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Protective Effect of Resveratrol against the Alveolar Bone Loss in Rats with Experimental Periodontitis and Acts Positively on the IL-17

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The resveratrol is a polyphenol known for its health benefits, which includes the ability to interfere in the osteoblastogenesis, which may foster adverse immunomodulators effects in the host response to periodontal disease. In the present study we evaluated the appearance of periodontal tissues of rats with experimentally induced periodontitis, by using resveratrol. Twenty-four male Wistar rats were used, in which half of the animals received a ligature around the first lower molars, then forming the groups with experimental periodontitis. Next, four groups were created: 1) Control Group (CON); 2) The Ligature Group (LIG); 3) Group Resveratrol (RSV); 4) Ligature-Resveratrol Group (LIG-RSV). The animals of the Resveratrol groups were daily dosed with 10

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mg/kg of body weight of polyphenol orally, during four weeks. After 105 days of experimental period, euthanasia was performed. The results showed a significantly lower alveolar bone loss ($p<0.05$) in animals that received resveratrol, and still, the polyphenol was able to reduce concentration of interleukin 17 (IL-17) in the groups dosed with it. Our conclusion is that dosing rats with experimental periodontitis with resveratrol could cause a protective effect on the alveolar bone loss, in addition to act positively on the IL-17.

Keywords: Periodontitis; polyphenol; alveolar bone; resveratrol.

1. INTRODUCTION

Periodontal disease (PD) is one of the most important oral diseases in the world, and poor oral hygiene remains as its biggest cause. According to the World Health Organization (WHO), a severe form of this disease affects approximately 10 to 20% of people as mild and moderate forms affect between 20 to 50% in the whole world, corresponding to 15% of adults aged between 21 and 50. In Brazil, prevalence of the moderate form of the disease in adults was 15.3% and the severe form was prevalent in 5.8% of them. In addition, individuals with low education and lowest social classes are the most affected [1-3]. Periodontal disease is no longer identified only as an oral health problem, but a public health issue as well, since it is associated with systemic health [4].

In the physiopathology of PD, the bacteria produce lipopolysaccharides (LPS) able to trigger the release of various pro-inflammatory cytokines, as well as systemic responses to oral inflammatory process, which includes the following: interleukin (IL) 1β, which stimulates production of prostaglandin E2 (PGE2); IL 6, which stimulatesproduction of immunoglobulins and bone resorption, and its secretion is enhanced on periodontal inflammation; tumor necrosis factor alpha (TNF-α), produced by monocytes and macrophages and that activates osteoclasts responsible for bone resorption, cementum and periodontal ligament, acting synergistically with IL 1 and IL 6, and C-reactive protein (CRP), which works as a marker for systemic inflammation. IL-17, described more recently, is also directly related to the disease progression and consequent tissue degradation in periodontitis [5-11].

After the inflammatory stimulus, there is an increase in the production of PGE2 and Matrix Metalloproteinases(MMP), which results in the destruction of the teeth supporting structures, stimulating the alveolar bone resorption. Furthermore, due to the disease progression and production of pro-inflammatory cytokines, periodontal pockets will be formed, increasing CRP and fibrinogen concentrations and generating a systemic response. In addition, the increase of MMPs happens, particularly MMP-8, which is the only proteinase that can fragment type I and III collagens, which are of utmost importance for the structural maintenance of the periodontium, closely linked to the disease progression and its worst prognosis [2,9,12,13.

Several plants or their active components used in traditional medicine may be useful to treat inflammatory conditions, so that there has been an increasing interest on resveratrol, through studies that have focused on its use to modulate immune-inflammatory diseases, such as the periodontitis [14,15].

Resveratrol compound (3,5,4'-trihydroxystilbene) is a polyphenol present in various species of plants used for human consumption and which can be especially found in grapes, red wine and nuts [16-18]. Its powerful antioxidant, antitumor and anti-inflammatory effect has been showing to be beneficial for prevention and treatment of some diseases such as cancer, diabetes, cardiovascular disorders as well as degenerative, autoimmune and metabolic diseases [19-21].

