/J.1600-051X.2006.00981.X

Chug, A., & Shukla, S. (2020). Placement of Sticky Bone™ in Patients with Generalized Periodontitis Previously Treated with Coenzyme Q10. *Journal of Contemporary Dental Practice*, *21*(2), 156–160. https://doi.org/10.5005/JP-JOURNALS-10024-2757

Crane, F. L. (2001). Biochemical functions of coenzyme Q10. *Journal of the American College of Nutrition*, *20*(6), 591–598. https://doi.org/10.1080/07315724.2001.10719063

Crane, F. L., Hatefi, Y., Lester, R. L., & Widmer, C. (1957). Isolation of a quinone from beef heart mitochondria. *Biochimica et Biophysica Acta*, *25*(1), 220–221. https://doi.org/10.1016/0006-3002(57)90457-2

Cuzzocrea, S., Riley, D. P., Caputi, A. P., & Salvemini, D. (2001). Antioxidant therapy: A new pharmacological approach in shock, inflammation, and ischemia/reperfusion injury. In *Pharmacological Reviews* (Vol. 53, pp. 135–159).

Dahlén, G., Lindhe, J., Sato, K., Hanamura, H., & Okamoto, H. (1992). The effect of supragingival plaque control on the subgingival microbiota in subjects with periodontal disease. *Journal of Clinical Periodontology*, *19*(10), 802–809. https://doi.org/10.1111/J.1600-051X.1992.TB02174.X

D'Aiuto, F., Nibali, L., Parkar, M., Patel, K., Suvan, J., & Donos, N. (2010). Oxidative stress, systemic inflammation, and severe periodontitis. *Journal of Dental Research*, *89*, 1241–1246. https://doi.org/10.1177/0022034510375830

Darveau, R. P. (2010). Periodontitis: A polymicrobial disruption of host homeostasis. In *Nature Reviews Microbiology* (Vol. 8, pp. 481–490). https://doi.org/10.1038/nrmicro2337

Darveau, R. P., Tanner, A., & Page, R. C. (1997). The microbial challenge in periodontitis. *Periodontology 2000*, *14*, 12–32. https://doi.org/10.1111/j.1600-0757.1997.tb00190.x

Darweesh, M. (2015). Doxycycline and Coenzyme Q10 Treatment Modalities for Chronic Periodontitis: A Preliminary Study. *International Journal of Oral and Dental Health*, *1*. https://doi.org/10.23937/2469-5734/1510014

Deinzer, R., Mossanen, B. S., & Herforth, A. (2000). Methodological considerations in the assessment of gingival crevicular fluid volume. *Journal of Clinical Periodontology*, *27*, 481–488. https://doi.org/10.1034/j.1600-051x.2000.027007481.x

Delima, A. J., & Van Dyke, T. E. (2003). Origin and function of the cellular components in gingival crevice fluid. In *Periodontology 2000* (Vol. 31, pp. 55–76). https://doi.org/10.1034/j.1600-0757.2003.03105.x

Dommisch, H., Kuzmanova, D., Jönsson, D., Grant, M., & Chapple, I. (2018). Effect of micronutrient malnutrition on periodontal disease and periodontal therapy. *Periodontology 2000*, *78*(1), 129–153. https://doi.org/10.1111/PRD.12233

Dyke, T. E. Van. (2008). The Management of Inflammation in Periodontal Disease. *Journal of Periodontology*, *79*(8S), 1601–1608. https://doi.org/10.1902/JOP.2008.080173

ElBarbary, A., Nadim, M. K., & Hussein, H. (2022). The Effect of Using Coenzyme Q10 With Non-Surgical Periodontal Treatment on MMP9 Gingival Crevicular Fluid Level in Patients With Periodontitis: Randomized Controlled Trial. *Advanced Dental Journal*, *4*(2), 85–95. https://doi.org/10.21608/ADJC.2022.98415.1113

Ernster, L., & Dallner, G. (1995). Biochemical, physiological and medical aspects of ubiquinone function. *Biochimica et Biophysica Acta*, *1271*(1), 195–204. https://doi.org/10.1016/0925-4439(95)00028-3

Ertugrul, A. S., Sahin, H., Dikilitas, A., Alpaslan, N., & Bozoglan, A. (2013). Comparison of CCL28, interleukin-8, interleukin-1β and tumor necrosis factor-alpha in subjects with gingivitis, chronic periodontitis and generalized aggressive periodontitis. *Journal of Periodontal Research*, *48*, 44–51. https://doi.org/10.1111/j.1600-0765.2012.01500.x

Fang, H., Han, M., Li, Q. L., Cao, C. Y., Xia, R., & Zhang, Z. H. (2016). Comparison of full-mouth disinfection and quadrant-wise scaling in the treatment of adult chronic periodontitis: a systematic review and meta-analysis. *Journal of Periodontal Research*, *51*, 417–430. https://doi.org/10.1111/jre.12326

Fei, Z., Gao, W., Xu, X., Sheng, H., Qu, S., & Cui, R. (2021). Serum superoxide dismutase activity: a sensitive, convenient, and economical indicator associated with the prevalence of chronic type 2 diabetic complications, especially in men. *Free Radical Research*, *55*, 275–281. https://doi.org/10.1080/10715762.2021.1937146

Fernandez, M. dos S., Martins, T. M., Meza-Mauricio, J., Ribeiro, M. C., Silva, F. H., Casarin, M., & Muniz, F. W. M. G. (2025). Clinical efficacy of adjunctive use of coenzyme Q10 in non-surgical periodontal treatment: A systematic review. In *European Journal of Oral Sciences*. John Wiley and Sons Inc. https://doi.org/10.1111/eos.70002

Figuero, E., Soory, M., Cerero, R., & Bascones, A. (2006). Oxidant/antioxidant interactions of nicotine, Coenzyme Q10, Pycnogenol and phytoestrogens in oral periosteal fibroblasts and MG63 osteoblasts. *Steroids*, *71*(13–14), 1062–1072. https://doi.org/10.1016/J.STEROIDS.2006.09.003

Frencken, J. E., Sharma, P., Stenhouse, L., Green, D., Laverty, D., & Dietrich, T. (2017). Global epidemiology of dental caries and severe periodontitis – a comprehensive review. *Journal of Clinical Periodontology*, *44*, S94–S105. https://doi.org/10.1111/jcpe.12677

G. Caton, J., Armitage, G., Berglundh, T., Chapple, I. L. C., Jepsen, S., S. Kornman, K., L. Mealey, B., Papapanou, P. N., Sanz, M., & S. Tonetti, M. (2018). A new classification scheme for periodontal and peri-implant diseases and conditions - Introduction and key changes from the 1999 classification. *Journal of Clinical Periodontology*, *45 Suppl 20*, S1–S8. https://doi.org/10.1111/JCPE.12935

Gaby, A. (1996). *The Role of Coenzyme Q 10 in Clinical Medicine: Part I*. Https://Www.Semanticscholar.Org/Paper/The-Role-of-Coenzyme-Q-10-in-Clinical-Medicine%3A-I-Gaby/87ce1b8131201eb04429be032a6b1720b2460633.

Garrido-Maraver, J., Cordero, M. D., Oropesa-Avila, M., Fernandez Vega, A., De La Mata, M., Delgado Pavon, A., Alcocer-Gomez, E., Perez Calero, C., Villanueva Paz, M., Alanis, M., De Lavera, I., Cotan, D., & Sanchez-Alcazar, J. A. (2014). Clinical applications of coenzyme Q10. *Frontiers in Bioscience (Landmark Edition)*, *19*(4), 619–633. https://doi.org/10.2741/4231

Gasmi Benahmed, A., Gasmi, A., Noor, S., Semenova, Y., Emadali, A., Dadar, M., Shanaida, Y., Avdeev, O., & Bjørklund, G. (2024). Hallmarks of Periodontitis. *Current Medicinal Chemistry*, *31*. https://doi.org/10.2174/0109298673302701240509103537

Genco, R. J. (1996). Current View of Risk Factors for Periodontal Diseases*. *Journal of Periodontology*, *67*, 1041–1049. https://doi.org/10.1902/jop.1996.67.10.1041

Genestra, M. (2007). Oxyl radicals, redox-sensitive signalling cascades and antioxidants. *Cellular Signalling*, *19*(9), 1807–1819. https://doi.org/10.1016/J.CELLSIG.2007.04.009

Ghasemi, S., Torab, Z., Shirmohammadi, A., Babaloo, A., Johari, R., Farhadi, F., Mobasseri, M., & Mohammadi, H. (2022). Evaluation of the effect of coenzyme Q10 supplementation along with scaling and root planing (SRP) on periodontal and gingival indices in controlled diabetic patients. *Journal of Advanced Periodontology & Implant Dentistry*, *14*(1), 32–37. https://doi.org/10.34172/JAPID.2022.003

Giuliana, G., Ammatuna, P., Pizzo, G., Capone, F., & D'Angelo, M. (1997). Occurrence of invading bacteria in radicular dentin of periodontally diseased teeth: microbiological findings. *Journal of Clinical Periodontology*, *24*(7), 478–485. https://doi.org/10.1111/J.1600-051X.1997.TB00215.X

Gomes Muniz, F. W. M., Nogueira, S. B., Vasconcelos Mendes, F. L., Rösing, C. K., Mendes Moreira, M. M. S., De Andrade, G. M., & De Sousa Carvalho, R. (2015). The impact of antioxidant agents complimentary to periodontal therapy on oxidative stress and periodontal outcomes: A systematic review. In *Archives of Oral Biology* (Vol. 60, pp. 1203–1214). Elsevier Ltd. https://doi.org/10.1016/j.archoralbio.2015.05.007

Gomes, S. C., Piccinin, F. B., Oppermann, R. V., Susin, C., & Marcantonio, R. A. C. (2009). The effect of smoking on gingival crevicular fluid volume during the treatment of gingivitis. *Acta Odontológica Latinoamericana : AOL*, *22*, 201–206.

