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Can Wine Modulate Apical Periodontitis Inflammation?

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Mini-Review

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ABSTRACT

There are a substantial number of studies suggesting possible benefits of the moderate wine consumption on human health. By the other side, it is known that chronic excessive alcohol consumption has a negative impact on bone health and in many organs. However, epidemiological evidence suggests that moderate consumption of alcoholic beverages may have beneficial effects on bone tissue. This mini-review aims to explore the relationship of wine and apical periodontitis inflammation.

INTRODUCTION

Apical periodontitis is the product resulting from persistent bacterial contamination of the root canal system in the face of combat led by the host's immune system, characterized by an inflammation of periradicular tissues[1]. When the dental pulp becomes infected, bacteria and their byproducts evoke nonspecific inflammatory responses, as well as specific immunological reactions, leading to the destruction of bone by osteoclasts and resorption of dental hard tissues (cementum and dentin) by multinucleated cells designated as odontoclasts[2,3].

Red wine and the isolated polyphenols (resveratrol and quercetin) have been established to alter the functioning of bone tissue and the immune system, both crucial elements for the development of apical periodontitis[4-10].

This mini-review aims to expose some scientific information regarding the effects of red wine on the development of apical periodontitis.

DISCUSSION

The wine

Wine consumption is a common habit throughout the world[11]. Wine is an alcoholic beverage popularly produced from fermented grape juice. Wines can be classified as red, rose (pink), or white based on their color, and they can also be classified as table (red, rose, or white), sparkling, or fortified based on their alcohol level or carbon dioxide content[12]. Table wines are wines that are neither fortified nor sparkling and are typically served with food; fortified wines are made by adding alcohol[13,14]. Wines can also be classified based on how much carbon dioxide they contain. Those that contain carbon dioxide are classified as sparkling wines or "still" wines[12,13]. Wines can also be classified as alcohol free (<0.5% v/v), low-alcohol (0.5% to 1.2% v/v), reduced-alcohol (1.2% to 5.5% or 6.5% v/v), lower-alcohol (5.5% to 10.5% v/v), and alcoholic wines (>10.5% v/v)[15,16]. In addition, wines are also classified according to their sugar content: dry (maximum of 4 g/L sugar), medium dry (between 4 g/L and 12 g/L sugar), semi-sweet (between 12 g/L and 45 g/L sugar), and sweet (minimum of 45 g/L sugar)[17]. These classifications may vary between countries and their legislations.

Wine is composed of water, ethanol, glycerol, polysaccharides, and different types of acids and, in addition, presents a complex mixture of bioactive compounds that are predominantly phenolic in nature[18]. It is one of the main sources of polyphenols through the diet; like that, drinkers red wine moderates consume polyphenols at levels well above the average of the 4 population[19]. The phenolic compounds in wine can be divided into flavonoids and non-flavonoids. Flavonoids represent more than 85% of the components phenolics in red wine, including different molecular families such as flavonols (quercetin), flavones and anthocyanidins. Non-flavonoid compounds include acids hydroxycinnamics, hydroxybenzoic acids, stilbenes and its derivative, resveratrol[20].

Wine and systemic health

It is estimated that the medicinal use of wine dates back to 2200 BC[21]. In the early 1990s, the discovery of the "French paradox" was reported, popularizing the Health benefits of red wine. This term was designed to describe the relationship inverse between coronary heart disease mortality and red wine consumption observed in French. This has been attributed to the so-called "Mediterranean diet", which includes an intake of constant wine[22].

Twenty years after the formulation of this concept, there have been a substantial number of studies suggesting possible benefits for the health that moderate wine consumption has on human health[23]. By the other side, it is known that chronic excessive alcohol consumption has a negative impact on bone health, in addition to deleterious effects on many organs. However, epidemiological evidence suggests that moderate consumption of alcoholic beverages may have beneficial effects on bone tissue[22].

Moderate consumption of alcohol has a positive impact on the immune system compared to excessive alcohol, also presenting an anti-inflammatory effect[24]. *In vitro* studies have shown that exposure to moderate doses of alcohol can inhibit the activation of NF-kB in human monocytes[25]. In addition, it was also reported that light alcohol consumption, preferably wine, resulted in an increase in bone mineral density of the spine and of the whole body in postmenopausal women[26]. In general, the beneficial effect of regular and moderate consumption of wine is obtained with approximately 150 ml/day for women and 300 ml/day for men[27,28].

There is evidence that ethanol increases the risk of cancer in the oral cavity, pharynx, larynx, esophagus and liver[29,30]. However it is possible that polyphenols and other potentially protective compounds present in wine may counteract the harm associated with ethanol.

It has been shown that red wine also promotes bone formation and prevents bone loss, inducing the proliferation of osteoblasts and inhibiting the differentiation of osteoclasts and, consequently, bone resorption. These mechanisms include the differentiation and proliferation of osteoblasts by mechanisms mediated by Receptors Estrogen (ER), activation of kinase 1/2 (ERK 1/2) and regulation of extracellular Wnt signal, increased osteoclast apoptosis and inhibition of factor activating receptor (RANKL) nuclear KB ligand[31-33].

