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Research article

The effectiveness of *Moringa oleifera* in the preservation of periodontium after radiation therapy: An experimental animal study

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ABSTRACT

Background: Radiation therapy produces reactive oxygen species, which have been linked to various degenerative conditions in periodontal attachment. This study aimed to assess the beneficial effects of aqueous *Moringa oleifera* leaf extract on the periodontium of albino rats exposed to fractionated gamma radiation.

Materials and methods: This experimental study involved 24 adult male albino rats divided into three groups: Group M received *M. oleifera* leaf extract (300 mg/kg) intraperitoneally for 14 days; Group R received 20 Gy fractionated gamma irradiation; and Group MR received the same *M. oleifera* regimen as Group M and then fractionated gamma irradiation dose as Group R. On the first and seventh days post-radiation, bone, cementum, and periodontal ligament samples were histologically and histomorphometrically examined.

Results: The periodontal ligament, alveolar bone, and cementum showed structural damage in Group R. A relative persistence of normal periodontal tissue structures was seen in Group MR, showing less disruption of the periodontal ligament and greater trabecular bone thickness than Group R. The histomorphometric analysis showed that the mean periodontal ligament width was highest in Group R7 (245.20 μm) and lowest in Group M7 (54.55 μm). In addition, the mean cementum width was highest in Group R1 (88.99 μm) and lowest in Group M1R1 (17.87 μm) and differed significantly between groups.

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Conclusion: Within the limitations of this study, *Moringa oleifera* leaf aqueous extract showed the potential to reduce the adverse effects of radiation, control inflammation, and support tissue healing in a rat model.

1. Introduction

Radiation therapy is one modality used to treat oral carcinomas [1]. While it is effective, despite the advances in technology, it adversely affects the normal oral structure surrounding the tumor directly and the entire body indirectly due to systemic toxicity and DNA damage [2]. Various complications of radiation therapy have been reported in the literature, such as trismus, osteoradionecrosis, irradiation caries, and changes in periodontium [3–6]. The consequences of radiation therapy include alterations in the cellularity and vascularity of hard and soft tissues and altered collagen synthesis [7–10]. Radiation effects on the blood vessels in the periodontal ligament (PDL) cause the widening of the PDL space and destruction of the adjacent trabecular bone [11–15]. The radiation-induced decreases in saliva production and alterations in the oral immune response can exacerbate periodontal disease and bone loss. The management of irradiated patients is challenging for health dental practitioners. The irradiated periodontium is more susceptible to periodontal attachment loss and gingival recession [16].

The use of naturally produced medicines in cancer adjuvant therapy has been thoroughly researched, and it is recommended because of their related therapeutic efficacy and minimal side effects [17,18]. *Moringa oleifera* (MO), known as the "miracle tree," can be consumed as a solid or a liquid [19,20]. Every part of the tree has potential herbal effects. MO has been used as an antihypertensive, antibacterial, anti-inflammatory, and immunostimulant [21–23]. Many studies have proven MO powders and leaf oil extracts to have anti-plaque, anticaries, and antioxidant effects [24–27]. MO extracts have been shown to protect normal cells against radiation therapy, which may increase treatment effectiveness [28]. MO extracts have also been shown to reduce chromosomal abnormalities and micronucleus production in bone marrow cells after gamma irradiation [29]. Additionally, MO extracts were found to protect the periodontium of male rats from gamma irradiation-induced oxidative stress and genotoxicity [30] by lowering pro-inflammatory cytokine levels in the gingival tissue [31].

Therefore, this study aimed to confirm the hypothesis that MO might help the periodontium (bone, PDL, and cementum) to withstand the adverse effects of radiation. Its objective was to evaluate the effects of ionizing radiation (IR) on the periodontium of rats and determine whether MO extracts protect the periodontium from the adverse effects of radiation.

2. Materials and Methods

2.1. Experiment design

This experimental animal study involved 24 adult male Wistar albino rats weighing 120–150 g obtained from the Experimental Animal House of the National Centre for Radiation Research and Technology (Cairo, Egypt). The irradiation procedures were conducted at the National Centre for Radiation Research and Technology of the Atomic Energy Authority (Nasr City, Cairo, Egypt) using a ^{137}Cesium source Gamma Cell-40 biological irradiator with a 0.39 Gy/min dose rate. The dose was adjusted using an alanine dosimetry system. The rats were housed in individual cages in a well-ventilated room at ambient temperature with good lighting. All rats were examined daily for behavioral, morphological, or physical changes. This study was approved by the Committee of Scientific Ethics at the National Centre for Radiation and Technology, following the guidelines for animal use (code number: P-PD-21-06).