Graves, D. T. (1999). The potential role of chemokines and inflammatory cytokines in periodontal disease progression. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America*, *28*(3), 482–490. https://doi.org/10.1086/515178

Graziani, F., Karapetsa, D., Alonso, B., & Herrera, D. (2017). Nonsurgical and surgical treatment of periodontitis: how many options for one disease? *Periodontology 2000*, *75*(1), 152–188. https://doi.org/10.1111/PRD.12201

Grellmann, A. P., Sfreddo, C. S., Maier, J., Lenzi, T. L., & Zanatta, F. B. (2016). Systemic antimicrobials adjuvant to periodontal therapy in diabetic subjects: a meta-analysis. *Journal of Clinical Periodontology*, *43*(3), 250–260. https://doi.org/10.1111/JCPE.12514

Griffiths, G. S. (2003). Formation, collection and significance of gingival crevice fluid. In *Periodontology 2000* (Vol. 31, pp. 32–42). https://doi.org/10.1034/j.1600-0757.2003.03103.x

Groneberg, D. A., Kindermann, B., Althammer, M., Klapper, M., Vormann, J., Littarru, G. P., & Döring, F. (2005a). Coenzyme Q10 affects expression of genes involved in cell signalling, metabolism and transport in human CaCo-2 cells. *The International Journal of Biochemistry & Cell Biology*, *37*(6), 1208–1218. https://doi.org/10.1016/J.BIOCEL.2004.11.017

Groneberg, D. A., Kindermann, B., Althammer, M., Klapper, M., Vormann, J., Littarru, G. P., & Döring, F. (2005b). Coenzyme Q10 affects expression of genes involved in cell signalling, metabolism and transport in human CaCo-2 cells. *The International Journal of Biochemistry & Cell Biology*, *37*(6), 1208–1218. https://doi.org/10.1016/J.BIOCEL.2004.11.017

Gumus, P., Huseyinalemdaroglu, B., & Buduneli, N. (2016). The role of oxidative stress in the interaction of periodontal disease with systemic diseases or conditions. *Oxidants and Antioxidants in Medical Science*, *5*(2), 33. https://doi.org/10.5455/OAMS.310516.RV.024

Gutteridge, J. M. C., & Halliwell, B. (2010). Antioxidants: Molecules, medicines, and myths. *Biochemical and Biophysical Research Communications*, *393*(4), 561–564. https://doi.org/10.1016/J.BBRC.2010.02.071

Haffajee, A. D., & Socransky, S. S. (1994). Microbial etiological agents of destructive periodontal diseases. *Periodontology 2000*, *5*(1), 78–111. https://doi.org/10.1111/J.1600-0757.1994.TB00020.X

Hajishengallis, G. (2015). Periodontitis: From microbial immune subversion to systemic inflammation. In *Nature Reviews Immunology* (Vol. 15, pp. 30–44). Nature Publishing Group. https://doi.org/10.1038/nri3785

Halliwell, B., Clement, M. V., & Long, L. H. (2000). Hydrogen peroxide in the human body. *FEBS Letters*, *486*(1), 10–13. https://doi.org/10.1016/S0014-5793(00)02197-9

Hanioka, T., Tanaka, M., Ojima, M., Shizukuishi, S., & Folkers, K. (1994a). Effect of topical application of Coenzyme Q10 on adult periodontitis. *Molecular Aspects of Medicine, 15*. https://doi.org/10.1016/0098-2997(94)90034-5

Hanioka, T., Tanaka, M., Ojima, M., Shizukuishi, S., & Folkers, K. (1994b). Effect of topical application of coenzyme Q10 on adult periodontitis. *Molecular Aspects of Medicine*, *15 Suppl*(SUPPL. 1). https://doi.org/10.1016/0098-2997(94)90034-5

Hans, M., Prakash, S., & Gupta, S. (2012). Clinical evaluation of topical application of perio-Q gel (Coenzyme Q10) in chronic periodontitis patients. *Journal of Indian Society of Periodontology*, *16*(2), 193. https://doi.org/10.4103/0972-124X.99261

Heasman, P. A., Collins, J. G., & Offenbacher, S. (1993). Changes in crevicular fluid levels of interleukin-1β, leukotriene B4, prostaglandin E2, thromboxane B2 and tumour necrosis factor α in experimental gingivitis in humans. *Journal of Periodontal Research*, *28*, 241–247. https://doi.org/10.1111/j.1600-0765.1993.tb02090.x

Heitz-Mayfield, L. J. A., & Lang, N. P. (2013). Surgical and nonsurgical periodontal therapy. Learned and unlearned concepts. *Periodontology 2000*, *62*, 218–231. https://doi.org/10.1111/prd.12008

Heitz-Mayfield, L. J. A., Trombelli, L., Heitz, F., Needleman, I., & Moles, D. (2002). A systematic review of the effect of surgical debridement vs non-surgical debridement for the treatment of chronic periodontitis. *Journal of Clinical Periodontology*, *29 Suppl 3*(SUPPL. 3), 92–102. https://doi.org/10.1034/J.1600-051X.29.S3.5.X

Highfield, J. (2009). Diagnosis and classification of periodontal disease. *Australian Dental Journal*, *54 Suppl 1*, S11–S26. https://doi.org/10.1111/J.1834-7819.2009.01140.X

Hope, C. K., & Wilson, M. (2004). Analysis of the Effects of Chlorhexidine on Oral Biofilm Vitality and Structure Based on Viability Profiling and an Indicator of Membrane Integrity. *Antimicrobial Agents and Chemotherapy*, *48*(5), 1461. https://doi.org/10.1128/AAC.48.5.1461-1468.2004

Ighodaro, O. M., & Akinloye, O. A. (2018). First line defence antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): Their

fundamental role in the entire antioxidant defence grid. *Alexandria Journal of Medicine*, *54*, 287–293. https://doi.org/10.1016/j.ajme.2017.09.001

Islam, M. N., Rauf, A., Fahad, F. I., Emran, T. Bin, Mitra, S., Olatunde, A., Shariati, M. A., Rebezov, M., Rengasamy, K. R. R., & Mubarak, M. S. (2022). Superoxide dismutase: an updated review on its health benefits and industrial applications. In *Critical Reviews in Food Science and Nutrition* (Vol. 62, pp. 7282–7300). Taylor and Francis Ltd. https://doi.org/10.1080/10408398.2021.1913400

Jacoby, B. H., & Davis, W. L. (1991). The Electron Microscopic Immunolocalization of a Copper-Zinc Superoxide Dismutase in Association with Collagen Fibers of Periodontal Soft Tissues. *Journal of Periodontology*, *62*, 413–420. https://doi.org/10.1902/jop.1991.62.7.413

Jervøe-Storm, P. M., Eberhard, J., Needleman, I., Worthington, H. V., & Jepsen, S. (2022). Full-mouth treatment modalities (within 24 hours) for periodontitis in adults. In *Cochrane Database of Systematic Reviews* (Vol. 2022). John Wiley and Sons Ltd. https://doi.org/10.1002/14651858.CD004622.pub4

Karim, S., Pratibha, P. K., Kamath, S., Bhat, G. S., Kamath, U., Dutta, B., Sharma, N., Archana, B., Bhat, K. M., & Guddattu, V. (2012). Superoxide dismutase enzyme and thiol antioxidants in gingival crevicular fluid and saliva. *Dental Research Journal*, *9*(3), 266–272. https://pubmed.ncbi.nlm.nih.gov/23087730/

Kim, T. S., Schenk, A., Lungeanu, D., Reitmeir, P., & Eickholz, P. (2007). Nonsurgical and surgical periodontal therapy in single-rooted teeth. *Clinical Oral Investigations*, *11*(4), 391–399. https://doi.org/10.1007/S00784-007-0144-X

Kinane, D. F., Stathopoulou, P. G., & Papapanou, P. N. (2017a). Periodontal diseases. *Nature Reviews Disease Primers 2017 3:1*, *3*(1), 1–14. https://doi.org/10.1038/nrdp.2017.38

Kinane, D. F., Stathopoulou, P. G., & Papapanou, P. N. (2017b). Periodontal diseases. In *Nature Reviews Disease Primers* (Vol. 3). Nature Publishing Group. https://doi.org/10.1038/nrdp.2017.38

Lamont, R. J., Koo, H., & Hajishengallis, G. (2018). The oral microbiota: dynamic communities and host interactions. *Nature Reviews. Microbiology*, *16*(12), 745. https://doi.org/10.1038/S41579-018-0089-X

Lamont, R. J., & Yilmaz, Ö. (2002). In or out: the invasiveness of oral bacteria. *Periodontology 2000*, *30*(1), 61–69. https://doi.org/10.1034/J.1600-0757.2002.03006.X

Lamprecht, M. (2014). Antioxidants in Sport Nutrition. *Antioxidants in Sport Nutrition*, 1–278. https://doi.org/10.1201/B17442/ANTIOXIDANTS-SPORT-NUTRITION-MANFRED-LAMPRECHT/ACCESSIBILITY-INFORMATION

Lamster, I. B., & Novak, M. J. (1992). Host mediators in gingival crevicular fluid: implications for the pathogenesis of periodontal disease. *Critical Reviews in Oral Biology and Medicine : An Official Publication of the American Association of Oral Biologists*, *3*(1–2), 31–60. https://doi.org/10.1177/10454411920030010501

Lang, N. P., & Tonetti, M. S. (2003). Periodontal risk assessment (PRA) for patients in supportive periodontal therapy (SPT). *Oral Health & Preventive Dentistry*, *1*, 7–16. https://doi.org/10.3290/j.ohpd.a8216

Linnane, A. W., Kios, M., & Vitetta, L. (2007). Coenzyme Q10 - Its role as a prooxidant in the formation of superoxide anion/hydrogen peroxide and the regulation of the metabolome. *Mitochondrion*, *7*. https://doi.org/10.1016/j.mito.2007.03.005

Littarru, G. P., Nakamura, R., Ho, L., Folkers, K., & Kuzell, W. C. (1971). Deficiency of coenzyme Q 10 in gingival tissue from patients with periodontal disease. *Proceedings of the National Academy of Sciences of the United States of America*, *68*, 2332–2335. https://doi.org/10.1073/pnas.68.10.2332

Loos, B., Claffey, N., & Egelberg, J. (1988). Clinical and microbiological effects of root debridement in periodontal furcation pockets. *Journal of Clinical Periodontology*, *15*(7), 453–463. https://doi.org/10.1111/J.1600-051X.1988.TB01600.X

Lowenguth, R. A., & Greenstein, G. (1995). Clinical and microbiological response to nonsurgical mechanical periodontal therapy. *Periodontology 2000*, *9*(1), 14–22. https://doi.org/10.1111/J.1600-0757.1995.TB00052.X