It has also been demonstrated that resveratrol can positively affect osteogenesis, contributing to the bone neoformation [22]. However, there is ongoing research to find out whether resveratrol can stimulate immunomodulatory effects in the host response with periodontal disease. Evidences have increasingly supported theories according to which immune-inflammatory response influences the biofilm composition and that control of inflammation may inhibit the emergence of a pathogenic biofilm, besides improving periodontal healing. Thus, new data on immune-inflammatory action of resveratrol may suggest it as a therapy for patients with periodontitis [14,23].

Therefore, the objective of this study was to evaluate the effect of resveratrol on the periodontal tissues of rats submitted or not to periodontal disease induced by ligature.

2. METHODOLOGY

Overall, 24 Wistar rats(body weight between 180-250 g) have been used, which were kept in the vivarium of Sectorial Physiology Laboratory of Endocrine and Metabolism of the CCBS in a light-dark cycle environment (12-hour cycle of course and 12 hours of dark7:00 a.m. to 7:00 p.m.) and controlled conditions of temperature (21 ± 2 °), grouped in individual cages in groups from 3 to 5 (41 cm in length, 34 cm width and 17 cm height). The animals received a standard diet and plenty of water throughout the experiment.

2.1 Experimental Groups

All the sample size calculation was based on the use of ANOVA test for calculating the size of samples, with 90%power and a 5% significance level, as well as based on preliminary studies [14,15].

The 24 animals were randomly divided, with half of the sample was submitted to induction of periodontitis by ligature. Then, the animals were subdivided, being 6 animals included in the ligature groups and 6 other animals in the groups without ligature received resveratrol. All the animals remained with a standard diet (Fig. 1).

2.2 Induction of Periodontal Disease

The 75 days of life, half of the total number of animals were anesthetized with xylazine 0.04mL/100g and ketamine 0.08mL/100g, and placed in the appropriate surgical table, which allowed keeping their mouths open, facilitating access to the teeth of the posterior region of the mandible. With the aid of forceps modified and an exploratory probe, a cotton yarn number 40 was placed around the first lower molars right and left of the animals. The ligature acted as gingival irritant for 30 days, favoring the accumulation of plaque and, consequently, the development of periodontal disease [24].

2.3 Resveratrol Administering

The animals belonging to the RSV and LIG-RSV groups started to receive resveratrol the very next day after the ligature was placed. The polyphenol powder was diluted in water at a dose of 10 mg/kg of body weight and was daily administered orally by gavage during 4 weeks [14,25].

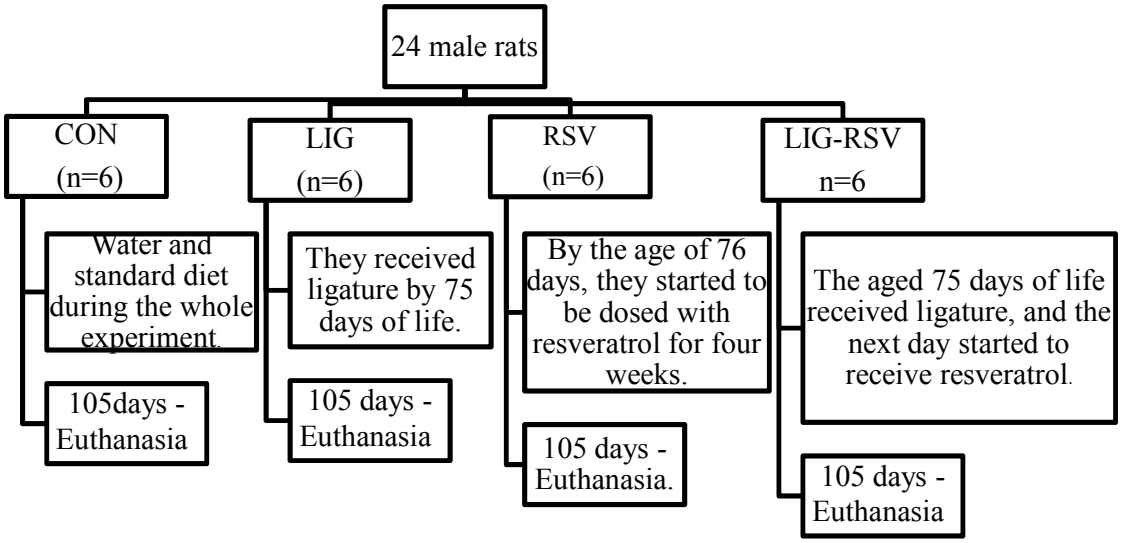

Fig. 1. Schematic figure representing the division of groups and performed experimental protocols