Before the study, a power calculation based on the collected data was used to establish the number of samples needed in each group [32,33]. A sample size of 24 rats ($n = 8$/group) was found to provide 80% power with a 95% confidence interval and 5% significance level using the G*Power program [34]. The experimental protocols were standardized and applied consistently to all groups to reduce bias. We used simple randomization by drawing random numbers for each rat and assigning them to treatment groups according to the sequence. To ensure blinding, we analyzed the data using assigned codes rather than treatment names until the analysis was completed.

Table 1
Experimental groups that were included in the study.

Group	Treatment
Moringa (Group M)	Moringa (300 mg/kg) for 14 consecutive days
M1	Rats euthanized 1 day after last M.O injection
M7	Rats euthanized 7 days after last injection
Irradiation (Group R)	Whole body γ- irradiation at dose 2 Gy/5 days/week for 2 weeks (20 Gy)
R1	Rats euthanized 1 day after last radiation session
R7	Rats euthanized 7 days after last radiation session
Moringa followed by irradiation. (Group MR)	Moringa (300 mg/kg) for 14 consecutive days followed by whole body γ- irradiation at dose 2 Gy/5 days/week for 2 weeks (20 Gy)
M1R1	Rats euthanized 1 day after last radiation session
M7 R7	Rats euthanized 7 days after last radiation session

The rats were randomly divided into three groups ($n = 8$/group). In **Group M**, the rats were intraperitoneally injected with MO extract (300 mg/kg; Genesis Today, Inc., USA) dissolved in saline for 14 days. All other chemicals and solvents used in the research procedures were of the highest purity available. In **Group R**, the rats were subjected to fractionated whole-body γ-irradiation at a total dose of 20 Gy (2 Gy daily, five days per week, for two weeks) [23]. In **Group MR**, the rats received the same MO regimen as Group M, followed by the same fractionated whole-body γ irradiation regimen as Group R, beginning 1 h after the last MO injection. The rats were further subdivided randomly into two subgroups ($n = 4$) according to their sacrifice date (one or seven days after the last treatment; Table 1). The mandibles were used for histological and histomorphological analyses.

2.2. Histopathological and histomorphometry examinations

The rat mandible samples were rinsed in running tap water after fixation in 4% paraformaldehyde for 24 h and then demineralized using demineralized solutions (25% formic acid and 10% trisodium citrate) for six months. Next, the samples were stained with hematoxylin and eosin according to routine protocols. The mounted slides were examined under a light microscope. The bone microarchitecture, cementum, and PDL were evaluated. Their widths were measured using the Leica Qwin 500 Image Analyzer software (Leica Microsystems, Germany).

2.3. Statistical analyses

The data were analyzed using SPSS software (version 18; IBM Corp.,NY, USA). The variables were compared among groups using a one-way analysis of variance, followed by Bonferroni's post hoc test. A p-value of <0.05 was considered statistically significant.

3. Results

3.1. Light microscopy

A normal bundle alveolar bone thickness and a well-developed Haversian system were observed in Group M1 (i.e., Group M euthanized one day after the last treatment). The osteocytes' quantity, size, and shape were all within the normal range. The nuclei were stained and of average size. Osteoblasts were identified on the bone surface. The PDL comprised well-ordered collagen fibers obliquely implanted into the bone and had a typical width. The cementum connected to the PDL showed uniform shapes and typical staining (Fig. 1).

In contrast, the alveolar process was noticeably weaker in Group R1. Numerous areas of osteoclastic resorption and osteoblastic disruption were observed in the bundled bone. Numerous empty lacunae were evident, along with a reduction in osteocyte size. While the cementum had a typical cellular-type cementum thickness, the PDL showed vacuolization and regions of degeneration (Fig. 2).

Cellularity was decreased, and areas of osteoblastic disruption in the alveolar process were evident in Group R7 (i.e., Group R sacrificed seven days after the last treatment). There were fewer and smaller osteocytes. Some of the gaps were also empty. The PDL was wide and showed vacuolization, fiber disarray, and areas of fiber detachment (Fig. 3).

In contrast, the alveolar process in Group M7 showed typical bone thickness and architecture. Consequently, there was an ordinary Haversian system. The number, size, and morphology of the osteocytes were all normal. The nuclei were stained, uniform, and of average size. The collagen fibers in the PDL were arranged normally and had a typical width (Fig. 4).