Magnusson, I., Lindhe, J., Yoneyama, T., & Liljenberg, B. (1984). Recolonization of a subgingival microbiota following scaling in deep pockets. *Journal of Clinical Periodontology*, *11*(3), 193–207. https://doi.org/10.1111/J.1600-051X.1984.TB01323.X

Mahanonda, R., & Pichyangkul, S. (2007). Toll-like receptors and their role in periodontal health and disease. *Periodontology 2000*, *43*(1), 41–55. https://doi.org/10.1111/J.1600-0757.2006.00179.X

Majeed, Z. N., Philip, K., Alabsi, A. M., Pushparajan, S., & Swaminathan, D. (2016). Identification of Gingival Crevicular Fluid Sampling, Analytical Methods, and Oral Biomarkers for the Diagnosis and Monitoring of Periodontal Diseases: A Systematic Review. In *Disease Markers* (Vol. 2016). Hindawi Limited. https://doi.org/10.1155/2016/1804727

Makkar, H., & Sriram, G. (2025). Advances in modeling periodontal host-microbe interactions: insights from organotypic and organ-on-chip systems. In *Lab on a Chip* (Vol. 25, pp. 1342–1371). Royal Society of Chemistry. https://doi.org/10.1039/d4lc00871e

Mamdouh, A., abdel gaber, hala, & AMR, A. (2024). Coenzyme Q10 local delivery as an adjunct to non-surgical periodontal treatment: A randomized controlled clinical study with biochemical assessment of IL-1β and IL-10 levels in the gingival crevicular fluid. *Egyptian Dental Journal*, *70*, 1173–1185. https://doi.org/10.21608/edj.2023.255428.2825

Manthena, S., Ramoji Rao, M. V., Penubolu, L. P., Putcha, M., & Sri Harsha, A. V. N. (2015). Effectiveness of CoQ10 Oral Supplements as an Adjunct to Scaling and Root Planing in Improving Periodontal Health. *Journal of Clinical and Diagnostic Research : JCDR*, *9*(8), ZC26–ZC28. https://doi.org/10.7860/JCDR/2015/13486.6291

Mark Bartold, P., & Van Dyke, T. E. (2013). Periodontitis: a host-mediated disruption of microbial homeostasis. Unlearning learned concepts. *Periodontology 2000*, *62*(1), 203–217. https://doi.org/10.1111/J.1600-0757.2012.00450.X

Martínez-García, M., & Hernández-Lemus, E. (2024). The Molecular Comorbidity Network of Periodontal Disease. *International Journal of Molecular Sciences*, *25*(18), 10161. https://doi.org/10.3390/IJMS251810161/S1

Merle, C. L., Lenzen, C., Schmalz, G., & Ziebolz, D. (2023). Systematic Review on Protocols of Coenzyme Q10 Supplementation in Non-Surgical Periodontitis Therapy. *Nutrients*, *15*(7). https://doi.org/10.3390/NU15071585

Michalowicz, B. S., Aeppli, D., Virag, J. G., Klump, D. G., Hinrichs, E., Segal, N. L., Bouchard, T. J., & Pihlstrom, B. L. (1991). Periodontal Findings in Adult Twins. *Journal of Periodontology*, *62*, 293–299. https://doi.org/10.1902/jop.1991.62.5.293

Mizutani, K., Buranasin, P., Mikami, R., Takeda, K., Kido, D., Watanabe, K., Takemura, S., Nakagawa, K., Kominato, H., Saito, N., Hattori, A., & Iwata, T. (2021). Effects of antioxidant in adjunct with periodontal therapy in patients with type 2 diabetes: A systematic review and meta-analysis. *Antioxidants*, *10*(8), 1304. https://doi.org/10.3390/ANTIOX10081304/S1

Mousquéegs, T., Listgarten, M. A., & Phillips, R. W. (1980). Effect of scaling and root planing on the composition of the human subgingival microbial flora. *Journal of Periodontal Research*, *15*(2), 144–151. https://doi.org/10.1111/J.1600-0765.1980.TB00268.X

Na, H.-J., Kim, O.-S., & Park, B.-J. (2006). Expression of Superoxide Dismutase Isoforms in Inflamed Gingiva. *The Journal of the Korean Academy of Periodontology*, *36*, 97. https://doi.org/10.5051/jkape.2006.36.1.97

Najeeb, S., Zafar, M. S., Khurshid, Z., Zohaib, S., & Almas, K. (2016). The role of nutrition in periodontal health: An update. In *Nutrients* (Vol. 8). MDPI. https://doi.org/10.3390/nu8090530

Nakamura, R., Littarru, G. P., Folkers, K., & Wilkinson, E. G. (1973). Deficiency of coenzyme Q in gingiva of patients with periodontal disease. *International Journal for Vitamin and Nutrition Research*, *43*, 84–92.

Newman, M. G., Takei, H. H., Klokkevold, P. R., & Carranza, F. A. (2019). *Newman and Carranza's clinical periodontology / [edited by] Michael G. Newman, Henry H. Takei, Perry R. Klokkevold, Fermin A Carranza.* 1–994.

Nguyen, N. H., Tran, G. B., & Nguyen, C. T. (2020). Anti-oxidative effects of superoxide dismutase 3 on inflammatory diseases. In *Journal of Molecular Medicine* (Vol. 98, pp. 59–69). Springer. https://doi.org/10.1007/s00109-019-01845-2

Nikalus P. Lang, & Jan Lindhe. (2015). *Clinical Periodontology and Implant Dentistry, 2 volume set*. John Wiley & Sons.

NOHL, H., & HEGNER, D. (1978). Do Mitochondria Produce Oxygen Radicals in vivo? *European Journal of Biochemistry*, *82*, 563–567. https://doi.org/10.1111/j.1432-1033.1978.tb12051.x

Novakovic, N., Todorovic, T., Rakic, M., Milinkovic, I., Dozic, I., Jankovic, S., Aleksic, Z., & Cakic, S. (2014). Salivary antioxidants as periodontal biomarkers in evaluation of tissue status and treatment outcome. *Journal of Periodontal Research*, *49*, 129–136. https://doi.org/10.1111/jre.12088

Ohlrich, E. J., Cullinan, M. P., & Seymour, G. J. (2009). The immunopathogenesis of periodontal disease. *Australian Dental Journal*, *54*(1), S2–S10. https://doi.org/10.1111/J.1834-7819.2009.01139.X

OJHA, M. O., Dr. Vartika Verma, Dr. Kapilesh Singh, & Dr. Darshana Sarkar. (2024). An Insight into Supportive Periodontal Therapy and Maintenance Care. *UNIVERSITY JOURNAL OF DENTAL SCIENCES*, *10*. https://doi.org/10.21276//ujds.2024.10.2.18

Okamoto, T., Matsuya, T., Fukunaga, Y., Kishi, T., & Yamagami, T. (1989). Human serum ubiquinol-10 levels and relationship to serum lipids. *International Journal for Vitamin and Nutrition Research. Internationale Zeitschrift Fur Vitamin- Und*

Ernahrungsforschung. Journal International de Vitaminologie et de Nutrition, *59*(3), 288–292. https://europepmc.org/article/med/2599795

Page, R. C. (1992). Host Response Tests for Diagnosing Periodontal Diseases. *Journal of Periodontology*, *63*, 356–366. https://doi.org/10.1902/jop.1992.63.4s.356

Palamakula, A., Soliman, M., & Khan, M. A. (2005). Regional permeability of coenzyme Q10 in isolated rat gastrointestinal tracts. *Pharmazie*.

Palmer, R. M., Wilson, R. F., Hasan, A. S., & Scott, D. A. (2005). Mechanisms of action of environmental factors - Tobacco smoking. *Journal of Clinical Periodontology*, *32*, 180–195. https://doi.org/10.1111/j.1600-051X.2005.00786.x

Papapanou, P. N., Sanz, M., Buduneli, N., Dietrich, T., Feres, M., Fine, D. H., Flemmig, T. F., Garcia, R., Giannobile, W. V., Graziani, F., Greenwell, H., Herrera, D., Kao, R. T., Kebschull, M., Kinane, D. F., Kirkwood, K. L., Kocher, T., Kornman, K. S., Kumar, P. S., … Tonetti, M. S. (2018a). Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Periodontology*, *89*, S173–S182. https://doi.org/10.1002/JPER.17-0721

Papapanou, P. N., Sanz, M., Buduneli, N., Dietrich, T., Feres, M., Fine, D. H., Flemmig, T. F., Garcia, R., Giannobile, W. V., Graziani, F., Greenwell, H., Herrera, D., Kao, R. T., Kebschull, M., Kinane, D. F., Kirkwood, K. L., Kocher, T., Kornman, K. S., Kumar, P. S., … Tonetti, M. S. (2018b). Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. *Journal of Periodontology*, *89 Suppl 1*, S173–S182. https://doi.org/10.1002/JPER.17-0721

Papucci, L., Schiavone, N., Witort, E., Donnini, M., Lapucci, A., Tempestini, A., Formigli, L., Zecchi-Orlandini, S., Orlandini, G., Carella, G., Brancato, R., & Capaccioli, S. (2003). Coenzyme Q10 prevents apoptosis by inhibiting mitochondrial depolarization independently of its free radical scavenging property. *Journal of Biological Chemistry*, *278*, 28220–28228. https://doi.org/10.1074/jbc.M302297200

Pedrazzoli, V., Kilian, M., Karring, T., & Kirkegaard, E. (1991). Effect of surgical and non-surgical periodontal treatment on periodontal status and subgingival microbiota. *Journal of Clinical Periodontology*, *18*(8), 598–604. https://doi.org/10.1111/J.1600-051X.1991.TB00096.X

Petersilka, G. J., Ehmke, B., & Flemmig, T. F. (2002a). Antimicrobial effects of mechanical debridement. *Periodontology 2000*, *28*(1), 56–71. https://doi.org/10.1034/J.1600-0757.2002.280103.X

Petersilka, G. J., Ehmke, B., & Flemmig, T. F. (2002b). Antimicrobial effects of mechanical debridement. *Periodontology 2000*, *28*(1), 56–71. https://doi.org/10.1034/J.1600-0757.2002.280103.X