2.4 Radiographic Analysis

Right after euthanasia, the left side hemimandible of each animal was removed and fixed in buffered formalin with pH 7.2 during 24 hours. After that, the hemimandibles were placed with the lingual side over the Kodak RVG 6100 digital radiographic sensor with 20 pl/mm image resolution,27.03 pl/mm sensor theoretical resolution, optic fiber 1, 22 x 30 mm active surface dimensions and (pixels) 1200 x 1600 (1.92 million) matrix dimensions. The jaws were positioned so that the buccal and vestibular cusps of the first molars were in the same vertical plane. The X-ray device (AGFA) was set to 100mA, 0,05s, 40KV and a focus/film distance of one meter, with incidence of X-rays perpendicular to the parts. In scanned images, three measurements were performed on Image Tools 3.0 program (University of Texas Health Science Center, San Antonio, TX, USA), by a linear measure, which covered the distance of the cementoenamel junction (CEJ) until the alveolar process of the mesial side of the lower left first molar. Besides, these measurements were performed once a day on three different days and the average was calculated. They were expressed in centimeters [24].

2.5 Histological Processing

The right hemimandibles obtained were fixed in a 10% formaldehyde solution for 24 hours and decalcified with 5% trichloroacetic acid (TCA), 10°C for 30 days. The parts were evaluated to determine the degree of decalcification expected, with renewal of TCA solutionevery five days. After the decalcification, the tissues were immersed in 5% sodium sulphate during approximately two hours to neutralize the TCA, washed up in tap water for two hours, kept in a 70% alcohol solution until the histological processing for inclusion in paraffin (PurifiedParaffin, code 1228, lot 1008459, VetecQuímica Fina, Rio de Janeiro, Brazil). Fragments of hemimandibles were dehydrated in ascending alcohol series, cleared in xylene and embedded in paraffin. The paraffin blocks were cut in manual microtome (Olympus, CUT 4055 - Charleston, South Carolina, USA) to obtain 7 µm thickness sections, which were assembled in histological slides and stained through the Hematoxylin and Eosin (HE) technique.

2.6 Histological Analyzes

Microscopic analysis was performed by a trained single examiner who evaluated stained histological sections. The plates were analyzed through a commonly transmitted light microscope (Leica Microsystems, Switzerland) for morphological observations of the gingival tissue, alveolar process and counting of osteoblasts, osteocytes and osteoclasts of the animals' hemimandibles.

2.7 Gingival Morphometry

Morphometric measurements were made on the buccal and lingual right marginal gums in all groups by using an image analyzer program (Image Tool 3.0), attached to a light microscope with 10x accuracy, at intervals of ten cuts between one count and another on the series of cuts (approximately 50 µm).The measurements were made from pre-determined morphological points in the marginal gingiva (Fig. 2). The results were expressed in µm.

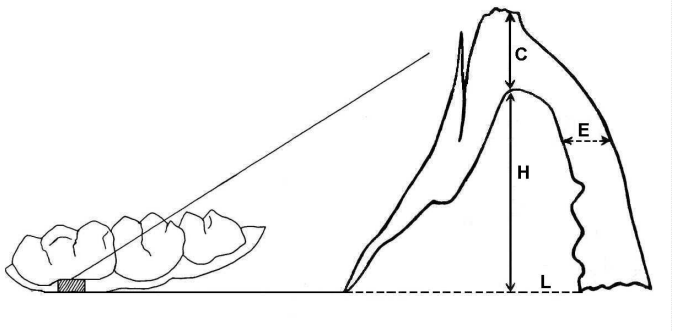

Fig. 2. Schematic of the rat's gingiva showingreference points used for morphometric measurements of oral epithelium, epithelial crest and connective tissue.

