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The Effect of *Zingiber, Alpinia Officinarum* with Periodontal Therapy on Clinical Outcome and Oxidative Stress

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Abstract: Many popular mouthwashes containing herbal products have helped to control dental plaque and gingivitis; however, they are used for a short time and only as an adjunct to other oral hygiene measures such as brushing and flossing. Recently, herbs such as Zingiber ginger and Alpinia officinarum, with antioxidant, antifungal, anti-inflammatory, and antibacterial properties apart from being cheap and safe, have been used as plant extracts in mouthwashes. The aim of this study was to assess the effect of both herbal mouthwashes and periodontal therapy on oxidative stress, total antioxidant capacity, and antioxidant enzyme activities in the saliva of patients with periodontitis as well as to investigate the association between oxidative stress, antioxidant enzymes, total antioxidant capacity, and periodontal parameters. 72 patients were selected using random sampling and divided into three categories. Each category consisted of 24 patients: the first group received non-surgical periodontal treatment and Zingiber ginger mouthwash, the second group received Alpine officinarum and non-surgical periodontal therapy, while the third control group received non-surgical periodontal therapy only. Periodontal parameters (Clinical Attachment Loss and Plaque Index) were recorded by a calibrated periodontal probe (William probe). Salivary oxidative stress (eight hydroxy deoxyguanosine) was measured by ELISA, and catalase and total antioxidant capacity were measured using a spectrophotometer. The concentration of salivary antioxidants significantly increased, and the periodontal parameter and eight hydroxy deoxyguanosine significantly decreased after two weeks. The p-value in the ginger group was ($P < 0.0001$). For the alpine officinarum group, the clinical parameters showed a significant decrease, and the p-value was ($P < 0.0001$). While catalase displayed a significant increase ($P < 0.0001$), the eight hydroxy deoxyguanosine markers showed a significant decrease ($P < 0.02$). Zingiber ginger and Alpine officinarum mouthwashes, in addition to periodontal therapy, can be effective in controlling inflammation, reducing oxidative stress, and improving dental health in patients with chronic periodontitis. Mostly positive associations were detected among clinical and biochemical parameters.

Keywords: oxidative stress, periodontitis, antioxidants.

生姜、高良姜配合牙周治疗对临床结果和氧化应激的影响

摘要：许多含有草药产品的流行漱口水有助于控制牙菌斑和牙龈炎；但是，它们的使用时间很短，并且仅作为其他口腔卫生措施（例如刷牙和使用牙线）的辅助手段。近来，生姜和高良姜等草本植物除了价格便宜和安全外，还具有抗氧化、抗真菌、抗炎和抗菌的特性，已被用作漱口水中的植物提取物。本研究的目的是评估草药漱口水和牙周治疗对牙周炎患者唾液中氧化应激、总抗氧化能力和抗氧化酶活性的影响，并研究氧化应激、抗氧化酶、总抗氧化能力和牙周参数。使用随机抽样方法选择了72名患者，并将其分为三类。每组24例：第一组接受非手术牙周治疗和姜姜漱口水，第二组接受高山药材和非手术牙周治疗，而第三组对照组仅接受非手术牙周治疗。牙周参数（临床附着损失和牙菌斑指数）由校准的牙周探针（威廉探针）记录。通过酶联免疫

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吸附试验测量唾液氧化应激（八羟基脱氧鸟苷），并使用分光光度计测量过氧化氢酶和总抗氧化能力。两周后唾液抗氧化剂浓度显着增加，牙周参数和八羟基脱氧鸟苷显着下降。生姜组的p值为(磷<0.0001)。高山药材组临床参数显着下降，p值为（磷<0.0001）。虽然过氧化氢酶显着增加（磷<0.0001），但八个羟基脱氧鸟苷标记物显着降低（磷<0.02）。生姜和高山药用漱口水，除了牙周治疗外，还可以有效控制慢性牙周炎患者的炎症、减少氧化应激和改善牙齿健康。在临床和生化参数之间检测到大多数正相关。
关键词：氧化应激，牙周炎，抗氧化剂。

Abbreviations

CP - chronic periodontitis; OS - oxidative stress; TAOC - total antioxidant capacity; CAT - catalase; CAL - clinical attachment loss; PI - plaque index; 8-OHdG - eight hydroxy deoxyguanosine; NSPT - nonsurgical periodontal therapy; ROS - reactive oxygen species.