Group M1R1 showed nearly regular thickness and structure. There was an ordinary Haversian system in the bundle bone. While there were fewer osteocytes, their size and morphology were both normal. The nuclei were stained and of average size. The PDL

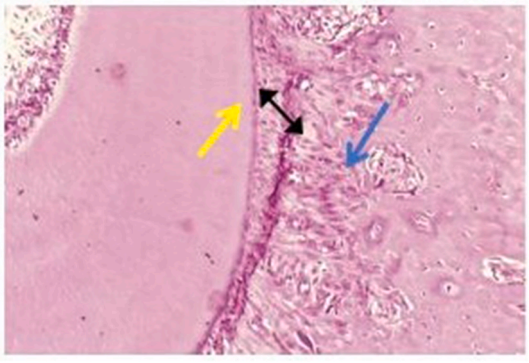

Fig. 1. A photomicrograph of mandibular bone showing normal bundle bone thickness, a normal Haversian system (circle), and normal osteocytes (arrow). The PDL is of normal thickness and has well-arranged collagen fibers obliquely inserted into the bone (double arrows). The osteoblastic distribution along the bone surface appeared normal (blue arrow). The cementum showed normal stainability and regular outlines (yellow arrow). Group M1 at 200 × magnification. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

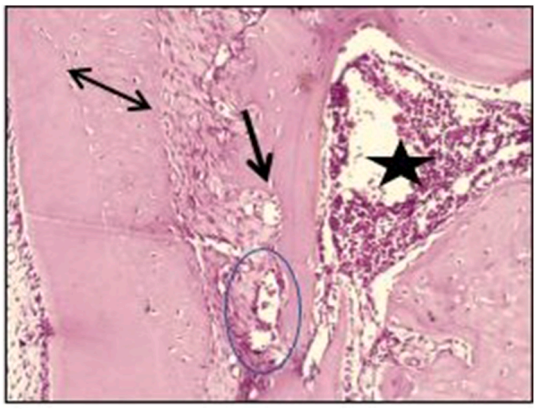

Fig. 2. A photomicrograph of the mandibular bone showing marked widening of Haversian canals (black arrows), widening of the fibrocellular bone marrow (star), numerous osteocytes in flattened lacunae (blue arrows), hyperchromatic nuclei (green arrows), slight irregularity, vacuolization, and areas of degeneration in the PDL (circle). The cementum had the typical thickness of cellular-type cementum (double arrows). Group R1 at 200 × magnification. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

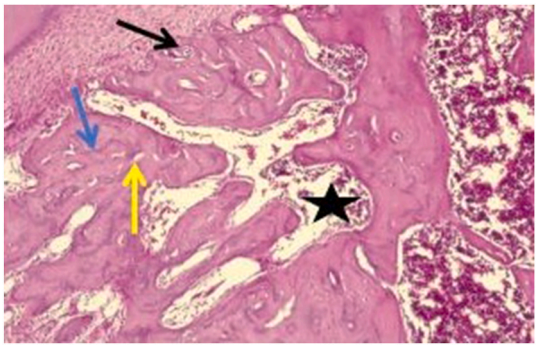

Fig. 3. A photomicrograph of mandibular bone showing a scalloped irregular bone surface (black arrows) with areas of bone resorption and reversal lines (blue arrows). The trabecular bone thickness was decreased (double arrow). Some empty lacunae without osteocytes were evident (yellow arrows). The fibrocellular marrow cavities were wide (star) and without osteoblastic lining cells. Numerous osteocytes were observed. The PDL showed widening and vacuolization, fiber disarrangement, and areas of fiber detachment. Group R7 at 200 × magnification. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

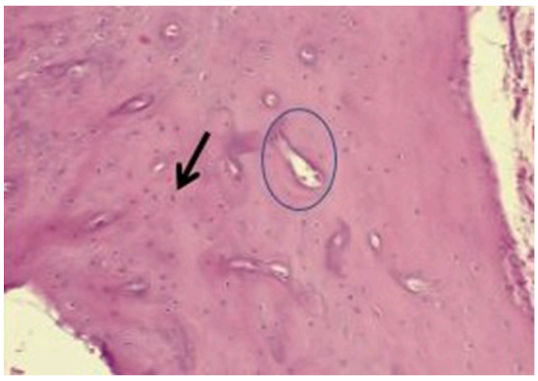

Fig. 4. A photomicrograph of mandibular bone showing normal bone thickness, a normal Haversian system (circle), and a normal number of osteocytes with uniform nuclei (black arrows). The PDL had a normal width and normally arranged collagen fibers. Group M7 at 200 × magnification.

showed evenly spaced collagen fibers, mild vacuolization, and normal thickness (Fig. 5).