Phull, A. R., Nasir, B., Haq, I. ul, & Kim, S. J. (2018). Oxidative stress, consequences and ROS mediated cellular signaling in rheumatoid arthritis. *Chemico-Biological Interactions*, *281*, 121–136. https://doi.org/10.1016/J.CBI.2017.12.024

Pihlstrom, B. L., Michalowicz, B. S., & Johnson, N. W. (2005). Periodontal diseases. *Lancet (London, England)*, *366*(9499), 1809–1820. https://doi.org/10.1016/S0140-6736(05)67728-8

Pisoschi, A. M., & Pop, A. (2015). The role of antioxidants in the chemistry of oxidative stress: A review. *European Journal of Medicinal Chemistry*, *97*, 55–74. https://doi.org/10.1016/J.EJMECH.2015.04.040

Prakash, S., Sunitha, J., & Hans, M. (2010a). Role of coenzyme Q10 as an antioxidant and bioenergizer in periodontal diseases. *Indian Journal of Pharmacology*, *42*(6), 334. https://doi.org/10.4103/0253-7613.71884

Prakash, S., Sunitha, J., & Hans, M. (2010b). Role of coenzyme Q(10) as an antioxidant and bioenergizer in periodontal diseases. *Indian Journal of Pharmacology*, *42*(6), 334–337. https://doi.org/10.4103/0253-7613.71884

Pranam, S., Palwankar, P., Pandey, R., & Goyal, A. (2020). Evaluation of Efficacy of Coenzyme Q10 as an Adjunct to Nonsurgical Periodontal Therapy and Its Effect on

Crevicular Superoxide Dismutase in Patients with Chronic Periodontitis. *European Journal of Dentistry, 14*(4), 551–557. https://doi.org/10.1055/S-0040-1716596

Qu, H. (2023). The association between oxidative balance score and periodontitis in adults: a population-based study. *Frontiers in Nutrition, 10*. https://doi.org/10.3389/fnut.2023.1138488

Quirynen, M., Bollen, C. M. L., Vandekerckhove, B. N. A., Dekeyser, C., Papaioannou, W., & Eyssen, H. (1995). Full- vs. partial-mouth disinfection in the treatment of periodontal infections: short-term clinical and microbiological observations. *Journal of Dental Research*, *74*(8), 1459–1467. https://doi.org/10.1177/00220345950740080501

Quirynen, M., Teughels, W., De Soete, M., & Van Steenberghe, D. (2002). Topical antiseptics and antibiotics in the initial therapy of chronic adult periodontitis: microbiological aspects. *Periodontology 2000*, *28*(1), 72–90. https://doi.org/10.1034/J.1600-0757.2002.280104.X

Ramesh, K., Swetha, P., Mohan Kumar, P., Sruthima, N., & Naresh Kumar, C. (2019). Estimation of superoxide dismutase levels in saliva and gingival crevicular fluid among smokers and non-smokers in periodontitis patients - An observational study. *Nigerian Medical Journal*, *60*, 133. https://doi.org/10.4103/nmj.nmj_56_19

Raut, C. P., & Sethi, K. S. (2016). *Comparative evaluation of co-enzyme Q10 and Melaleuca alternifolia as antioxidant gels in treatment of chronic periodontitis: A clinical study*. https://doi.org/10.4103/0976-237X.188572

Raut, C. P., Sethi, K. S., Kohale, B., Mamajiwala, A., & Warang, A. (2019). Subgingivally delivered coenzyme Q10 in the treatment of chronic periodontitis among smokers: A randomized, controlled clinical study. *Journal of Oral Biology and Craniofacial Research*, *9*(2), 204–208. https://doi.org/10.1016/J.JOBCR.2018.05.005

Reddy, V. N., Kasahara, E., Hiraoka, M., Lin, L. R., & Ho, Y. S. (2004). Effects of variation in superoxide dismutases (SOD) on oxidative stress and apoptosis in lens epithelium. *Experimental Eye Research*, *79*, 859–868. https://doi.org/10.1016/j.exer.2004.04.005

Rowshani, B., Timmerman, M. F., & Van Der Velden, U. (2004). Plaque development in relation to the periodontal condition and bacterial load of the saliva. *Journal of Clinical Periodontology*, *31*(3), 214–218. https://doi.org/10.1111/J.0303-6979.2004.00468.X

Sagar, A. (2014). Full mouth versus quadrant treatment in chronic periodontitis. *Primary Dental Journal*, *3*(3), 66–69. https://doi.org/10.1308/205016814812736853

Saini, R. (2014). A clinical and microbiological study to evaluate the effect of dietary supplement of coenzyme Q10 in nonsurgical treatment outcome of chronic periodontitis patients after phase 1 periodontal therapy. *European Journal of General Dentistry*, *3*, 194–198. https://doi.org/10.4103/2278-9626.141669

Sale, S., Parvez, H., Yeltiwar, R., Vivekanandan, G., Pundir, A., & Jain, P. (2014). A comparative evaluation of topical and intrasulcular application of coenzyme Q10 (Perio Q^{TM}) gel in chronic periodontitis patients: A clinical study. *Journal of Indian Society of Periodontology*, *18*(4), 461–465. https://doi.org/10.4103/0972-124X.138690

Sanz, M., Herrera, D., Kebschull, M., Chapple, I., Jepsen, S., Beglundh, T., Sculean, A., Tonetti, M. S., Merete Aass, A., Aimetti, M., Kuru, B. E., Belibasakis, G., Blanco, J., Bol-van den Hil, E., Bostanci, N., Bozic, D., Bouchard, P., Buduneli, N., Cairo, F., … Wennström, J. (2020). Treatment of stage I–III periodontitis—The EFP S3 level clinical practice guideline. *Journal of Clinical Periodontology*, *47*, 4–60. https://doi.org/10.1111/jcpe.13290

Sbordone, L., Ramaglia, L., Gulletta, E., & Iacono, V. (1990). Recolonization of the subgingival microflora after scaling and root planing in human periodontitis. *Journal of Periodontology*, *61*(9), 579–584. https://doi.org/10.1902/JOP.1990.61.9.579

Schmelzer, C., Lindner, I., Rimbach, G., Niklowitz, P., Menke, T., & Döring, F. (2008). Functions of coenzyme Q10 in inflammation and gene expression. *BioFactors (Oxford, England)*, *32*(1–4), 179–183. https://doi.org/10.1002/BIOF.5520320121

Scopp, I. W., Froum, S. J., Sullivan, M., Kazandjian, G., Wank, D., & Fine, A. (1980). Tetracycline: a clinical study to determine its effectiveness as long-term adjuvant. *Journal of Periodontology*, *51*(6), 328–330. https://doi.org/10.1902/JOP.1980.51.6.328

Shaheen, M. A., Elmeadawy, S. H., Bazeed, F. B., Anees, M. M., & Saleh, N. M. (2020). Innovative coenzyme Q10-loaded nanoformulation as an adjunct approach for the management of moderate periodontitis: preparation, evaluation, and clinical study. *Drug Delivery and Translational Research*, *10*(2), 548–564. https://doi.org/10.1007/S13346-019-00698-Z

Sharma, P. (2023). Supportive Periodontal Therapy. In *Practical Periodontal Diagnosis and Treatment Planning* (pp. 135–137). Wiley. https://doi.org/10.1002/9781119830344.ch10

Shigenaga, M. K., Hagen, T. M., & Ames, B. N. (1994). Oxidative damage and mitochondrial decay in aging. In *Proceedings of the National Academy of Sciences of the United States of America* (Vol. 91, pp. 10771–10778). National Academy of Sciences. https://doi.org/10.1073/pnas.91.23.10771

Sies, H. (1991). Role of reactive oxygen species in biological processes. *Klinische Wochenschrift*, *69*, 965–968. https://doi.org/10.1007/BF01645140

Silva, N., Abusleme, L., Bravo, D., Dutzan, N., Garcia-Sesnich, J., Vernal, R., Hernández, M., & Gamonal, J. (2015). Host response mechanisms in periodontal diseases. *Journal of Applied Oral Science : Revista FOB*, *23*(3), 329–355. https://doi.org/10.1590/1678-775720140259

Siti, H. N., Kamisah, Y., & Kamsiah, J. (2015). The role of oxidative stress, antioxidants and vascular inflammation in cardiovascular disease (a review). *Vascular Pharmacology*, *71*, 40–56. https://doi.org/10.1016/J.VPH.2015.03.005

Socransky, S. S., & Haffajee, A. D. (2005). Periodontal microbial ecology. *Periodontology 2000*, *38*, 135–187. https://doi.org/10.1111/J.1600-0757.2005.00107.X

Soni, S., Agarwal, P., Sharma, N., & Chander, S. (2012). "Coenzyme Q10 And Periodontal Health"- A Review. *International Journal of Oral and Maxillofacial Pathology*.

Sukhtankar, L., Kulloli, A., Kathariya, R., & Shetty, S. (2013). Effect of non-surgical periodontal therapy on superoxide dismutase levels in gingival tissues of chronic

periodontitis patients: A clinical and spectophotometric analysis. *Disease Markers*, *34*, 305–311. https://doi.org/10.3233/DMA-130978

Sulijaya, B., Takahashi, N., & Yamazaki, K. (2019). Host modulation therapy using anti-inflammatory and antioxidant agents in periodontitis: A review to a clinical translation. *Archives of Oral Biology*, *105*, 72–80. https://doi.org/10.1016/J.ARCHORALBIO.2019.07.002

Suvan, J., Leira, Y., Moreno Sancho, F. M., Graziani, F., Derks, J., & Tomasi, C. (2020). Subgingival instrumentation for treatment of periodontitis. A systematic review. In *Journal of Clinical Periodontology* (Vol. 47, pp. 155–175). Blackwell Munksgaard. https://doi.org/10.1111/jcpe.13245

Teughels, W., Dekeyser, C., Van Essche, M., & Quirynen, M. (2009). One-stage, full-mouth disinfection: fiction or reality? *Periodontology 2000*, *50*(1), 39–51. https://doi.org/10.1111/J.1600-0757.2008.00292.X

Tonetti, M. S., Greenwell, H., & Kornman, K. S. (2018). Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *Journal of Periodontology*, *89 Suppl 1*, S159–S172. https://doi.org/10.1002/JPER.18-0006