C- height of the epithelium of the gingival crest, E -Width of the oral epithelium
H - height of connective tissue in the middle region, L - width of the connective tissue in the basal region

2.8 Histological Analysis and Counting of Cells

After obtaining the histological plates, quantity of osteoblasts, osteocytes and osteoclasts present in five consecutive fields of vestibular alveolar bone crest has been calculated, starting from the highest point of the crest. The 100 times increase in immersion in the microscope was used for the observation, so that two observations per field were performed, and then the average of values for each animal and for each group was calculated.

A measurement of the smallest distance between the apex of the vestibular alveolar bone crest and the cementoenamel junction was also performed. The measurements (in pixels) were repeated once a day, on three different days to obtain the average among the values. To do it so, we used a microscope attached to a computer, which allowed us to capture the images, through the LazEz® software.

2.9 Analysis of the Expression of IL-17

A portion of the gum tissue around the teeth, from the hemimandible left side, subjected or not to the ligature placing was removed and used for analysis by Enzyme Linked ImmunoSorbent Assay (ELISA) with the addition of the IL-17 cytokine. For the dosage, previously sensitized plates with monoclonal antibodies (Biosource, INVITROGEN ®, California, USA) were used in accordance with the manufacturer's instructions. The plates were incubated with the supernatants of gingival tissue or with different concentrations of the IL-17 cytokine, recombinant, at the concentrations indicated by the manufacturer. The detection antibody conjugated to the specific peroxidase of the cytokine was added to the plates and after the incubation time, they were washed and the reactivity revealed by adding the revealing solution, according to the manufacturer's instructions. The reaction was blocked with a stop solution and the reading was carried out at 450 nm through a microplate reader. The cytokine concentration was calculated using the linear regression curve, starting from a standard curve performed for the respective cytokine. The results were expressed in pg;mL.

2.10 Statistical Analysis

For the statistical analysis, all numerical values were expressed as mean ± standard deviation. At first, by using the program Bioestat 5.3 (Instituto Mamiraua, Amazonas, Brazil), The normality of the data was analyzed by the Shapiro-Wilk test; after checking the normality distribution, Parametric tests ANOVA- Oneway were subsequently performed followed by applying the Tukey's multiple comparison test. Differences observed were considered significant when $p < 0.05$ (5%).

3. RESULTS

3.1 Radiographic Analysis and Histomorfometric of the Alveolar Bone

Radiographic (Chart1) and histomorphometric (Table 1) analyzes of the alveolar bone of the first lower molars has shown that the animals of the LIG group (0.26±0.07) had a higher and significant alveolar bone loss ($p<0.05$), proving the efficacy of induction of periodontal disease on the bone tissue. However, the animals that received the resveratrol treatment, even associated with periodontal disease induced (LIG-RSV(0.18±0.07)), had a significant lower bone loss ($p<0.05$), when compared to those who have not received the treatment, which suggests the possibility of a protective effect of resveratrol against periodontal disease. The resveratrol(0.119±0.05) and control groups(0.11±0.05) have not shown statistically significant differences when comparing to each other.

3.2 Histomorphometric Measurement of Gingival Tissue

Analysis of measures of gingival morphometry has demonstrated no statistically significant difference between the LIG and LIG-RSV groups ($p>0.05$) (Table 2), as well as between the CON and RSV groups. However, these measures are statistically higher ($p>0.05$) when the groups of rats submitted to ligature (LIG and LIG-RSV) are compared to the groups without induced periodontitis (CON and RSV). Therefore, that implies resveratrol has not acted on gingival tissues.

3.3 Histological Analysis of the Right Hemimandible

3.3.1 Control group

In the histological analysis of this group, the oral, junctional and sulcular epithelia, as well as the

connective tissue were found within the normal range, with no inflammatory tissue. The alveolar bone was intact, compact and regular, with spongy central portion with normal appearance. Cementum, periodontal ligament and cementum-enamel junction also showed anatomical features within the pattern normality. Presence of osteoblasts and osteoclasts has been observed, which indicates resorption process and bone neoformation, in a balanced condition. Bone crests were thick and at the level of the root cervical third, evidenced by measurement of the distance from the cementum-enamel junction to the alveolar bone crest (Fig. 3-A).