1. Introduction

Precisely 10% of the overall population is hugely exposed to severe periodontitis, 10-15% deny their exposure to it, and the rest alter between these two conditions. Periodontitis is the universal term for the extensive pathology of the human oral cavity [1]. It has been documented that periodontitis leads to tooth mobility and tooth loss; it impedes mastication, food tearing, and speech. Cosmetically, it can detract from smile esthetics due to gingival recession, negatively impacting self-confidence and social relations. The main characteristic of periodontitis is a lack of periodontal tissue support, known as clinical attachment loss, whereby a loss of alveolar bone, the existence of periodontal pockets, and the bleeding of gingiva are discernible through X-ray [2]. Oxidative stress, or excess oxygen reactive species (ROS), plays a critical role in the development and evolution of tissue injury and periodontal inflammation, which leads to tissue destruction and the creation of a proinflammatory state in periodontitis. This is because ROS can stimulate the production of proinflammatory molecules, regulate apoptosis, and activate immune cells that produce more ROS, resulting in a vicious circle of inflammation and enhanced tissue injury. In addition, ROS can stimulate bone resorption through osteoclastogenesis, leading to tooth mobility and eventual tooth loss. However, it is difficult to determine whether oxidative stress is a factor prior to the development of periodontitis, or whether it is only triggered as a result of periodontal inflammation [3]. Current interest in the use of herbal medicines is growing steadily in an effort to combat and prevent diseases, including periodontal diseases [4]. A study by Ahmad et al. [5] reported ginger supplementation, along with nonsurgical periodontal therapy (NSPT), decreased oxidative stress, improved the inflammatory and periodontal status, and increased the serum levels of antioxidant enzymes. It is therefore suggested that ginger supplementation combined with NSPT may be more effective in the control of systemic inflammation in T2DM patients with CP [5]. The active ingredients in ginger, such as β-bisabolene, shogaol, gingerol, and paradol have glycemic control, anti-inflammatory, antioxidant, anti-cancer, and anti-obesity properties [6]. The effectiveness of ginger in treating such diseases as nausea, rheumatism [7], and lipid profile disorders [8] has been proposed in some studies. Another study explained how ginger supplementation can significantly increase TAC levels. TAC is an antioxidant defense system indicator [9], and it is reasonable to suppose that when the determinants of TAC, namely GPx, CAT, and MDA, have improved due to ginger supplementation, TAC levels would increase as well [10]. An important member of the family Zingiberaceae, *Alpinia officinarum* (lesser galangal), is widely present in the tropical and subtropical regions of Southeast Asia. Its rhizomes are used as an anti-inflammatory, analgesic, and antioxidant agent in conventional medicine [11]. The major active component of *Alpinia officinarum*, the flavonoid galangin, was proven to exert strong antioxidative and radical scavenging effects [12]. To date, however, there is no comprehensive review on the effects of *Alpinia officinarum* on periodontal diseases in our community. To the best of our knowledge, moreover, there are no clinical trial studies that assess the effects of ginger and *Alpinia officinarum* mouthwashes, when combined with NSPT, on periodontal parameters, oxidative stress, and antioxidants. It is with a view to supply this information, as well as to investigate the association between periodontal parameters and biochemical markers in patients with chronic periodontitis, that this study has been conducted.

2. Material and Methods

All procedures involving human patients were approved by the ethics committees of the University of Duhok, Number 28012020-1 (28/1/2020). Furthermore, verbal informed consent was obtained from all the patients.

2.1. Subjects

The study population consisted of 72 patients (39 male and 33 female), aged 25-55, with chronic periodontitis (mild, moderate). NSPT was performed by a single dentist, who also collected the data. The selected patients were randomly divided into three groups. Each group consisted of 24 patients; each patient was given the same toothpaste and brush, and the mouth was washed after toothbrushing:

- *Group 1*: Patients who will receive NSPT and *Zngiber ginger* mouth wash (20 ml) 2 times per day for two weeks. The patients will advise swishing mouthwash for 30 seconds with oral hygiene instructions;
- *Group 2*: Patients who will receive NSPT and *Alpinia officinarum* mouth wash (20 ml) 2 times per day for two weeks. The patients will advise swishing mouthwash for 30 seconds with oral hygiene instructions;
- *Group 3*: Patients who received NSPT, with rinsing with normal water and oral hygiene instruction only. The salivary antioxidant parameter and periodontal measurement were measured at baseline and after two weeks.

2.2. Diagnosis

The patients were diagnosed at the College of Dentistry, Department of Periodontology.

2.3. Exclusion

History of systemic disease**,** taken antibiotics, anti-inflammatory or any other drugs for at least two months, smokers (cigarette and nergela)**,** vitamin supplement**,** those who had undergone any form of nonsurgical or surgical periodontal therapy in the last six months, pregnant and lactating mothers.

2.4. Type of Sample

Saliva.

2.5. Clinical Analysis

2.5.1. Periodontal Status Examination

The dental examination was done by one of the authors, a specialist dentist in a standardized environment, manipulating a calibrated periodontal probe, disposable mouth mirror, masks, gloves, tweezer, and tray. In the current study, the periodontal status of the participants is determined by the following indices. The PI system by Sillness defined four levels of quantity and quality of soft deposits: Score 0 - no plaque, Score 1 - a film of plaque adhering to the free gingival margin and adjacent areas of the tooth, Score 2 - moderate accumulation of soft deposits within the gingival pocket or on the tooth and gingival margin which can be seen with the naked eye, Score 3 - abundance of soft matter within the gingival pocket or on the tooth and gingival margin [13].

2.5.2. Clinical Attachment Loss Index

Clinical attachment loss was assessed by measuring the distance from the cementoenamel junction (CEJ) to the base of the probing pocket depth by using Williams graduated periodontal probe (William probe) [14]. The criteria of CAL included: 1-2 mm - mild periodontitis, 3-4 mm - moderate periodontitis, ≥ 5 mm - severe periodontitis.