Wine and apical periodontitis

Recently our group investigated the effects of red wine on the development of apical periodontitis in a rat model study and we observed that red wine decreases the inflammatory intensity, the marking of TRAP in the periapical lesion, while the administration of isolated Resveratrol/Quercetin increased the expression of OPG and IL-10, in addition to decreasing TRAP[34]. One possibility to explain the attenuation of the beneficial effects of wine may be related to the presence of alcohol, as we observed a negative effect of alcohol on the development of periapical lesions when in concentrations above 15%[35].

The pathogenesis of the apical periodontitis is related to inflammation and immune responses promoting bone resorption in the apical region[36]. When the periapical lesion is installed, inflammatory cytokines or interleukins play an important role in the immune response, initiating and coordinating cellular events and regulating the host's response to endotoxins. Furthermore, the bone resorption that occurs in these pathologies appears as a determining factor for the expansion of these lesions, being initiated by the proliferation of immature osteoclast precursor cells and their differentiation into mature osteoclastic cells that promote the degradation of organic and inorganic bone components. RANKL is a key molecule in osteoclast activation and OPG is a receptor for RANKL. The increase in RANKL/OPG rate favors bone resorption through osteoclastogenesis and osteoclast activation[37].

The beneficial effect of resveratrol consumption in reducing alveolar bone loss seems to be associated with the modulation of the host's immune-inflammatory reaction, as indicated by other studies using different experimental models. The modulatory action exerted by resveratrol seems to be attributed to its inhibitory effect on the production of pro-inflammatory cytokines of the Th17 immune response, as the administration of this natural agent promoted a significant reduction in IL-17 levels[38,39].

Similarly to the observation regarding the apical periodontitis, periodontal disease is also benefited with wine or its phenolic compounds administration in different study models. A prospective cohort study found that intake of wine is inversely associated with clinical attachment loss in men[40]. It was also evidenced a beneficial effect of wine on periodontal status of southern Brazilian adults[41]. In animals, periodontitis was down regulated with the use of the polyphenols present in the red wine once continuous administration of resveratrol decreased periodontal breakdown induced experimentally in rats[42]. Moreover, resveratrol administered to rats caused a significant reduction in bone resorption[43]. Even when administrated subcutaneously it protected rats from periodontal tissue damage by inhibiting inflammatory responses and by stimulating antioxidant defense systems[44]. The same results observed when administered freely in drinking water[45]. Moreover, resveratrol decreased periodontal breakdown during smoking in rats[46].

Quercetin also could exhibit protective effects in bacterial-induced periodontitis, reducing the alveolar bone loss by mechanisms involving the reduction of pro-inflammatory cytokine production and down-regulation of the osteoclastogenic cytokine RANKL[47]. In addition, it could reduce alveolar bone loss in ligature-induced periodontitis

by increasing osteoblastic activity, decreasing osteoclastic activity, apoptosis, and inflammation[48]. This flavonoid has been reported to decrease osteoclastogenesis *via* inhibition of the activating nuclear factor-kB ligand receptor (RANKL), involved in osteoclastic differentiation; can directly induce apoptosis of mature osteoclasts; and furthermore, the local use of quercetin in a collagen matrix caused greater new bone formation[49, 50]. 6 Quercetin is able to increase Alkaline Phosphatase (ALP) activity in osteoblasts of the MG-63 lineage; the quercetin-supplemented diet can also reverse osteopenia in diabetic rats as well as inhibit bone loss in ovariectomized mice, confirming its beneficial effect on bone tissue in bone disorders[51-54].

CONCLUSION

This review spotlights a promising approach using the red wine or its phenolic compounds to modulate the inflammation during the periapical periodontitis development. Although numerous studies have looked at a wide range of molecules in the context of AP, the involvement of TLR2, MyD88, MMP2, and MMP9 in the spread of infection, pulpal necrosis, and AP development is still unknown. Our research revealed some new details about the chemicals involved in the evolution of AP. However, further research in animals and humans is needed to better understand the relationship between bacteria, MMPs, and the innate immune system.

REFERENCES

1. Kakehashi S, et al. The Effects of Surgical Exposures of Dental Pulps in Germ-Free and Conventional Laboratory Rats. Oral Surg Oral Med Oral Pathol. 1965;20:340-349. [PubMed] [Google Scholar] [Cross Ref]

2. Nair PN. Apical periodontitis: a dynamic encounter between root canal infection and host response. Periodontology. 1997;13:121-148. [PubMed] [Google Scholar] [Cross Ref]

3. Liapatas S, et al. Inflammatory infiltrate of chronic periradicular lesions: an immunohistochemical study. Int Endod J. 2003;36:464-471. [PubMed] [Google Scholar] [CrossRef]

4. Das S, et al. Anti-inflammatory responses of resveratrol. Inflamm Allergy Drug Targets. 2007;6:168-173. [PubMed] [Google Scholar] [CrossRef]