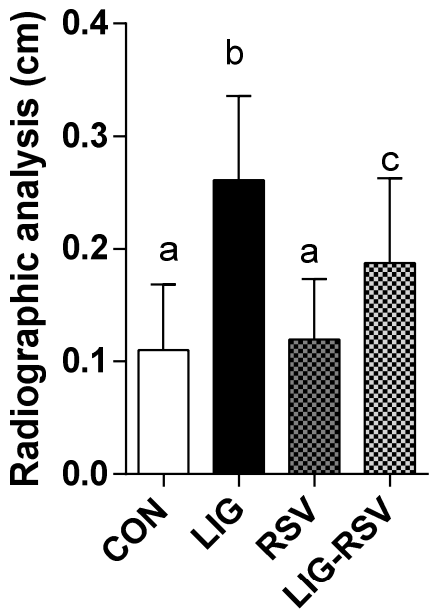

Chart 1. Radiographic analysis of distance from the cementoenamel junction up to the alveolar bone crest of the mesial side of the left first molar of rats from all the groups. Values represent the mean ± standard deviation and are expressed in centimeters
**Different letters, statistically different groups (p<0.05) after ANOVA test and Tukey's test.*

3.3.2 Ligature group

In the LIG group alterations on the cementum and periodontal ligament were observed, in addition to the crest bone which was irregular, with extensive alveolar bone loss occurring exposure of the tooth cervical third. Regarding bone cells, we notice enhanced presence of osteoclasts, which revealed bone reabsorption activity. Junctional, oral and sulcular epithelia were found in a state of abnormality in relation to their morphology, with migration to the apical region and presence of inflammatory infiltrate in the connective tissue (Fig. 3-C).

Table 1. Histomorphometric analysis of distance from the cementoenamel junction up to the alveolar bone crest of the mesial side of left first molar of rats from all the groups. Values represent the mean ± standard deviation and are expressed in pixels

Groups	Mean ± standard deviation
CON	196.07±43.35 A
LIG	369.38±76.73 B
RSV	198.38±25.92 A
LIG-RSV	269.84±56.21 C

**Different Letters, statistically different groups (p<0.05 after the ANOVA test and Tukey test*

3.3.3 Resveratrol group

In this group we observed normality on periodontal tissues and morphology of oral, junctional and sulcular epithelia, as well as in the connective tissue, which did not present any inflammatory aspect. We observed osteoblasts and osteoclasts in normal conditions for the processes of formation and bone reabsorption. The crest bone remained close to the CEJ, in homeostasis conditions (Fig. 3-D).

3.3.4 Ligature-resveratrol group

Small changes in oral, junctional and sulcular epithelia could be observed in this group, and the connective tissue presented inflammatory aspect. The crest bone also showed irregularities, both in relation to the amount of bone resorption, in which there was more reabsorption in relation to the groups without experimental periodontitis as to its location, in which, in this case it was close to the tooth third cervical. There was an increase of osteoclasts when compared to the Resveratrol group, revealing activity of bone reabsorption, but smaller than in the LIG group (Fig. 3-B).

In the quantification of bone cells (Table 3) of the alveolar bone of the first lower molars, it was found that in animals of the LIG group there was a significant increase in the number of osteoclasts ($p<0.05$), with consequent significant reduction of the number of osteoblasts and osteocytes ($p<0.05$). However, the animals that

received treatment with resveratrol, although associated with induced periodontal disease (LIG-RSV), had a smaller number of osteoclasts and significant increase of osteoblasts and osteocytes ($p<0.05$) when compared to those that did not get the treatment. Control and resveratrol groups had no statistically significant differences between them ($p>0.05$) regarding quantification of bone cells.

3.4 Analysis of the Expression of IL-17

The concentration of IL-17 was assessed from the supernatant of gingival tissue of animals from all groups. The results showed that the concentration of IL-17 was higher in groups without resveratrol when comparing to the other groups ($p<0.05$), demonstrating a positive result of resveratrol on this interleukin (Table 4).