2.6. Biochemical Analysis

For the collection of samples, participants were instructed not to eat, drink, chew gum, or brush teeth for at least 30 min before sampling after rinsing their mouths with water (to remove any food residue); then they were to wait 10 min before collection of saliva to avoid diluting it. Five milliliters of unstimulated saliva was collected from patients between 9 and 11 a.m. to minimize diurnal variation [15]. The participants were asked to sit comfortably and were instructed to allow the saliva to pool in the bottom of their mouth and drain it into plastic containers for 5 min and store it in ice. Then after collecting samples, in order to separate impurities and squamous cells of the oral mucosa, the samples were centrifuged at 4000 rpm for 10 min at room temperature. Then the supernatant was transferred to a laboratory and frozen at -20°C until it was tested for TAOC, 8OHdG, and CAT.

- *TAOC*: TAC measurements on saliva samples were carried out using the commercially available antioxidant assay kit (Rel Assay Diagnostics, MEGA TIP group, Turkey). Measurements were done as instructed by the manufacturer. The TAC assay was based on the measurements of the reduction of 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid; ABTS) radical. For the measurements of salivary TAC, 225 µl of assay Reagent 1 (acetate buffer; pH 5.8) was mixed with 5 µl of saliva and the absorbance was measured at 420 nm after 30 s of incubation. Afterwards, 20 µl of Reagent 2 (ABTS, 30 mM in acetate buffer; pH 3.6) was added into each sample and the absorbance at 420 nm was measured after 5 min of incubation. TAC was calculated based on differences in absorbance at 420 nm before and after adding Reagent 2. The assay was calibrated using Trolox, and the results were expressed in terms of mM Trolox equivalent per liter (mmol Trolox equiv/L) [16];

- *Human (CAT) enzyme:* The CAT assay mixture of 3 ml consisted of 0.05 ml extract, 1.5 ml phosphate buffer (100 mM buffer, pH 7.0), 0.5 ml H2O2, and 0.95 ml distilled water. A decrease in the absorbance was recorded at 240 nm. The CAT activity was expressed as μmol of H2O2 oxidized per minute per gram FW [17];
- *8-OHdG Elisa kit*: Salivary 8-OHdG levels were also measured by an ELISA kit (OxiSelect™ Oxidative DNA Damage ELISA Kit, Cat# STA-320, Cell Biolabs, Inc. San Diego, USA), according to the manufacturer's instructions. A volume of 50 μl of saliva or 8-OHdG standard was used for the assay. At the end reaction, the absorbance was read spectrophotometrically at 450 nm, and the concentrations of 8-OHdG in the samples were determined by comparison against a pre-determined standard curve [18].

2.7. Preparation of Plant Extract

2.7.1. Cold Aqueous Extract Preparation

Rhizomes of the plant were obtained from the local Duhok market, Duhok, Iraqi Kurdistan Region, from April 8 to June 8, 2020. Authentication for the plant was performed at Agricultural Engineering College, Department of Forestry, Duhok University. The rhizomes were cleaned and peeled where fresh peels were minced to very fine pieces for extraction. Fifty grams of peeled rhizomes were mixed with 200 ml of distilled water using an electrical blender, and the mixture will then be stirred magnetically for 24 h at room temperature. The residue will be removed by filtration using filter paper (Whattman No. 1), and the filtrate will be concentrated using a rotary evaporator at 40◦C [19].

2.7.2. Preparation of 2% Herbal Mouthwash Solution

Two grams of plant water extract will be put in a 100-ml volumetric flask, and the volume will complete to 100 ml using distal water [20].

2.8. Statistical Analyses

The data were entered in the SPSS software (Ver. 18). The analyses were conducted using an independent t-test, unpaired T-test, and Pearson's correlation. The significance level was ≤ 0.05 in all tests.

3. Result

3.1. Profile for the Study Population

Our results showed that (CAL, PI) and 8-OHdG parameters between baseline and after two weeks were very highly significant (p-value ≤ 0.0001). In addition, there were highly significant changes in the levels of CAT and TAOC after two weeks (p-value ≤ 0.001 and ≤ 006, respectively) (Table 1).

Table 1 General characteristic feature of the study population

	M ± SD		
	Baseline	**2 wks**	**P-value**
CAL (mm)	2.02 ± 0.58	1.61 ± 0.56	0.0001***
PI	2.27 ± 0.54	1.56 ± 0.56	0.0001***
TAOC (mmol/L)	0.40 ± 0.14	0.47 ± 0.14	0.001**
CAT (u/L)	0.29 ± 0.10	0.33 ± 0.13	0.006**
8OHdG (ng/ml)	2.44 ± 0.87	2.03 ± 0.70	0.0001***

*** p ≤ 0.0001
** p ≤ 0.001 and ≤ 006

3.2. Zingiber Ginger

After two weeks, there was a highly significant difference in all parameters (CAL, PI, TAO, CAT, and 8-OHdG) (p-value < 0.001 for *the ginger* group as in Table 2).