Group M7R7 showed a reduced alveolar process. In the bundle bone, numerous regions showed osteoclastic resorption and osteoblastic disruption. Numerous osteocytes had shrunk in size, and lacunae were empty. The PDL showed degenerative areas, hyalinized fibers, and vacuolization (Fig. 6).

3.2. Histomorphometry

3.2.1. PDL

The mean PDL width was greatest in Group R7 (245.20 μm), followed by Group R1 (210.20 μm), Group M7R7 (191.39 μm), Group M1R1 (165.89 μm), Group M1 (88.03 μm), and Group M7 (54.55 μm). The mean PDL widths differed significantly among the groups ($p = 0.001$; Table 2). The pairwise Bonferroni post hoc tests indicated that mean PDL widths did not differ significantly between Groups R7, R1, M7R7, and M1R1. In addition, Group M1R1 did not differ significantly from Group M1, and Group M1 did not differ significantly from Group M7.

3.2.2. Cementum

The mean cementum width was greatest in Group R1 (88.99 μm), followed by Group M7R7, Group R7, Group M1, Group M7, and Group M1R1 (17.87 μm). The mean cementum widths differed significantly along the groups ($p = 0.00$). The pairwise Bonferroni post hoc tests indicated that mean cementum widths did not differ significantly between Groups M7R7, R7, M1, M7, and M1R1 (Table 3).

3.2.3. Trabecular bone

The mean trabecular bone width was greatest in Group M7 (341.46 μm), followed by Group M1, Group M1R1, Group M7R7, Group R1, and Group R7 (62.93 μm). The mean trabecular bone widths differed significantly among the groups ($p = 0.00$). The pairwise Bonferroni post hoc tests indicated that mean trabecular bone widths did not differ significantly between Groups M7R7, R7, and R1 or between Groups M7 and M1 (Table 4).

4. Discussion

This study aimed to assess the hypothesis that MO extract might help the periodontium to withstand the adverse effects of radiation. It used a rat model because it is the most widely used model for evaluating the secondary effects of radiotherapy and mimicking humans [2].

Histological examination of the mandibles from Group R revealed fewer osteocytes. This observation is consistent with **He et al.**, who found destroyed osteocytes in radioactively damaged bone tissues and justified this by IR reducing osteocyte viability and increasing cell apoptosis [35]. Our observation is also consistent with **Amira et al.**, who demonstrated that γ-radiation causes decreased bone cells, osteoblastic resorption, and loss of bone thickness [36].

Regarding the trabecular bone, our study observed increased trabecular bone thickness, which was also observed in the marrow cavities. The amount of radiation absorbed, beam intensity, the patient's age and developmental stage, and other factors could affect bone quality [37,38]. After radiation, osteoclasts may be more radioresistant than osteoblasts, potentially explaining why they predominate in cementum-related resorption sites and cells. Consequently, proportional increases in lytic activity and resorption sites have been previously observed [39,40].

Our study found no apparent differences in the mean trabecular bone widths of **Groups M1 and M7**, which had the greatest widths. This finding might reflect the short period between the last MO dose and tissue analysis. Osteocytes, the most numerous bone cells, typically have peak lacunar sizes between 200 and 330 μm^3 [41]. These cells show appreciable variation in density and shape. In

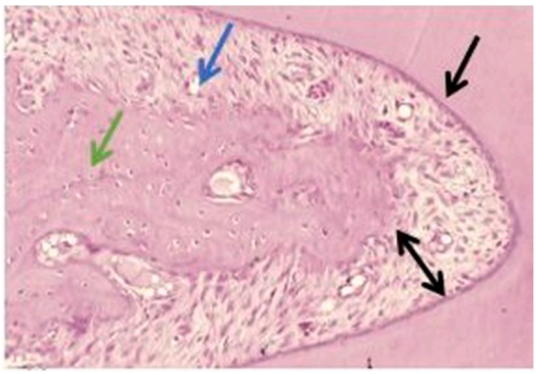

Fig. 5. A photomicrograph of mandibular bone showing a slightly regular bone surface with some reversal lines (black arrows), indicating bone remodeling. The trabecular bone showed increased thickness. Osteoblasts lined the bone surface, and the osteocyte lacunae appeared relatively normal (blue arrows). There were slightly undulated resting lines (green arrow). Group R1. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