Table 2. Histomorphometric analysis of right hemimandible gingiva of animals from all groups. Values represent mean ± standard deviation and are expressed in micrometers (µm)

Groups	Height of the epithelium of the gingival crest (C)	Width of the oral epithelium (E)	Height of the connective tissue (H)	Width of the connective tissue (W)
CON	51.61 ± 7.10	59.83 ± 5.69[a]	199.02 ± 11.80[a]	98.10 ± 18.03 A
RSV	51.43 ± 8.86 A	58.31 ± 9.18[a]	196.57 ± 21.16[a]	98.07 ± 14.04[a]
LIG	62.93 ± 6.60 B	74.14 ± 14.25B	228.04 ± 9.81B	134.04 ± 20.38B
LIG-RSV	63.92 ± 6.36 B	75.71 ± 13.08B	234.67 ± 21.78B	136.62 ± 27.29B

**The letters correspond to the comparisons within the same parameter. Different letters: statistically different groups ($p<0.05$) after ANOVA test and Tukey's test.*

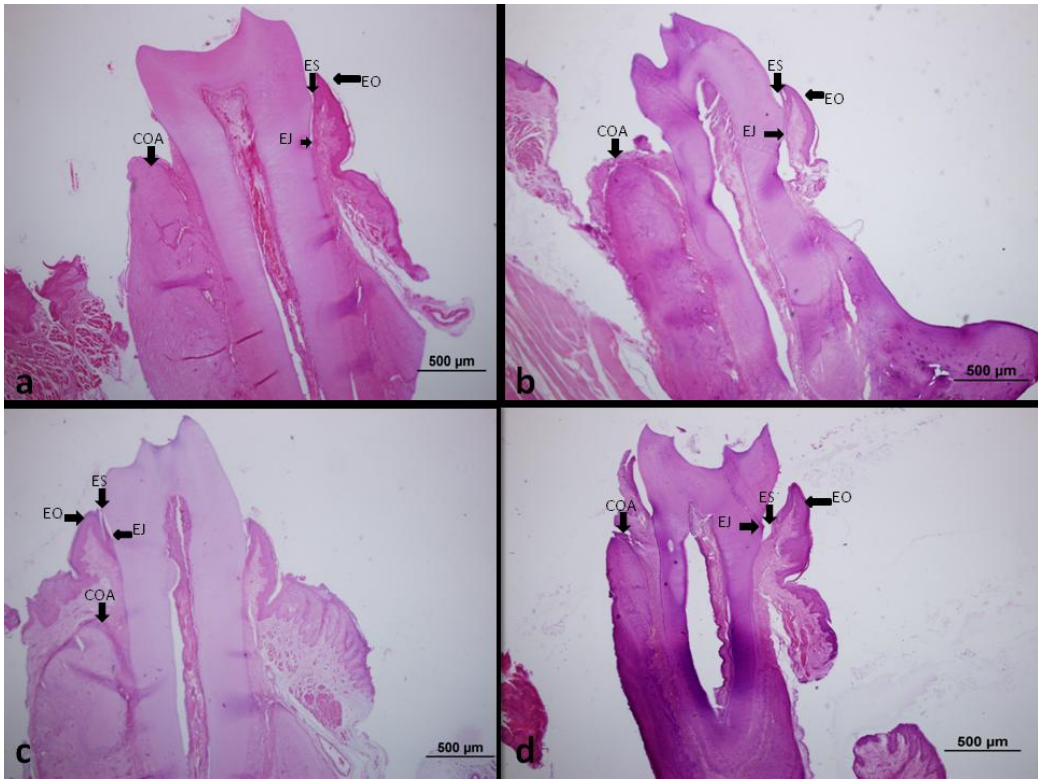

Fig. 3. Representative photomicrography of an animal from the CON group (A). Representative photomicrography of an animal of the LIG-RSV group. (B) Representative photomicrography of an animal from the LIG group (C). Photomicrography representative of an animal of the RSV group (D). COA: Alveolar bone crest; EJ: Junctional epithelium; ES: Sulcular epithelium; EO: Oral epithelium . Hematoxylin and Eosin (HE). Magnification 40xs