Tóthová, L., & Celec, P. (2017). Oxidative Stress and Antioxidants in the Diagnosis and Therapy of Periodontitis. *Frontiers in Physiology*, *8*, 1055. https://doi.org/10.3389/fphys.2017.01055

Tran, M. T., Mitchell, T. M., Kennedy, D. T., & Giles, J. T. (2001). Role of coenzyme Q10 in chronic heart failure, angina, and hypertension. *Pharmacotherapy*, *21*(7), 797–806. https://doi.org/10.1592/PHCO.21.9.797.34564

Trindade, D., Carvalho, R., Machado, V., Chambrone, L., Mendes, J. J., & Botelho, J. (2023). Prevalence of periodontitis in dentate people between 2011 and 2020: A systematic review and meta-analysis of epidemiological studies. In *Journal of Clinical Periodontology* (Vol. 50, pp. 604–626). John Wiley and Sons Inc. https://doi.org/10.1111/jcpe.13769

Tsai, C. C., Chen, H. S., Chen, S. L., Ho, Y. P., Ho, K. Y., Wu, Y. M., & Hung, C. C. (2005). Lipid peroxidation: a possible role in the induction and progression of chronic periodontitis. *Journal of Periodontal Research*, *40*(5), 378–384. https://doi.org/10.1111/J.1600-0765.2005.00818.X

Valko, M., Leibfritz, D., Moncol, J., Cronin, M. T. D., Mazur, M., & Telser, J. (2007). Free radicals and antioxidants in normal physiological functions and human disease. *The International Journal of Biochemistry & Cell Biology*, *39*(1), 44–84. https://doi.org/10.1016/J.BIOCEL.2006.07.001

Van der Weijden, G. A., Dekkers, G. J., & Slot, D. E. (2019). Success of non-surgical periodontal therapy in adult periodontitis patients: A retrospective analysis. *International Journal of Dental Hygiene*, *17*, 309–317. https://doi.org/10.1111/idh.12399

Van Der Weijden, G. A., & Timmerman, M. F. (2002a). A systematic review on the clinical efficacy of subgingival debridement in the treatment of chronic periodontitis. *Journal of Clinical Periodontology*, *29 Suppl 3*(SUPPL. 3), 55–71. https://doi.org/10.1034/J.1600-051X.29.S3.3.X

Van Der Weijden, G. A., & Timmerman, M. F. (2002b). A systematic review on the clinical efficacy of subgingival debridement in the treatment of chronic periodontitis. In *Journal of Clinical Periodontology* (Vol. 29, pp. 55–71). https://doi.org/10.1034/j.1600-051X.29.s3.3.x

van Winkelhof, A. J., van der Velden, U., & de Graaff, J. (1988a). Microbial succession in recolonizing deep periodontal pockets after a single course of supra- and subgingival debridement. *Journal of Clinical Periodontology*, *15*(2), 116–122. https://doi.org/10.1111/J.1600-051X.1988.TB01004.X

van Winkelhof, A. J., van der Velden, U., & de Graaff, J. (1988b). Microbial succession in recolonizing deep periodontal pockets after a single course of supra- and subgingival debridement. *Journal of Clinical Periodontology*, *15*(2), 116–122. https://doi.org/10.1111/J.1600-051X.1988.TB01004.X

Van Winkelhoff, A. J., Van der Velden, U., Clement, M., & De Graaff, J. (1988). Intra-oral distribution of black-pigmented Bacteroides species in periodontitis patients. *Oral Microbiology and Immunology*, *3*(2), 83–85. https://doi.org/10.1111/J.1399-302X.1988.TB00087.X

Vandekerckhove, B. N. A., Bollen, C. M. L., Dekeyser, C., Darius, P., & Quirynen, M. (1996). Full- Versus Partial-Mouth Disinfection in the Treatment of Periodontal Infections. Long-Term Clinical Observations of a Pilot Study. *Journal of Periodontology*, *67*, 1251–1259. https://doi.org/10.1902/jop.1996.67.12.1251

Varela-Lopez, A., Bullon, P., Battino, M., Ramirez-Tortosa, Mc., Ochoa, J. J., Cordero, M. D., Ramirez-Tortosa, C. L., Rubini, C., Zizzi, A., & Quiles, J. L. (2016). Coenzyme Q Protects Against Age-Related Alveolar Bone Loss Associated to n-6 Polyunsaturated Fatty Acid Rich-Diets by Modulating Mitochondrial Mechanisms. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, *71*(5), 593–600. https://doi.org/10.1093/GERONA/GLV063

Vo, T. T. T., Chu, P. M., Tuan, V. P., Te, J. S. L., & Lee, I. T. (2020). The Promising Role of Antioxidant Phytochemicals in the Prevention and Treatment of Periodontal Disease via the Inhibition of Oxidative Stress Pathways: Updated Insights. *Antioxidants 2020, Vol. 9, Page 1211*, *9*(12), 1211. https://doi.org/10.3390/ANTIOX9121211

Waddington, R. J., Moseley, R., & Embery, G. (2000). Periodontal Disease Mechanisms: Reactive oxygen species: a potential role in the pathogenesis of periodontal diseases. *Oral Diseases*, *6*(3), 138–151. https://doi.org/10.1111/J.1601-0825.2000.TB00325.X

Wei, D., Zhang, X. L., Wang, Y. Z., Yang, C. X., & Chen, G. (2010a). Lipid peroxidation levels, total oxidant status and superoxide dismutase in serum, saliva and gingival crevicular fluid in chronic periodontitis patients before and after periodontal therapy. *Australian Dental Journal*, *55*(1), 70–78. https://doi.org/10.1111/J.1834-7819.2009.01123.X

Wei, D., Zhang, X. L., Wang, Y. Z., Yang, C. X., & Chen, G. (2010b). Lipid peroxidation levels, total oxidant status and superoxide dismutase in serum, saliva and gingival crevicular fluid in chronic periodontitis patients before and after periodontal therapy.

Australian Dental Journal, *55*, 70–78. https://doi.org/10.1111/j.1834-7819.2009.01123.x

Youssef, M., Shoukheba, M., El-Sayed, S., & El-Kholy, M. (2019). Coenzyme Q10 Food Supplement on the Treatment of Chronic Periodontitis in Patients with Type II Diabetes Mellitus: A Randomized Control Study. *Egyptian Dental Journal*, *65*(Issue 1-January (Oral Medicine, X-Ray, Oral Biology & Oral Pathology)), 253–261. https://doi.org/10.21608/EDJ.2015.71409

Yucel-Lindberg, T., & Båge, T. (2013). Inflammatory mediators in the pathogenesis of periodontitis. *Expert Reviews in Molecular Medicine*, *15*. https://doi.org/10.1017/ERM.2013.8

APPENDICES

APPENDIX A

A.1 ETHIC COMMITTEE APPROVAL

KLİNİK ARAŞTIRMALAR ETİK KURULU KARAR FORMU

ARAŞTIRMANIN AÇIK ADI	Cerrahi Olmayan Periodontal Tedaviye Ek Olarak Kullanılan Koenzim Q10'un Klinik ve Biyokimyasal Etkinliğinin Değerlendirilmesi
ARAŞTIRMANIN PROTOKOL KODU (VARSA)	2024-196

KLİNİK ARAŞTIRMALAR ETİK KURULUNA AİT BİLGİLER

Etik Kurulun Adı:
BAKIRKÖY DR. SADİ KONUK EĞİTİM VE ARAŞTIRMA HASTANESİ KLİNİK ARAŞTIRMALAR ETİK KURULU

TİTCK Tarafından Verilen Etik Kurul Kodu [1]

Açık Adresi	Telefon	E-Posta
Zuhuratbaba Mh. Tevfik Sağlam Cd. No:11 Bakırköy İstanbul	(0212) 414 74 04	

KLİNİK ARAŞTIRMALAR ETİK KURULUNA YAPILAN BAŞVURUYA AİT BİLGİLER

Etik Kurula Başvuru Tarihi	18.06.2024
Koordinatör/Sorumlu Araştırmacı Unvanı/Adı/Soyadı [2]	Prof. Dr. Şebnem Dirikan İPÇİ
Koordinatör/Sorumlu Araştırmacının Uzmanlık Alanı	Periodonteloji
Koordinatör/Sorumlu Araştırmacının Bulunduğu Merkez	Altınbaş Üniversitesi
Destekleyici	BAP Başvurulacaktır.
Destekleyicinin Yasal Temsilcisi	Mevcut Değildir.
Sözleşmeli Araştırma Kuruluşu	Mevcut Değildir.
Başvuru Sahibi	Yasal Temsilci — Lütfen başvuru sahibini belirtiniz (Ad soyad Sponsor (Firma) adı)
Araştırmanın Fazı	Düşük Riskli Bilimsel Çalışma
Araştırmanın Türü (Tıbbi Cihaz Araştırma/Çalışmaları İçin)	Bir öğe seçin.
Destekleyicinin Statüsü	Bir öğe seçin.