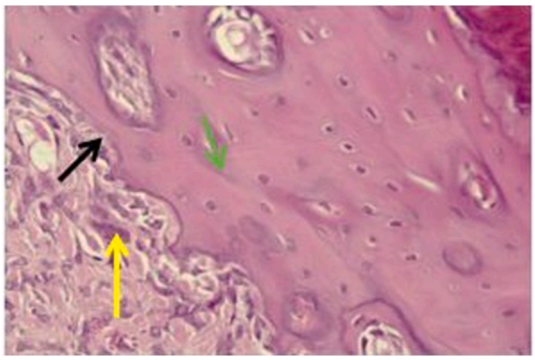

Fig. 6. A photomicrograph of mandibular bone showing a slightly regular bone surface with some reversal lines (black arrows), indicating bone remodeling. The trabecular bone showed increased thickness. Osteoblasts lined the bone surface (yellow arrows), and the osteocyte lacunae appeared relatively normal. There were slightly undulated resting lines (green arrows). Group R7 at 200 × magnification. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table (2)
Descriptive statistics and comparison of periodontal ligament width in different groups (ANOVA test).

Width/μm	Mean	Std. Dev	95% Confidence Interval for Mean		Min	Max	P
			Lower Bound	Upper Bound			
Group "M1"	$88.03^{y,z}$	27.42	68.42	107.64	55.85	139.64	0.000*
Group "R1"	210.20^{x}	53.01	172.28	248.12	128.47	301.61	
Group "M1R1"	$165.89^{x,y}$	58.16	124.28	207.49	93.09	277.41	
Group "M7"	54.55^{z}	33.60	30.52	78.58	1.86	87.51	
Group 'R7"	245.20^{x}	118.35	160.54	329.86	63.30	418.91	
Group "M7R7"	191.39^{x}	92.26	125.39	257.39	55.85	322.09	

Significance level $p \leq 0.05$, *significant.

Table (3)
Descriptive statistics and comparison of cementum width in different groups (ANOVA test).

Width/um	Mean	Std. Dev	95% Confidence Interval for Mean		Min	Max	P
			Lower Bound	Upper Bound			
Group "M1"	25.32^{y}	14.56	14.90	35.74	1.86	42.82	0.000*
Group "R1"	88.99^{x}	39.77	60.55	117.44	24.20	124.74	
Group "M1R1"	17.87^{y}	3.19	15.59	20.16	13.03	22.34	
Group "M7"	20.48^{y}	2.48	18.71	22.25	16.76	22.34	
Group 'R7"	34.26^{y}	21.30	19.02	49.50	1.86	63.30	
Group "M7R7"	38.73^{y}	12.37	29.87	47.58	18.62	52.13	

Significance level $p \leq 0.05$, *significant.

Table (4)
Descriptive statistics and comparison of osteocytes bony width in different groups (ANOVA test).

Width/um	Mean	Std. Dev	95% Confidence Interval for Mean		Min	Max	F	P
			Lower Bound	Upper Bound				
Group "M1"	278.53^{x}	113.22	197.53	359.53	128.47	389.12	25.93	0.000*
Group "R1"	88.99^{z}	56.61	48.49	129.49	14.89	145.22		
Group "M1R1"	185.44^{y}	70.96	134.68	236.20	98.68	290.44		
Group "M7"	341.46^{x}	73.93	288.57	394.34	268.10	450.56		
Group 'R7"	62.93^{z}	29.67	41.71	84.15	29.79	102.40		
Group "M7R7"	92.34^{z}	53.12	54.34	130.34	1.86	154.53		

Significance level $p \leq 0.05$, *significant.

contrast, mean trabecular bone widths were smaller in **Groups M1R1 and M7R7**, followed by **Groups R1 and R7**. These findings suggest that radiation reduces alveolar bone width and that MO extract might provide immediate protection against radiation damage since the group given MO and radiation (Group MR) had greater alveolar bone widths than the group given radiation alone (Group R).

Group R1 had the greatest cementum width. Higher magnification images of the middle and apical thirds of the cementum revealed surface abnormalities. As mentioned in the literature, increasing the radiation dose above 1 Gy causes observable surface abnormalities and a decrease in Sharpey's fiber sites. Sharpey's fiber sites were further reduced at irradiation doses above 2 Gy, and resorption was apparent on the cementum surface [42]. In Group R1, the cementum appeared to be entirely devoid of cells, and its healing potential was reduced [43], which might be explained by changes in the extracellular matrix of the tissue resulting from radiation-induced reductions in hydration levels in the root matrices. The primary chain of collagen macromolecules is split during this process.