Table 2 Comparison within the group (Zingiber ginger) after two weeks (p ≤ 0.001)

	Ginger		
	Baseline	**2 wks**	**p-value**
CAL (mm)	2.15 ± 0. 60	1.53 ± 0.49	< 0.001
PI	2.32 ± 0.55	1.41 ± 0.60	< 0.001
TAOC (mmol/L)	0.43 ± 0.13	0.56 ± 0.12	< 0.001
8OHdG (ng/ml)	2.93 ± 1.03	2.07 ± 0.95	< 0.001
CAT (u/L)	0.32 ± 0.12	0.44 ± 0.15	< 0.001

According to the Pearson correlation between CAL and TAOC for the ginger group, although it was a positive correlation (r = 0.19), it was nonsignificant (p-value = 0.36) (Fig. 1).

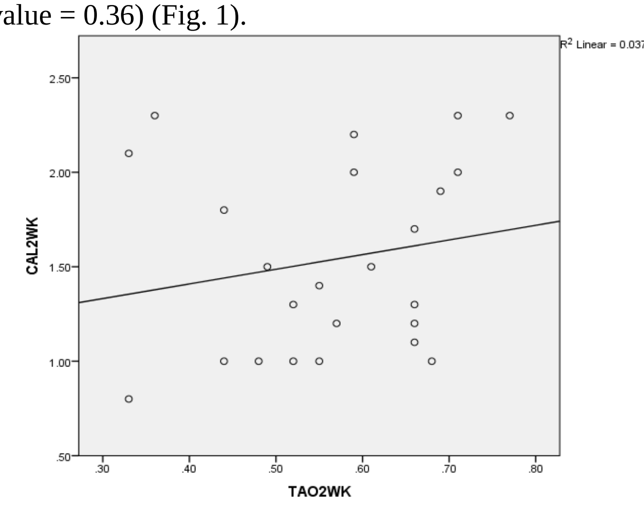

Fig. 1 Correlation between CAL and TAOC after two weeks (The authors' elaboration)

After two weeks, there was a weak positive correlation (r = 0.02) between CAL and 8-OHdG. The result was nonsignificant (p-value = 0.9) (Fig. 2).

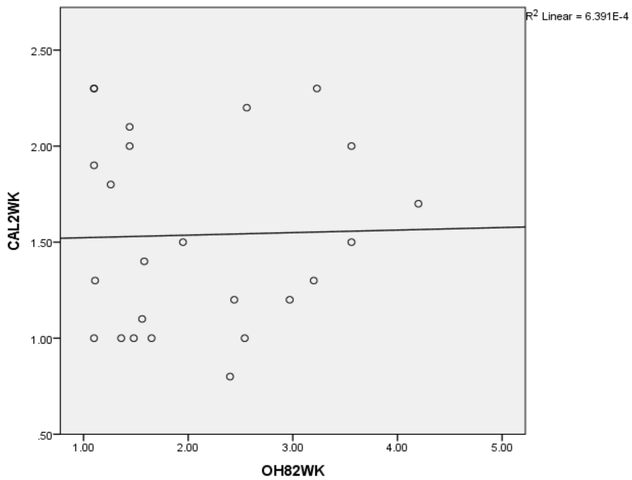

Fig. 2 Correlation between CAL and 8OHdG after two weeks (The authors' elaboration)

The same as for CAL and CAT, the Pearson correlation was positive (r = 0.24). The data was nonsignificant (p-value = 0.25) (Fig. 3).

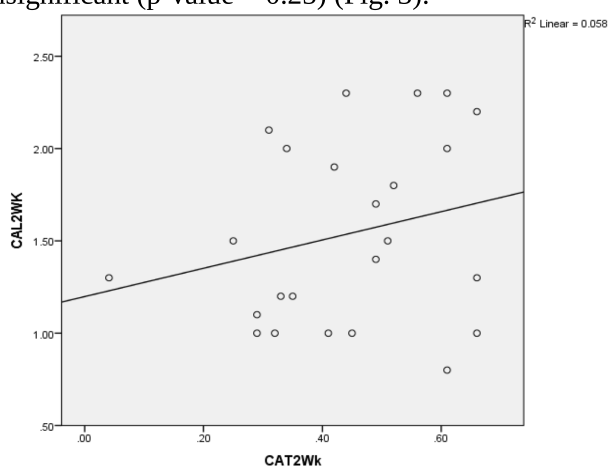

Fig. 3 Correlation between CAL and CAT after two weeks (The authors' elaboration)

For PI and TAOC, the correlation was positive (r = 0.23), and the p-value was 0.26, nonsignificant (Fig. 4).