UYGUNLUĞU DEĞERLENDİRİLEN BELGELER				
Araştırma Protokolü	18.06.2024	00	Türkçe	Uygun ☒ Uygun Değil [3] ☐
Bilgilendirilmiş Gönüllü Olur Formu (BGOF)[4]	18.06.2024	00	Türkçe	Uygun ☒ Uygun Değil ☐
Değerlendirilmek üzere Bilgi Amaçlı Belgeler	Doküman Tarihi	Versiyon Numarası	Bir öğe seçin.	Uygun ☐ Uygun Değil ☐
Değerlendirilmek üzere Bilgi Amaçlı Belgeler	Doküman Tarihi	Versiyon Numarası	Bir öğe seçin.	Uygun ☐ Uygun Değil ☐
Yazılı Rıza Formu (varsa)	Doküman Tarihi	Versiyon Numarası	Bir öğe seçin.	Uygun ☐ Uygun Değil ☐
Araştırmacı Broşürü (AB)				Uygun ☐ Uygun Değil ☐
Fayda-Risk Değerlendirilmesine İlişkin Plan/Rapor	Doküman Tarihi	Versiyon Numarası	Bir öğe seçin.	Uygun ☐ Uygun Değil ☐
Pedıyatrik Araştırma Planı (geçerli ise)	Doküman Tarihi	Versiyon Numarası	Bir öğe seçin.	Uygun ☐ Uygun Değil ☐
Ara Analiz Raporu (geçerli ise)	Doküman Tarihi	Versiyon Numarası	Bir öğe seçin.	Uygun ☐ Uygun Değil ☐

Bağımsız Veri İzleme Komitesi Raporu (varsa)	Doküman Tarihi	Versiyon Numarası	Bir öğe seçin	Uygun ☐ Uygun Değil ☐
Araştırma Ürünü Dosyası	Doküman Tarihi	Versiyon Numarası	Bir öğe seçin	Uygun ☐ Uygun Değil ☐
Olgu Rapor Formu (ORF)	18.06.2024	00	Türkçe	Uygun ☒ Uygun Değil ☐

Sigorta [5] (ilgili mevzuat gereği sigorta gerektiren araştırmalar için)

Sigorta Poliçesi	Sigorta poliçe numarası	Poliçe dönemi	Tanzim tarihi	Uygun ☐ Uygun Değil ☐
Sigorta Sertifikası	Sigorta poliçe numarası	Poliçe dönemi	Tanzim tarihi	Uygun ☐ Uygun Değil ☐
Sigorta Zeyilnameleri (varsa)	Sigorta poliçe numarası	Poliçe dönemi	Tanzim tarihi	Uygun ☐ Uygun Değil ☐
Genel ve Özel Şartlar, vb.	Sigorta poliçe numarası	Poliçe dönemi	Tanzim tarihi	Uygun ☐ Uygun Değil ☐
Araştırma Bütçesi	37.381 Tl Araştırma Bütçesi BAP Başvurulacaktır. Tarih 18.06.2024 versiyon 00			Uygun ☒ Uygun Değil ☐
Araştırmanın Yeniden Başlatılması	Gerekçesini belirtiniz.			Uygun ☐ Uygun Değil ☐
Araştırmanın Geçici Durdurulması	Gerekçesini belirtiniz.			Uygun ☐ Uygun Değil ☐

Araştırma Merkezi Eklenmesi	*Merkez adını/adlarını belirtiniz.*	*Sorumlu araştırmacı/araştırmacıları belirtiniz.*	Uygun ☐	Uygun Değil ☐
Araştırma Ekibi (Özgeçmişler)	**Dr.Öğrt.Üyesi İlknur ÖZENCİ, As.Dr.Berkay Ali BİLGİN**		Uygun ☒	Uygun Değil ☐
Monitör	*Monitör (İzleyici) atanması CE işareti taşımayan Tıbbi Cihazlar ve İn-Vitro Tanı Amaçlı Tıbbi Cihazlar ile yürütülen araştırmalarda zorunludur. Destekleyici tarafından atanacak monitörün yetkinliği ile araştırma merkezinden bağımsız olması hususlarının incelenmesi yapılmalıdır.*		Uygun ☐	Uygun Değil ☐

Diğer Dokümanlar;

Varsa değerlendirilen diğer belgeleri belirtiniz	**Doküman Tarihi**	*Versiyon Numarası*	Bir öğe seçin.	Uygun ☐	Uygun Değil ☐
Varsa değerlendirilen diğer belgeleri belirtiniz	**Doküman Tarihi**	*Versiyon Numarası*	*Bir öğe seçin.*	Uygun ☐	Uygun Değil ☐
Varsa değerlendirilen diğer belgeleri belirtiniz	**Doküman Tarihi**	*Versiyon Numarası*	*Bir öğe seçin.*	Uygun ☐	Uygun Değil ☐
Varsa değerlendirilen diğer belgeleri belirtiniz	**Doküman Tarihi**	*Versiyon Numarası*	*Bir öğe seçin.*	Uygun ☐	Uygun Değil ☐

GÖNÜLLÜ DOKÜMANLARI

Gönüllü Kartı	*Tarih/Varsa Versiyon*	Uygun ☐	Uygun Değil ☐
Gönüllü Günlüğü	*Tarih/Varsa Versiyon*	Uygun ☐	Uygun Değil ☐

Anketler;

Değerlendirilen anketin adını giriniz.	Tarih/Varsa Versiyon	Uygun ☐	Uygun Değil ☐
Değerlendirilen anketin adını giriniz.	Tarih/Varsa Versiyon	Uygun ☐	Uygun Değil ☐
Değerlendirilen anketin adını giriniz.	Tarih/Varsa Versiyon	Uygun ☐	Uygun Değil ☐
Değerlendirilen anketin adını giriniz.	Tarih/Varsa Versiyon	Uygun ☐	Uygun Değil ☐

Gönüllüye verilecek diğer dokümanlar[6] ;

Değerlendirilen dokümanın adını giriniz.	Tarih/Varsa Versiyon	Uygun ☐	Uygun Değil ☐
Değerlendirilen dokümanın adını giriniz.	Tarih/Varsa Versiyon	Uygun ☐	Uygun Değil ☐
Değerlendirilen dokümanın adını giriniz.	Tarih/Varsa Versiyon	Uygun ☐	Uygun Değil ☐

Gönüllü hizmetleri ile ilgili (evde bakım/hemşire/sağlık hizmetleri, araştırma ürünü teslim hizmeti, araştırma merkezine transfer hizmeti vb.) dokümanlar:

Değerlendirilen dokümanın adını giriniz.	Tarih/Varsa Versiyon	Uygun ☐	Uygun Değil ☐
Değerlendirilen dokümanın adını giriniz.	Tarih/Varsa Versiyon	Uygun ☐	Uygun Değil ☐
Değerlendirilen dokümanın adını giriniz.	Tarih/Varsa Versiyon	Uygun ☐	Uygun Değil ☐

Gönüllülere verilecek olan elektronik cihaz ve materyaller (tablet, telefon, çanta vb.)	Türünü belirtiniz.	Uygun ☐ Uygun Değil ☐

DİĞER DOKÜMANLAR

Yıllık Bildirim	Dönemini belirtiniz.	Uygun ☐	Uygun Değil ☐
Araştırma Sonuç Raporu	Tarihini belirtiniz.	Uygun ☐	Uygun Değil ☐
Güvenlilik Bildirimleri	Tarihini /dönemini belirtiniz.	Bir öğe seçin.	Bir öğe seçin.
Araştırmanın Tamamlanması Bildirimi	Tarihini belirtiniz.	Uygun ☐	Uygun Değil ☐
Diğer	-	Uygun ☐	Uygun Değil ☐

ARAŞTIRMAYA İLİŞKİN DEĞERLENDİRME

Araştırmada plasebo kullanılıyor mu?	Evet	Evet ise; plasebo kullanımı etik ve bilimsel açıdan uygun mu? Uygun ☒ Uygun Değil ☐ Açıklama:
Araştırmada tüm DNA analizi yapılıyor mu?	Hayır	Evet ise; DNA analizi yapılması etik ve bilimsel açıdan uygun mu? Uygun ☐ Uygun Değil ☐

		Açıklama:
Araştırmaya kısıtlılar, çocuklar, gebeler, johusalar ve emziren kadınlar, yoğun bakımdaki ve bilinci kapalı kişiler ile şahsen olur veremeyecek kişiler veya etkilenebilir özneler gibi hassas bir popülasyon dahil edilecek mi?	Hayır	**Evet ise; araştırmanın bu popülasyonda yapılmasına dair gerekçe ve seçilen bu popülasyona yönelik alınacak tedbirler uygun mu?** Uygun ☐ Uygun Değil ☐ Açıklama:
Araştırma pediatrik popülasyonda yürütülen bir klinik araştırma mı?	**Hayır**	
Evet ise; Çocuk sağlığı ve hastalıkları uzmanının görüşü alındı mı?	Bir öğe seçin.	Bir öğe seçin.
Çocuk sağlığı ve hastalıkları uzmanı tarafından araştırmanın pediatrik popülasyonda yürütülmesi bilimsel ve etik açıdan uygun bulundu mu?	Bir öğe seçin.	**Hayır ise gerekçesini belirtiniz;**
Araştırma yenidoğanlarda yürütülen bir klinik araştırma mı?	**Hayır**	
Evet ise; yenidoğan uzmanının görüşü alındı mı?	Bir öğe seçin.	Bir öğe seçin.
Yenidoğan uzmanı tarafından araştırmanın yenidoğanlarda yürütülmesi bilimsel ve etik açıdan uygun bulundu mu?	Bir öğe seçin.	**Hayır ise gerekçesini belirtiniz;**
Araştırma diş hekimliği alanında bir klinik araştırma mı?	**Evet**	
Evet ise; ilgili alanda uzman diş hekimi görüşünün alınması gerekli mi?	**Hayır**	Bir öğe seçin.
Evet ise; Diş hekimi tarafından araştırmanın yürütülmesi bilimsel ve etik açıdan uygun bulundu mu?	**Evet**	**Hayır ise gerekçesini belirtiniz;**

KARAR BİLGİLERİ

Karar No:	2024-11- 03	Tarih:	24.06.2024

İlk Uygunluk Başvurusu:

Uygun ☒

Yukarıda bilgileri verilen başvuru dosyası ile ilgili belgeler araştırmanın/çalışmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiş ve uygun bulunmuş olup araştırmanın/çalışmanın başvuru dosyasında belirtilen merkezlerde gerçekleştirilmesinde etik ve bilimsel sakınca bulunmadığına toplantıya katılan etik kurul üye tam sayısının salt çoğunluğu ile karar verilmiştir.