Significant evidence shows that the cementoenamel junction gradually disappears with increasing radiation doses [44,45]. While the cementum appeared most affected in Group R1, no differences were observed in the MO-only (M1 and M7) or combined-treatment (M1R1 and M7R7) groups. The effects of radiation therapy on cementum width are complicated. Almehdi et al. reported structural deterioration and thermal changes in radiotherapy-treated cementum [46]. Mjöberg et al. observed an increase in the radiolucent zone adjacent to bone cement, which may have been a sign of variations in cementum width [47]. Research generally indicates that radiation therapy and associated interventions may greatly affect cementum width, possibly resulting in structural layer melting and increased widths (20–140 μm) depending on the type of radiation used.

Our study observed the greatest mean PDL width in **Group R7**, whereas the other studied tissues showed no statistically significant difference. Radiation damages periodontal blood vessels, enlarges the PDL space, and destroys the bony trabeculae, potentially increasing the risk of periodontal disease, disrupting healing, and reducing the ability to remodel and repair bone. The PDL space increases because of decreased periodontal vascularization [48,49]. Comparable results were reported by **El-Faramawy et al. and Kassim et al.**, who noticed the same features in the periodontium, which was damaged by radiation [43,50].

Based on our observations, treatment with MO leaf extract before irradiation enhanced alveolar bone osteogenesis, potentially due to the antioxidant properties of MO, which promote the scavenging of free radicals produced indirectly by IR [51–54]. MO leaf extract also activates phosphatidyl inositol-3 kinase, which helps to promote the osteogenic differentiation of H_2O_2-damaged bone marrow stem cells [55]. MO leaf extract has been found to have various positive benefits on bone and periodontal tissue. Boonanantanasarn et al. [56] discovered that MO leaf extract stimulated osteogenic differentiation and mineralization in human PDL cells, showing its potential for tissue regeneration. Elwan et al. reported the radioprotective characteristics of MO leaf extract, which improved bone marrow electrical properties and blood antioxidant levels [57]. Burali et al. also mentioned the ability of MO leaf extract to prevent bone loss, implying that it could help mitigate the effects of radiation therapy on the PDL, cementum, and bone [58,59,60].

4.1. Limitations

Our study had some limitations. Firstly, it lacked a preoperative width for a reference group. Establishing baseline mean widths for each tissue before the intervention and including them in the comparisons could help clarify some results. Secondly, the short interval between treatment and analysis and the limited sample size potentially limit our findings. Therefore, studies with larger sample sizes and longer evaluation periods are needed to accurately determine the effects of MO leaf extract on the periodontium.

5. Conclusions

Our results have shown that exposure to gamma radiation can damage the alveolar bone, cementum, and PDL in albino rats, reflected by their decreased trabecular bone thickness, fewer osteoblasts, altered cementum thickness, and increased PDL thickness. However, they also showed that MO leaf extract could attenuate these effects since the bone, cementum, and PDL were histologically normal in rats pre-administered with MO leaf extract before radiation exposure.

Ethics approval and consent to participate

The animal treatment protocol was approved by the Animal Care Committee of the National Center for Radiation Research and Technology (Cairo, Egypt) and followed the guidelines of the National Institute of Health. This study was approved by the Committee of Scientific Ethics at the Faculty of Oral and Dental Medicine, Al-Azhar University, Girls' Branch (Nasr City, Egypt; code number: P-PD-21-06), and followed the guidelines for animal use.

Consent for publication

Not applicable.

Data availability statement

The dataset are available from the corresponding author upon reasonable request. Researchers interested in accessing the data may contact Shadia Elsayed via email at shadiaelsayed@azhar.edu.eg.

CRediT authorship contribution statement

Noura Mohammed Bakr: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization.

Gihan A. Balboa: Writing – review & editing, Writing – original draft, Resources, Methodology, Formal analysis, Conceptualization. **Nora Abdel Gawad Mohamed:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Nehad A. Ahmed:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Conceptualization. **Ahmed Mohammed Sapri:** Writing – review & editing, Writing – original draft, Software, Methodology, Investigation. **Eihab A. Mously:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization. **Doaa Feleman:** Writing – review & editing, Writing – original draft, Software, Resources, Funding acquisition. **Shadia A. Elsayed:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Data curation. **Sandy Hassan:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The authors declare no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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