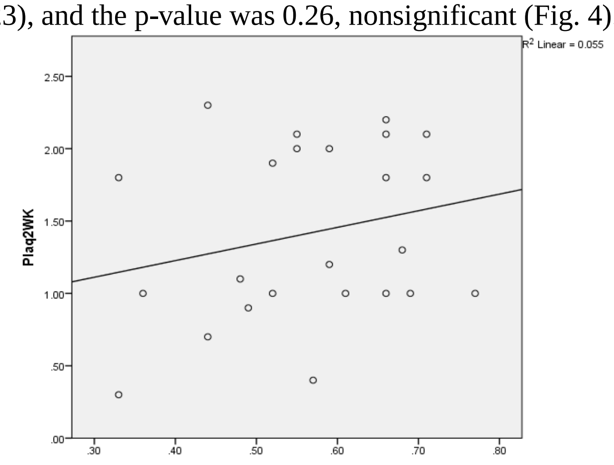

Fig. 4 Correlation between PI and TAOC after two weeks (The authors' elaboration)

There was a negative correlation between PI and 8-OHdG (r = - 0.157), and the data were nonsignificant (p-value = 0.46) (Fig. 5).

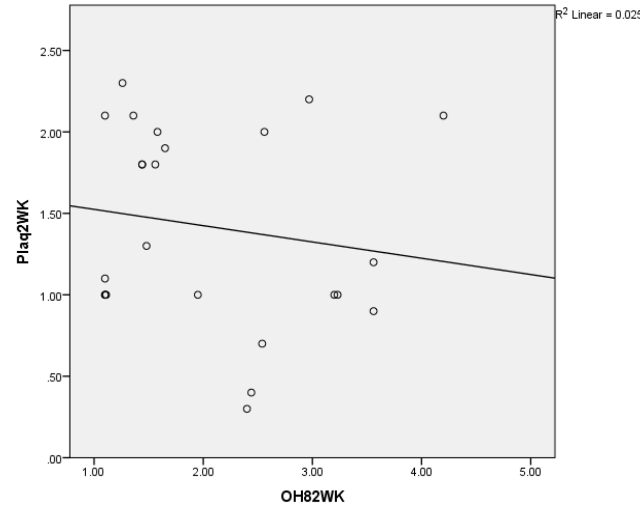

Fig. 5 Correlation between PI and 8OH-dG after two weeks (The authors' elaboration)

Also, there was a negative correlation between PI and CAT after two weeks (r = - 0.022), and the p-value of 0.91 was nonsignificant (Fig. 6).

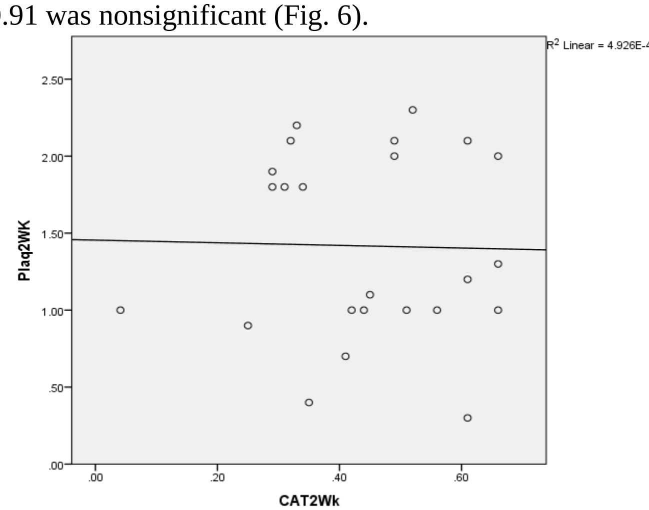

Fig. 6 Correlation between PI and CAT after two weeks (The authors' elaboration)

3.3. Alpine Officinarum

Within-group comparison in the intervention group showed a significant difference in the mean of CAL and plaque index (p-value < 0.001).

The mean of CAT was significantly higher after two weeks, 0.28 ± 0.09 (p-value < 0.001), while there was no significant difference in TAO pre- and post-intervention. In addition, the mean changes in salivary levels of 8-OHdG were significantly decreased in the post-intervention group to 1.90 ± 0.36 (p-value < 0.02) (Table 3).

Table 3 Comparison within the group (*Alpine officinarum*) after two weeks

	Alpine officinarum		
	Baseline	**2 wks**	**p-value**
CAL (mm)	2.05 ± 0.60	1.45 ± 0.61	< 0.001
PI	2.38 ± 0.46	1.38 ± 0.41	< 0.001
TAOC (mmol/L)	0.41 ± 0.12	0.43 ± 0.13	NS
8OHdG (ng/ml)	2.02 ± 0.49	1.90 ± 0.36	< 0.02
CAT (u/L)	0.26 ± 0.09	0.28 ± 0.09	< 0.001

Notes: NS – nonsignificant; p < 0.001

There was a positive correlation (r = 0.13) between CAL and TAOC after two weeks of treatment, but it was nonsignificant (p-value = 0.54) (Fig. 7).