Table 3. Histologic analysis of right hemimandible of rats from the experimental groups for quantification of osteocytes, osteoblasts and osteoclasts. Values represent mean ± standard deviation and are expressed in units

	Osteoblast	Osteocyte	Osteoclast
CON	12.57±2.14 A	32.23±9.98 A	0.37±0.08 A
LIG	6.95±0.69 B	10.67±4.62 B	3.46±0.16 B
RSV	12.05±0.63 A	34.25±12.10 A	0.46±0.08 A
LIG-RSV	8.64±1.03 C	18.45±4.23 C	1.71±0.14 C

**Different letters in the same column indicate statistically significant differences (p<0.05) between the groups within the same parameter*

Table 4. Concentration of IL-17 in gingival samples of rats from experimental groups. Values represent mean ± standard deviation and are expressed in pg/mL

Groups	Mean ± standard deviation
CON	27.47±8.23 A
LIG	41.37±7.47 B
RSV	12.47±2.30 C
LIG-RSV	15.98±2.33 D

**Different letters represent statistically different groups (p<0.05) after ANOVA test and Tukey's test.*

4. DISCUSSION

Periodontitis is a chronic inflammatory response associated to subgingival plaque, being one of the main causes of tooth loss [26]. It leads to formation of periodontal pockets, which stimulates loss of adhesion between teeth, gums and also induces the resorption of the alveolar bone [27]. Currently, there is a growing interest in the use of natural products to prevent oral diseases such as the periodontitis [28]. Among these products, the resveratrol is a natural compound, non flavonoid polyphenol that is found in more than 72 plants, and may have an anti-inflammatory and antimicrobial effect in the treatment of periodontal disease [29]. Therefore, our study aimed at a therapeutic natural alternative, such as resveratrol, which could be used to assist protection against the alveolar bone loss caused by the periodontal disease development.

Resveratrol is a phytoalexin naturally produced by some spermatocytes, extensively found in the skin of red grapes and wine [16,18]. Among its many benefits, it can even positively affect the osteogenesis, contributing to new bone formation [22,30-33].

The literature shows resveratrol use against periodontal disease, such as the study performed by Atmanspacher [34], which aimed to determine, through immunoenzymatic assessments, the influence of resveratrol in the systemic inflammatory process of experimental periodontitis in rats induced to the disease. The IL-17 was significantly lower in the group test, in which the rats received the polyphenol, when compared to the control group (p= 0.014), corroborating the results of our study (Table 4), in which the group that received the ligature associated with treatment with resveratrol showed lower concentrations of this interleukin, when compared to the LIG group, which is also demonstrated in the CON and RSV groups, and RSV showed lower concentration of IL-17 in relation to the CON group. Casati et al. [14] also demonstrated that the action of modulation of resveratrol seems to be attributed to its inhibitory effect on the pro-inflammatory activity in the production of cytokines of the immune response of type Th17, because the administering this natural agent led to a significant reduction in the levels of IL-17.

According to Xuzhu et al. [35] and Casati et al. [14], resveratrol can directly inhibit the development of TH17 cells or indirectly by suppressing the production of main cytokines of Th17 such as polarization IL-1. In fact, corroborating the present study, we observed a tendency toward a greater inhibition of IL-17 in the group that received the resveratrol. Thus, although the inhibition of IL-17 has been achieved mainly by the consumption of resveratrol in our study, a trend in reduction of levels of other cytokines, such as IL-1β, may also have contributed to the positive impact of resveratrol on the destructive processes of the alveolar bone tissue [14,36].

Regarding histomorphometry of the alveolar bone, we noticed that once more the resveratrol was effective against experimental periodontitis. Evidenced by both radiographic (Chart 1) and the histomorphometric analysis (Table 1), which distance from the CEJ until the alveolar bone

crest of the mesial side of the left first molar was lower in the rats of the LIG-RSV group, where the animals received daily administration of resveratrol associated with periodontal disease, when compared to the LIG group in which the animals did not receive the polyphenol and had bigger bone loss. These findings are similar to those of Casati et al. [14] who evaluated the effect of continuous resveratrol in the progression of periodontal disease experimentally induced in 24 rats. In these same analyzes, the CON and RSV groups showed no statistical differences among them.