☐ *Uygun bulunan araştırmanın 27 Mayıs 2023 tarih ve 32203 sayılı Resmi Gazete'de yayımlanarak yürürlüğe giren Beşeri Tıbbi Ürünlerin Klinik Araştırmaları Hakkında Yönetmelik kapsamında yer alması nedeni ile araştırmanın başlatılabilmesi için Türkiye İlaç ve Tıbbi Cihaz Kurumu'ndan izin alınması gerekmektedir.*

☐ *Uygun bulunan araştırmanın 02.06.2021 tarihli ve 31499 sayılı Resmi Gazete' de yayımlanan Tıbbi Cihaz Yönetmeliği kapsamında CE işareti taşımayan tıbbi cihaz ile yapılan Tıbbi Cihaz Klinik Araştırması olması nedeniyle araştırmanın başlatılabilmesi için etik kurul onayı alındıktan sonra Türkiye İlaç ve Tıbbi Cihaz Kurumu'ndan izin alınması.*

☐ *Uygun bulunan araştırmanın/çalışmanın 02.06.2021 tarihli ve 31499 sayılı Resmi Gazete' de yayımlanan Tıbbi Cihaz Yönetmeliği kapsamında CE işareti taşıyan ve teknik dokümantasyonunda belirtilen kullanım amacına uygun olarak kullanılan tıbbi cihazla yapılan Tıbbi Cihaz Klinik Araştırması ve Tıbbi Cihazlar ile Yürütülen Piyasaya Arz Sonrası Çalışma olması nedeni ile araştırmanın/çalışmanın başlatılabilmesi için etik kurul onayı alındıktan sonra Türkiye İlaç ve Tıbbi Cihaz Kurumu'na bildirim yapılması gerekmektedir.*

☐ *Uygun bulunan çalışmanın 02.06.2021 tarihli ve 31499 sayılı Resmi Gazete' de yayımlanan İn Vitro Tanı Amaçlı Tıbbi Cihaz Yönetmeliği kapsamındaki İn Vitro Tanı Amaçlı Tıbbi Cihazlar İle Yürütülen;*

- *Amacı yalnızca performans değerlendirmek olan ve cerrahi prosedürler yoluyla numune alımının yapıldığı Performans Değerlendirme Çalışması,*
- *Yürütülmesinde ilave girişimsel prosedürler veya gönüllüler için başka riskler bulunan Performans Değerlendirme Çalışması,*
- *Test sonuçlarının hasta yönetimi kararlarını etkileyebildiği veya tedaviye yön vermek üzere kullanılabildiği Performans Değerlendirme Çalışması,*

olması nedeni ile çalışmanın başlatılabilmesi için etik kurul onayı alındıktan sonra Türkiye İlaç ve Tıbbi Cihaz Kurumu'ndan izin alınması gerekmektedir.

☐ *Uygun bulunan çalışmanın 02.06.2021 tarihli ve 31499 sayılı Resmi Gazete' de yayımlanan İn Vitro Tanı Amaçlı Tıbbi Cihaz Yönetmeliği kapsamındaki;*

- *Destek tanı cihazına ilişkin sadece artık numune kullanılarak yapılan Performans Değerlendirme Çalışması,*
- *Teknik dokümantasyonunda belirtilen kullanım amacına uygun olarak kullanılan ve gönüllülerin ilave olarak girişimsel veya külfetli prosedürlere tabi tutulduğu İn-Vitro Tanı Amaçlı Tıbbi Cihazlar İle Yürütülen Piyasaya Arz Sonrası Çalışması,*

olması nedeni ile çalışmanın başlatılabilmesi için etik kurul onayı alındıktan sonra Türkiye İlaç ve Tıbbi Cihaz Kurumu'na bildirim yapılması gerekmektedir.

☐ *Uygun bulunan 02.06.2021 tarihli ve 31499 sayılı Resmi Gazete' de yayımlanan İn Vitro Tanı Amaçlı Tıbbi Cihaz Yönetmeliği kapsamındaki İn Vitro Tanı Amaçlı Tıbbi Cihazlar ile yürütülen yukarıda yer alan çalışmalar dışında kalan Performans Değerlendirme Çalışmaları etik kurul kararı ile başlatılabilir, Türkiye İlaç ve Tıbbi Cihaz Kurumu izni veya Türkiye İlaç ve Tıbbi Cihaz Kurumu' na bildirim yapılması gerekmemektedir.*

☐ *Uygun bulunan çalışmanın Sağlık Hizmetleri Genel Müdürlüğünün 5/4/2018 tarihinde yayımladığı 2018/10 sayılı Genelge kapsamında yer alan kök hücreler ile yapılan klinik araştırma olması nedeni ile araştırmanın başlatılabilmesi için Sağlık Hizmetleri Genel Müdürlüğü'nden izin alınması gerekmektedir.*

☐ *Uygun bulunan beşeri tıbbi ürünlerin gözlemsel çalışması etik kurul kararı ile başlatılabilir, Bakanlık izni gerektirmemektedir.*

☐ *Uygun bulunan çalışmanın 3359 sayılı Sağlık Hizmetleri Temel Kanunu Ek 10. Madde kapsamında yer alan*
•Geleneksel ve tamamlayıcı tıp uygulamalarına ilişkin araştırmalar dışındaki tedavi yöntemlerine ilişkin çalışma,
•Özel tıbbi amaçlı gıdalarda kullanım amacına ilişkin çalışma,
•Gıda ve takviye edici gıdalarda sağlık beyanı kullanımına ilişkin çalışma
•Düşük riskli bilimsel çalışma
olması nedeni ile çalışmanın başlatılabilmesi için Türkiye İlaç ve Tıbbi Cihaz Kurumu'na başvuru yapılması gerekmektedir.

Uygun Değil ☐

Yukarıda bilgileri verilen başvuru dosyası ile ilgili belgeler araştırmanın/çalışmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiş ve araştırmanın/çalışmanın yürütülmesi uygun bulunmamıştır.

Gerekçe:

Revizyon ☐

Yukarıda bilgileri verilen başvuru dosyası ile ilgili belgeler araştırmanın/çalışmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiş olup aşağıda belirtilen eksiklikler tespit edilmiştir;

Talep edilen revizyonları belirtiniz.

Etik Kurul Başk
Unvanı/Adı/Soy
İmza:

SİL

Değişiklik/Önemli Değişiklik Başvurusu:

Uygun ☐

Araştırmanın yürütülmesine ilişkin yukarıda belirtilen bilgi/belge değişikliği/önemli değişikliği talebi/talepleri araştırmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiş ve uygun bulunmuş olup değişikliğin/değişikliklerin uygulanmasında etik ve bilimsel sakınca bulunmadığına toplantıya katılan etik kurul üye tam sayısının salt çoğunluğu ile karar verilmiştir.

Uygun Değil ☐

Araştırmanın yürütülmesine ilişkin yukarıda belirtilen bilgi/belge değişikliği/önemli değişikliği talebi/talepleri araştırmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiş ve değişikliklerin uygulanması uygun bulunmamıştır.

Gerekçe:

Revizyon ☐

Yukarıda belirtilen bilgi/belge değişikliği/önemli değişikliği talebi/talepleri araştırmanın gerekçe, amaç, yaklaşım ve yöntemleri dikkate alınarak incelenmiş olup aşağıda belirtilen eksiklikler tespit edilmiştir;

Revizyon talep edilen dokümanı belirtiniz.

Etik Kurul Başk
Unvanı/Adı/Soy
İmza

VGÜNSEL

[redacted]

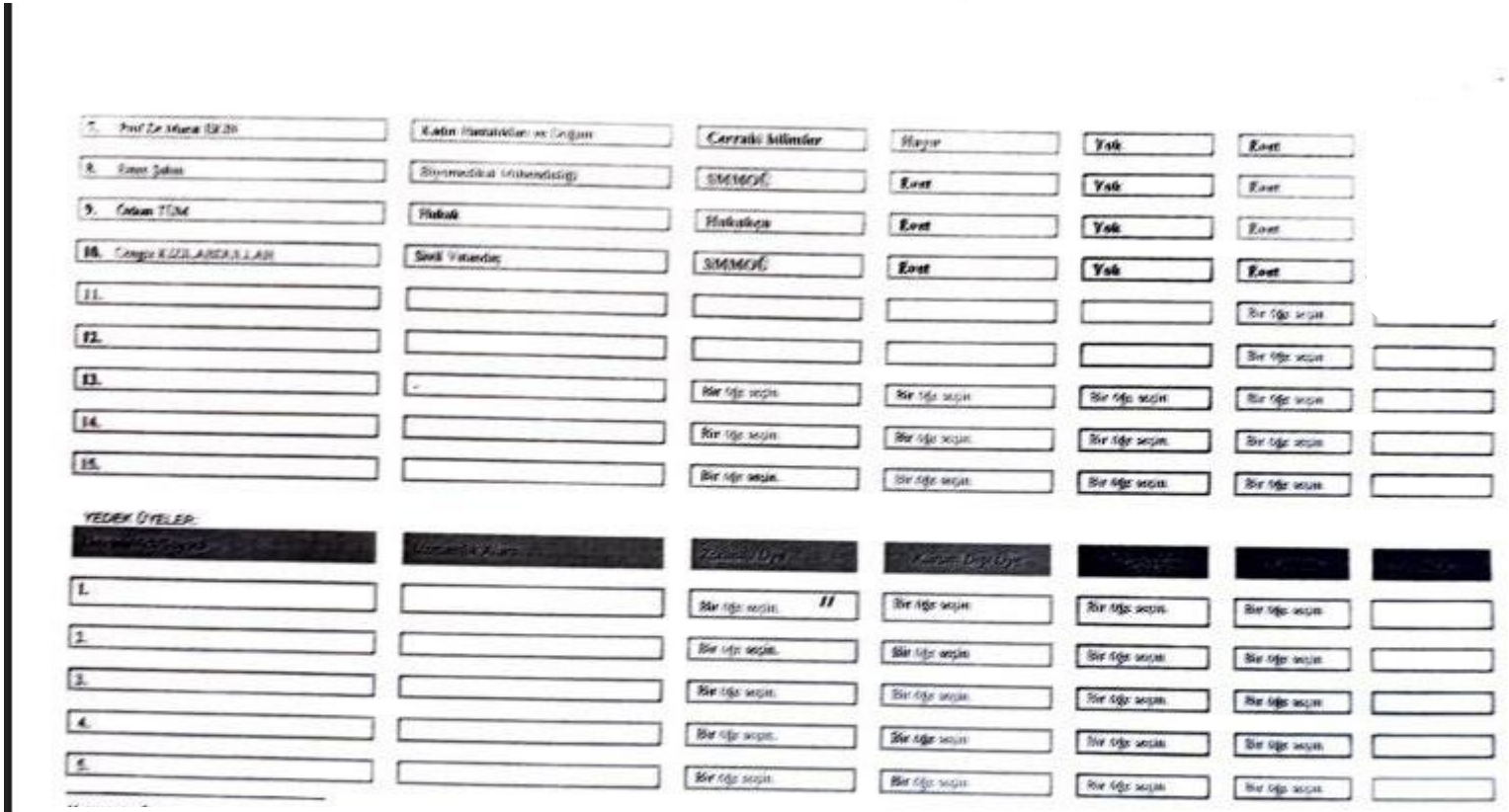
- *Biyoloji ve Tıbbın Uygulanması Bakımından İnsan Hakları ve İnsan Haysiyetinin Korunması Sözleşmesi: İnsan Hakları ve Biyotıp Sözleşmesi*
- *Biyotıp Araştırmalarına İlişkin İnsan Hakları ve Biyotıp Sözleşmesine Ek Protokol*
- *Sağlık Hizmetleri Temel Kanununun Ek 10 uncu maddesi*
- *Beşeri Tıbbi Ürünlerin Klinik Araştırmaları Hakkında Yönetmelik*
- *İyi Klinik Uygulamaları Kılavuzu*
- *Klinik Araştırmalar ve Biyoyararlanım / Biyoeşdeğerlik Çalışmaları Etik Kurullarının Standart Çalışma Yöntemi Esasları*