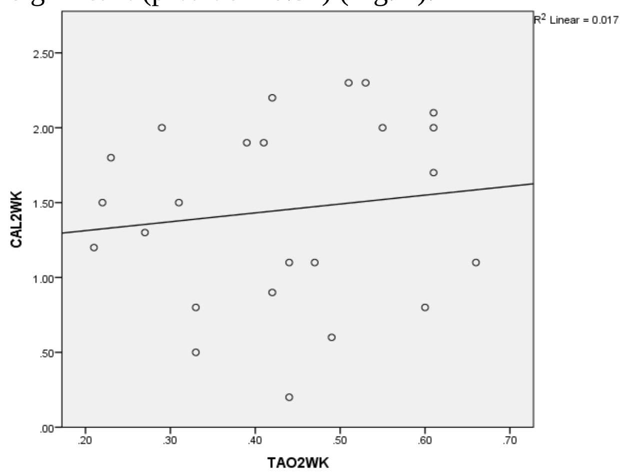

Fig. 7 Correlation between CAL and TAOC after two weeks (The authors' elaboration)

Although there was a strong positive relation (r = 0.39) between CAL and 8-OHdG, it was significant (p-value = 0.05) (Fig. 8).

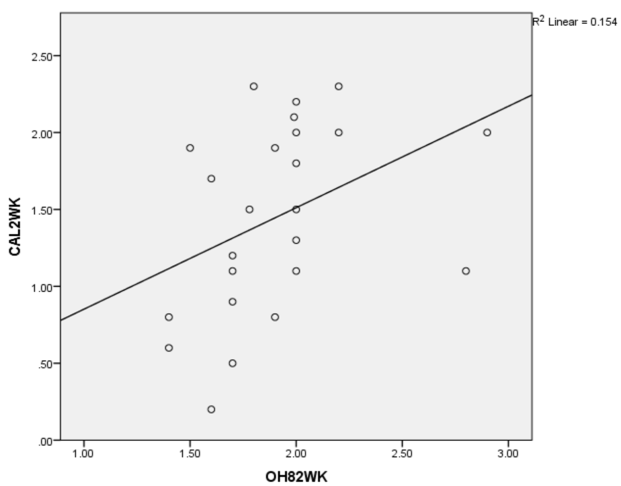

Fig. 8 Correlation between CAL and 8OHdG after two weeks (The authors' elaboration)

For CAT and CAL, there was a positive correlation (r = 0.10), but the result was nonsignificant (p-value = 0.62) (Fig. 9).

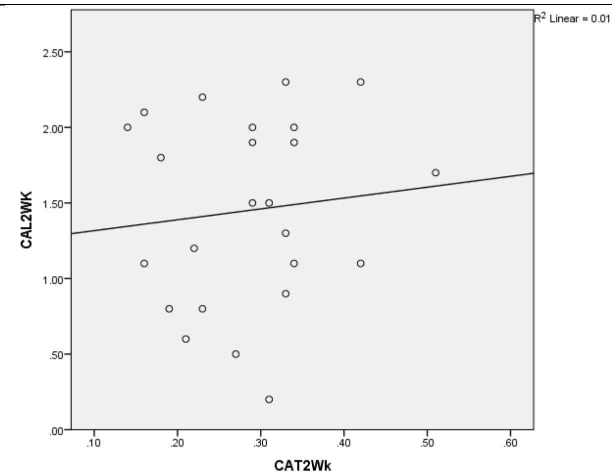

Fig. 9 Correlation between CAL and CAT after two weeks (The authors' elaboration)

A positive correlation was found between PI and TAOC (r = 0.07), but it was nonsignificant (p-value = 0.72) (Fig. 10).

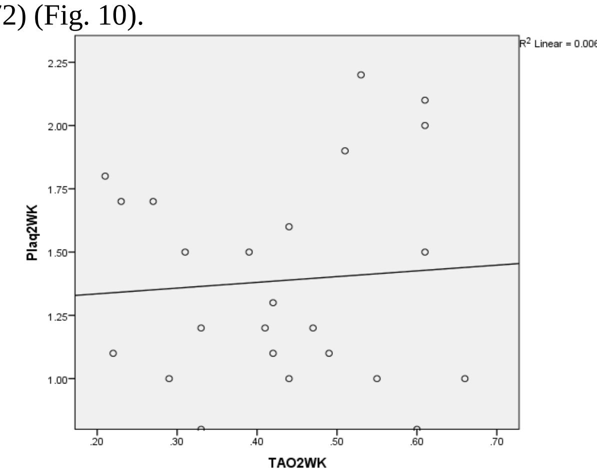

Fig. 10 Correlation between PI and TAOC after two weeks (The authors' elaboration)

Also, a positive relationship was found between PI and 8-OHdG (r = 0.38), but it was nonsignificant (p-value = 0.06) (Fig. 11).

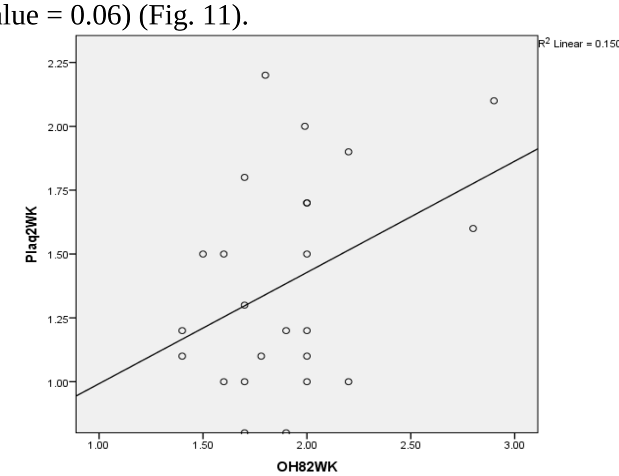

Fig. 11 Correlation between PI and 8OHdG after two weeks (The authors' elaboration)

Finally, the correlation between CAT and PI was positive (r = 0.25) and nonsignificant (p-value = 0.23) (Fig. 12).