In this study, resveratrol did not influence the morphology of gingival tissues (Table 2). When performed measurements on pre-determined points shown on Fig. 3, the CON and RSV groups were statistically similar, as well as the LIG and LIG-RSV groups, i.e., the animals that were induced to periodontal disease and that in addition to the induction received resveratrol as a possible treatment for the disease, showed no statistical differences between them when analyzed the gingival morphometry was analyzed. Thus, the polyphenol has not acted as a protective agent on the gingival tissues. These data differ from the findings of Minagawa et al. [37], who demonstrated that the resveratrolsuppressed inflammatory responses of human gingival epithelial cells probably by the suppression of reactive oxygen species or inhibition of the nuclear factor-kB (NF-kB).

With regard to the activity of resorption, by quantifyingbone cells, as demonstrated on table 3, groups CON and RSV showed a marked quantity of osteoblasts and osteocytes and a very small quantity of osteoclasts, showing a relationship of balance between neoformation processes of bone resorption in both groups. Specimens of the LIG group, which were induced to periodontal disease, had a marked quantity of osteoclasts (Table 3), justifying the large bone resorption observed both in x-ray analysis (Chart 1), and in the histomorphometric analysis (Table 1). The LIG RSV group showed a lower number of osteoclasts and greater number of osteoblasts and osteocytes than the animals of the LIG group, which justifies the effectiveness of resveratrol preventing bone loss in ligature. These findings corroborate Bhattarai et al. [38] study who researched resveratrol action in the modulation of inflammation and concluded through histological analysis that resveratrol (5mg/kg of body weight) improved the alveolar bone loss mediated by ligature in rats.

Although there is in fact a therapeutic potential of resveratrol in inflammatory modulation, the exact mechanisms of this substance that stimulates such effect is not enough clarified. Casati et al. [14] stated that additional mechanisms need clarification, but some findings demonstrated that resveratrol can reduce expression of other markers, including IL-2, IL-6, IL-8, IL-12, tumor necrosis factor (TNF) -α, colony stimulating factor granulocyte-macrophage colony-stimulating factor (GM-CSF) and interferon (INF) -γ, in different experimental models, although many other inflammatory mediators (IL-6, IL-8, IL-10, IL-23, INF-γ and TNF-α) and factors related to bone (osteoprotegerin [OPG], RANK AND RANK ligand [RANKL]) are related to the establishment of the periodontitis. Thus, these findings may partially suggest the modulation of immune inflammatory response by resveratrol.

The study conducted by Bhattarai et al. [38], had as an objective to investigate whether the resveratrol would be able to protect rats with a model of induced periodontitis by ligature against alveolar bone loss. Histological analyzes and micro-CT showed that the administering 5 mg/kg of body weight of the polyphenol was effective to decrease alveolar bone loss in these animals, contributing and corroborating the findings of this study. Furthermore, the authors showed that the resveratrol, among other benefits, reduced production of proteins related to inflammation and formation of osteoclasts. According to same authors, these results suggest that the resveratrol would protect rats of tissue damage caused by periodontitis, inhibiting the inflammatory diseases and stimulating the antioxidant defense systems. In this sense, we propose the use of resveratrol as a therapeutic drug for the treatment of periodontitis, as well as other inflammatory bone diseases, such as osteoporosis and arthritis.

Although further studies need to be performed, resveratrol has been recently studied as a therapeutic natural alternativeto assist periodontal disease treatment, as demonstrated in our study. Recently, Nishii [39] has clinically proven that systemic use of polyphenol was efficient to reduce the probing depth and increase the level of insertion clinic, thus promoting clinical benefits for the periodontal treatment.

5. CONCLUSION

Thus, it can be concluded with these results, that the use of resveratrol could cause a protective

effect over the alveolar bone loss in rats with experimental periodontitis and it acted positively over the IL-17. However, it has presented no effect on the gingival tissues in the groups with the presence of periodontal disease.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

All the experimental protocol was approved by the Ethics Committee on Animal Use (CEUA) from UNIOESTE, being in accordance with the Ethical Principles in Animal Experimentation, adopted by the National Council for Control of Animal Experimentation (CONCEA).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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