ETİK KURUL ÜYELERİ

ASİL ÜYELER:

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
1. Doç.Dr.Gülsüm Oya HERGÜNSEL	Anestezi ve Reanimasyon	Cerrahi bilimler [10]	Hayır	Yok	Evet
2. Prof.Dr.Sadık Sami HATİPOĞLU	Çocuk Sağlığı ve Hastalıkları	Dahili bilimler	Hayır	Yok	Evet
3. Prof.Dr.Asuman GEDİKBAŞI	Biyokimya	Temel bilimler	Evet	Yok	Evet
4. Prof.Dr.Ufuk EMEKLİ	Plastik, Rek. Ve Estetik Cerrahi	Cerrahi bilimler	Evet	Yok	Evet
5. Uz.Dr.Gülay ÖZGÖN	Farmakolog	Farmakolog	Evet	Yok	Evet
6. Uz.Dr.Kaya Sami NİZAMOĞLU	Halk Sağlığı	Temel bilimler	Evet	Yok	Evet

[9] Üyenin araştırma ile ilişkisi bulunması durumunda araştırmaya ilişkin görüşmelerin yapıldığı sırada tartışmalara katılamaz ve kararı imzalayamaz. Katılım durumunun da işaretlenmesi gerekmektedir.
[10] SMMOÜ: Sağlık Meslek Mensubu Olmayan Üye



7.	[redacted]	Cerrahi bilimler	Hayır	Yok	Evet	
8.	[redacted]	[redacted]	Evet	Yok	Evet	
9.	[redacted]	Histoloji	Evet	Yok	Evet	
10.	[redacted]	[redacted]	Evet	Yok	Evet	
11.					Bir öğe seçin.	
12.					Bir öğe seçin.	
13.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
14.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
15.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	

YEDEK ÜYELER

1.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
2.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
3.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
4.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
5.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	

6.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
7.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
8.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
9.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
10.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
11.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
12.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
13.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
14.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	
15.		Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	Bir öğe seçin.	

Toplantıya katılım sağlayan yedek üye/üyeler varsa katılım gerekçesini (ilanı ile ilgili görüş almak, zorunlu üyenin toplantıya katılım sağlayamaması, yeterli üye sayısına ulaşmak vb) belirtiniz. Yedek üye asil üye olarak atanmadığı sürece asil üyeler arasında ismi belirtilememelidir.	
** *Kararı uygun bulmayan üye varsa katılım durumu evet işaretlenmeli ancak kararı imzalamamalıdır!*	
Kararı uygun bulmayan üye var mı?	**Hayır**
*Kararı uygun bulmayan üyenin gerekçesini şerh düşmesini dayanakları ile birlikte belirtiniz.**	

Danışman Görüşü [1]	
Danışman Görüşü Alındı mı?	Hayır
Danışmanın Uzmanlık Alanı	
Danışmanın çıkar çatışması var mı?	Bir öğe seçin.
Danışman Görüşü	Bir öğe seçin.
Açıklama	Bu bölümde danışmanın görüşünü ayrıntılı şekilde belirtiniz.

A.2 MINISTRY OF HEALTH OF THE REPUBLIC OF TÜRKIYE TITCK RESEARCH START APPROVAL

T.C.
SAĞLIK BAKANLIĞI
Türkiye İlaç ve Tıbbi Cihaz Kurumu

Sayı : E-66175679-514.04.01-5581825 05.02.2025
Konu : Klinik Çalışma [24-AKD-254]

Sayın Prof. Dr. Şebnem DİRİKAN İPÇİ
Altınbaş Üniversitesi Diş Hekimliği Fakültesi
Periodontoloji Anabilim Dalı
Bakırköy/İSTANBUL

İlgi : a) 12.12.2024 tarihli, E-85521274-000-3545788 sayılı yazınız.
b) 30.12.2024 tarihli, E-66175679-514.04.01-1742408 sayılı yazınız.
c) 16.01.2025 tarihli, E-85521274-000-3605016 sayılı yazınız.

Aşağıda bilgileri verilen klinik araştırma başvurunuz ilgili mevzuat gereğince incelenmiş olup;

Araştırmanın Adı:	Cerrahi Olmayan Periodontal Tedaviye Ek Olarak Kullanılan Koenzim Q10'un Klinik ve Biyokimyasal Etkinliğinin Değerlendirilmesi
Koordinatör:	Prof. Dr. Şebnem DİRİKAN İPÇİ
Koordinatör Merkez:	Altınbaş Üniversitesi Diş Hekimliği Fakültesi
Onay Veren Etik Kurulun Adı:	Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu

Araştırmanın güncel Helsinki Bildirgesi'ne, iyi klinik uygulamalar ilkelerine ve ilgili mevzuata uygun olarak yürütülmesi,

Araştırma ekibinde yer alan sorumlu araştırmacıların ilgili mevzuat hükümleri gereğince araştırma süresince tam zamanlı olarak araştırma merkezinde bulunması,

Araştırma sırasında kullanılan araştırma ürünlerinden, araştırmada uygulanan işlemlerden ya da rutin tedavilerinde klinik araştırma gereğince uygulanacak kısıtlamalardan dolayı araştırmaya katılan gönüllülerde oluşabilecek zararlar ile araştırmada protokol dâhilinde kullanılacak tüm ürünlerin ve tetkiklerin destekleyici, destekleyici yoksa araştırmacı tarafından karşılanması,

Güvenlilik bildirimlerinin ilgili mevzuat gereği belirtilen sürelerde Kurumumuza ve ilgili etik kurula bildirilmesi,

Araştırmada kullanılan ürünlere ait Türkçe etiket örneğinin hazırlanması ve araştırma ürünlerinin üretiminin İyi İmalat Uygulamaları Kılavuzuna uygun olarak yapılması,

Kişisel verilerin gizliliğine riayet edilmek kaydıyla, izin verilen bu araştırmanın kamuya açık bir veri tabanına kaydedilmesi,

Araştırma ürünü ithal edilecek ise Kurumumuza ilgili başvuru formu ve ekleri ile müracaat edilmesi,

Araştırma sonunda artan araştırma ürünü olması halinde araştırma ürünü imha işlemlerinin ilgili mevzuata göre yapılması,

Araştırmanın başlamaması, iptali, durdurulması veya sonlandırılması halinde Kurumumuza ve ilgili etik kurula bildirilmesi ilgili mevzuata uygun şekilde ve belirtilen süreler dâhilinde bilgi verilmesi,

Bu belge, güvenli elektronik imza ile imzalanmıştır.
Belge Doğrulama Kodu: ZW56Q3NRYnUyZmxXSHY3Z1AxRG83YnUy Belge Takip Adresi:https://www.turkiye.gov.tr/saglik-titck-ebys

Söğütözü Mahallesi, 2176.Sokak No:5 06520 Çankaya/ANKARA
Telefon No: (0 312) 218 30 00 Faks No: (0 312) 218 34 60
e-Posta: halkla.iliskiler@titck.gov.tr İnternet Adresi: https://www.titck.gov.tr
Kep Adresi: titck@hs01.kep.tr

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T.C.
SAĞLIK BAKANLIĞI
Türkiye İlaç ve Tıbbi Cihaz Kurumu

Araştırma sonlandırıldığında, sorumlu araştırmacı tarafından araştırma ürününün yararlı olduğu belirlenirse ve alternatif bir tedavi seçeneği mevcut değilse araştırma ürünü ülkemiz piyasasında bulunana kadar destekleyici tarafından temin edilmesi,

Araştırma ile ilgili kayıtların tamamının araştırmanın bütün merkezlerde tamamlanmasından sonra en az 14 yıl süre ile saklanması,

Araştırma konusu ile ilgili ödemelerin, araştırma boyunca yapılacak olan eş zamanlı tedavi ve kurtarma tedavilerinin gönüllüye ödetilmeyeceği hususuna dikkat edilmesi gerekmektedir.

Uygun bulunan dokümanların listesi aşağıdaki tabloda verilmiştir. Bu dokümanların herhangi birinde değişiklik olduğu takdirde ilgili mevzuat hükümleri doğrultusunca başvuru yapılması gerekmektedir.

Dokümanın Adı	Tarih	Versiyon No
Araştırma Protokolü	18.06.2024	00
Bilgilendirilmiş Gönüllü Olur Formu	18.06.2024	00
Olgu Rapor Formu	18.06.2024	00
Bütçe	18.06.2024	00
Etik Kurul Kararı	24.06.2024	Karar No: 2024-11-03

İlgi (a) yazı ekindeki başvuru formunda belirtilen merkezde araştırmanın başlaması uygun bulunmuştur. Araştırma sürecinde yukarıda belirtilen hususların yerine getirilmesi gerekmektedir.

İlgili araştırma onayı, sunulan klinik araştırma tasarımının güncel Klinik Araştırma mevzuatına ve etik ilkelere uygun olduğunu belirtmekte olup, ruhsata esas teşkil edecek verilerin elde edilmesi için yeterli ve uygun tasarımda planlandığı anlamını taşımamaktadır.

Yazımızın bir örneğinin ilgili Etik Kurula iletilmesi hususunda gereği bilgilerinize sunulur.

Fatih TOPUZ
Kurum Başkanı a.
Daire Başkanı V.

Bu belge, güvenli elektronik imza ile imzalanmıştır.
Belge Doğrulama Kodu: ZW56Q3NRYnUyZmxXSHY3Z1AxRG83YnUy Belge Takip Adresi:https://www.turkiye.gov.tr/saglik-titck-ebys

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Kep Adresi: titck@hs01.kep.tr