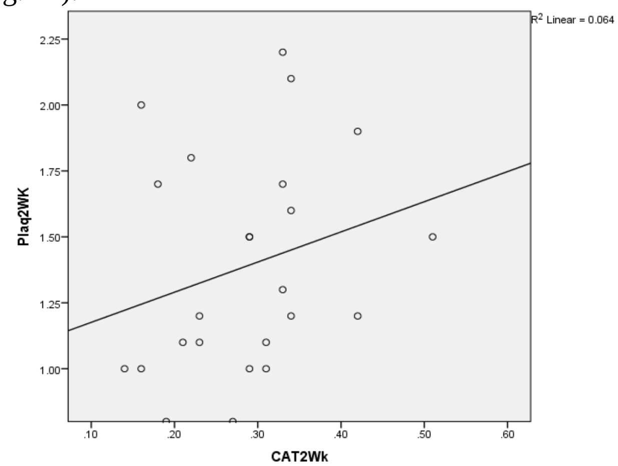

Fig. 12 The correlation between PI and CAT after two weeks (The authors' elaboration)

3.4. Comparison between Two Groups after Two Weeks (*Zingiber Ginger* and *Alpine Officinarum*)

After two weeks, there was no significant difference in the CAL index, plaque index, and 8-OHdG for both groups (Table 4). The mean of CAT showed a significant difference between the two groups, 0.44 ± 0.15 and 0.28 ± 0.09, respectively (p-value < 0.001). Patients under ginger and *Alpine* mouthwash showed significant differences in TAOC (p-value < 0.001) (Table 4).

Table 4 Comparison between Zingiber ginger and Alpine officinarum after two weeks

	Ginger	Alpine officinarum	p-value
CAL mm	1.53 ± 0.49	1.45 ± 0.61	NS
PI	1.41 ± 0.60	1.38 ± 0.41	NS
TAOC mmol/L	0.56 ± 0.12	0.43 ± 0.13	< 0.001
8OHdG ng/ml	2.07 ± 0.95	1.90 ± 0.36	NS
CAT u/L	0.44 ± 0.15	0.28 ± 0.09	< 0.001

4. Discussion

The effectiveness of plant extracts and natural products has been demonstrated in numerous studies concerning their use in the treatment of oral diseases [21]. However, to the best of our knowledge, no prior study has investigated the effects of *Z. officinale* and *A. officinarum* in combination with NSPT on parameters such as the antioxidant, inflammatory, and periodontal statuses of subjects with CP. In the present randomized clinical trial, which involved 72 participants with CP, significant statistical differences were identified between the concentrations of the salivary antioxidant and the levels of OS before and after periodontal therapy, in addition to significant upsurges in the levels of antioxidants following treatment. Moreover, significant progress was observed in relation to dental parameters. Periodontal therapy decreases the OS biomarker levels to values similar to those detected in periodontally healthy individuals [22]. Most previous saliva studies have confirmed a significant reduction in the 8-OHdG levels among non-smokers following periodontal treatment [23]. The salivary antioxidant levels in subjects with generalized severe to moderate CP are known to be considerably elevated following the etiotropic phase of periodontal therapy, which indicates the potentially beneficial effect of periodontal therapy on the salivary antioxidant levels of subjects with periodontitis, as suggested by the findings of our study [24]. By contrast, Saufi et al. [25] stated that scaling and root planning had no effect on the total antioxidant status of the saliva and gingival crevicular fluid in patients with CP. Neha et al. [26] found that the mean plasma TAC level was lower in CP patients when compared with healthy controls, although it increased following NSPT. Nonsurgical therapy can restore and control the antioxidant capacity by locally and systemically modifying the levels of ROS and antioxidant molecules generated.

4.1. Zingiber Ginger and Periodontal Parameters

A member of the *Zingiberaceae* family, ginger (*Z. officinale*) is a spice commonly used in traditional diets worldwide [27]. The results of our study revealed that the use of ginger mouthwash for two weeks in combination with NSPT significantly reduced the participants' mean PI and CAL after the intervention. In accordance with our findings, Zari et al. [5] reported that the consumption of a ginger supplement for eight weeks along with NSPT considerably decreased the subjects' mean CAL and PD following the intervention. A PubMed-based survey of studies conducted in the last ten years (2005–2016) using the keywords "properties of ginger," "uses of ginger in dentistry," and "ginger extract in oral diseases" yielded 15 studies that established the antibacterial, antifungal, antineoplastic, antioxidant, and anti-inflammatory properties of ginger in the field of dentistry [29]. Swamy et al. [30] reported the effectiveness of ginger against selective human pathogenic bacteria due to the diverse secondary metabolites present in the spice, which provided evidence of the antimicrobial efficiency of ginger.

4.2. Correlations between the Parameters

The relationships between the clinical periodontal and biochemical parameters were assessed in the ginger group after two weeks. Interestingly, no noteworthy relationships were identified between the biochemical and clinical periodontal information concerning the participants' CAL. Yet, the participants' salivary 8-OHdG levels and CAT were found to be adversely correlated with their dental PI, while their salivary

TAOC levels were positively related to their dental PI. By contrast, in the *A. officinarum* group, no noteworthy relationships were found after therapy between the biochemical and clinical parameters and the participants' PI, except for a positive relationship between their CAL and 8-OHdG levels. Thus, the association between antioxidant levels, OS, and periodontal infection severity observed in this study may be attributed to a disequilibrium between the participants' antioxidants and ROS levels. Only a limited number of prior studies have investigated the association between subjects' saliva antioxidant capacity and their periodontal clinical parameters. For example, in one study, the saliva and serum obtained from the participants revealed no significant associations between the clinical and biochemical parameters [31].

4.3. Ginger, Antioxidant Levels, and Oxidative Stress

The identification of characteristic compounds for the avoidance of ROS-related disorders by inflammatory cells represents a critical methodology for antioxidant treatment, while the suppression of ROS generation by shogaols and gingerols could be attributed to various pharmacological actions on the part of ginger [32]. In combination with NSPT, ginger supplementation has previously been found to decrease OS, improve the inflammatory and periodontal status, and increase the serum levels of antioxidant enzymes [5]. In the present study, ginger intake was found to be related to decreased OS and periodontal parameters. However, contrary to the findings of our study, Abdul Hanif et al. [34] found ginger to have no impact on OS, although it should be remembered that their research involved an in vitro study. In this study, after two weeks, the impact of Zingiber ginger on the participants' OS and antioxidant levels appeared to be significant. Other studies involving the manipulation of the ethanol extract of ginger for 30 days noted a drastic increase in the subjects' CAT, GR, GPx, and SOD activity [35], which accords with the findings of our study.

4.4. *Alpine Officinarum,* Antioxidant Levels, and Oxidative Stress

All the different parts of *A. officinarum* (aerial sections, leaves, rhizomes, and roots) have previously been utilized for medicinal resolution, either directly or through extract preparation involving numerous nonpolar and polar solvents [33]. Many prior studies have successfully cleared up the bioactive compounds found in *A. officinarum*. The dry root and rhizome of *A. officinarum* have been used to achieve antioxidant, antidiabetic, anti-inflammatory, antiulcer, antidiarrhea, analgesic, antiemetic, and anticoagulation effects [28]. Due to the lack of studies concerning the impact of *A. officinarum* mouthwash on the periodontal status, antioxidant levels, and OS of people in our community, further studies and larger sample sizes are required to extend knowledge in this area. In the present study, the data revealed a significant reduction in the participants' CAL, PI, CAT, and 8-OHdG marker levels, while no change was identified in relation to the participants' TAOC, which indicates that further studies are required to explain the mechanisms of action of *A. officinarum* in those with CP. In fact, this finding warrants further investigation to identify the bioactive plant components in *A. officinarum*, principally in relation to both its anti-inflammatory and antioxidant activities due to its potential employment in disease therapy. Furthermore, immunological and toxicological studies of *A. officinarum* should serve to authenticate classical claims regarding the usage of this plant species and provide evidence of its potential in relation to clinical drug development. Finally, in terms of the comparison between Zingiber ginger and *A. officinarum* with regard to the studied clinical and biochemical parameters, no significant changes in the participants' PI, CAL, and 8-OHdG marker levels were identified. However, a statistically significant increase in the participants' salivary CAT and TAOC following periodontal therapy was observed in both groups. No data are available to compare with the findings of our study, so we recommend that further studies be conducted to identify the effects of Zingiber ginger and *A. officinarum* on subjects' periodontal status, antioxidant levels, and OS.

5. Conclusion

1. *Zingiber ginger* and *Alpine officinarum* mouthwash and NSPT decreased oxidative stress, improved periodontal status, and increased saliva levels of antioxidant enzymes;
2. It is suggested that ginger and *Alpine officinarum* mouthwash and NSPT may be more effective in controlling inflammation in patients with CP and can be used as an alternative for chemical mouthwash;
3. More positive correlations were found between biochemical and clinical parameters;
4. A few limitations were obvious such as short duration, small sample size;
5. No adverse events or side effects were reported or observed in both groups at the end of the period.

5.1. Recommendation

1. More longitudinal research to establish our study's findings and assess the efficacy of periodontal therapy with plant mouthwash in different systemic diseases related to periodontitis;

2. The effect of the combination of antioxidants and periodontal therapy in terms of antioxidant/oxidative

stress parameters needed further investigation with longer follow-up, and a bigger sample could strengthen the study;

3. Taking X-rays before and after periodontal therapy to support the study.

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