5. Wong RW, et al. Effect of quercetin on bone formation. J Orthop Res. 2008;26: 1061-1066.
[PubMed] [Google Scholar] [CrossRef]

6. Wong RW, et al. Effect of quercetin on preosteoblasts and bone defects. Open Orthop J. 2008;2:27-32.
[PubMed] [Google Scholar] [CrossRef]

7. Wong SK, et al. Quercetin as an Agent for Protecting the Bone: A Review of the Current Evidence. Int J Mol Sci. 2020;21:6448. [PubMed] [Google Scholar] [CrossRef]

8. Pervaiz S, et al. Resveratrol: its biologic targets and functional activity. Antioxid Redox Signal. 2009;11:2851-2897. [PubMed] [Google Scholar] [CrossRef]

9. Li Y, et al. Quercetin, Inflammation and Immunity. Nutrients.2016;8:167.
[PubMed] [Google Scholar] [CrossRef]

10. Esteban-Fernández A, et al. The role of wine and food polyphenols in oral health. Trends Food Sci Technol. 2017; 69,118-30. [PubMed] [Google Scholar] [CrossRef]

11. Kutlesa Z, et al. Wine and bone health: a review. J Bone Miner Metab. 2016;34:11-22.
[PubMed] [Google Scholar] [CrossRef]

12. Joshi VK, et al. Wines: White, Red, Sparkling, Fortified, and Cider. Curr Develop Biotechnol Bioeng: Food and Beverages Industry; Elsevier: Amsterdam, The Netherlands, 2016; 353-406.
[PubMed] [Google Scholar] [CrossRef]
13. Jackson RS, et al. Wines: Types of Table Wines. (1st eds.). Elsevier: Amsterdam, The Netherlands. 2015
[PubMed] [Google Scholar] [CrossRef]

14. Pereira V, et al. Emerging Trends in Fortified Wines: A Scientific Perspective. In Alcoholic Beverages: The Science of Beverages; Elsevier: Amsterdam, The Netherlands. 2019;7:419-470.
[PubMed] [Google Scholar] [CrossRef]
15. Pickering GJ. Low and Reduced-Alcohol Wine: A Review. J Wine Res. 2000;11:37-41.
[PubMed] [Google Scholar] [CrossRef]
16. Saliba AJ, et al. Consumer Demand for Low-Alcohol Wine in an Australian Sample. Int J Wine Res. 2013;5:1-8.
[PubMed] [Google Scholar] [CrossRef]
17. International Standard for the Labelling of Wines. (2022nd eds.). OIV Publications: Paris, France. 2021;1:1-12.
[PubMed] [Google Scholar] [CrossRef]
18. Soleas GJ, et al. Wine as a biological fluid: history, production, and role in disease prevention. J Clin Lab Anal. 1997;11:287-313. [PubMed] [Google Scholar] [CrossRef]
19. Waterhouse AL. Wine Phenolics. Ann N Y Acad Sci. 2002;957:21-36. [PubMed] [Google Scholar] [CrossRef]
20. Stockley C, et al. Bioavailability of wine-derived phenolic compounds in humans: a review. Food Funct. 2012;3:995-1007. [PubMed] [Google Scholar] [CrossRef]
21. Robinson J. The Oxford companion to wine (4th eds.). Oxford, United Kingdom; New York NY: Oxford University Press. 2015.
22. Renaud S, et al. Wine, alcohol, platelets, and the French paradox for coronary heart disease. Lancet.1992;339:1523-1526.
[PubMed] [Google Scholar] [CrossRef]
23. Giacosa A, et al. Alcohol and wine in relation to cancer and other diseases. Eur J Cancer Prev. 2012;21:103-108.
[PubMed] [Google Scholar] [CrossRef]
24. Liberman DN, et al. Low concentration alcohol intake may inhibit spontaneous alveolar bone loss in Wistar rats. Arch. Oral Biol. 2011;56:109-113.
[Google Scholar] [CrossRef]
25. Mandrekar P, et al. Inhibition of lipopolysaccharide-mediated NFkappaB activation by ethanol in human monocytes. Int Immunol. 1999;11:1781-1790.
[PubMed] [Google Scholar] [CrossRef]
26. Ilich JZ, et al. To drink or not to drink: how are alcohol, caffeine and past smoking related to bone mineral density in elderly women? J Am Coll Nutr. 2002;21:536-544.
[PubMed] [Google Scholar] [CrossRef]
27. Rotondo S, et al. The relationship between wine consumption and cardiovascular risk: from epidemiological evidence to biological plausibility. Ital Heart J. 2001;2:1-8.

[PubMed] [Google Scholar]

28. Walzem RL. (2008). Wine and health: state of proofs and research needs. Inflammopharmacology. 2008;16:265-271.

[PubMed] [Google Scholar] [CrossRef]

29. Baan R, et al. Carcinogenicity of alcoholic beverages. Lancet Oncol. 2007;8:292-293.

[PubMed] [Google Scholar] [CrossRef]

30. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Alcohol consumption and ethyl carbamate. IARC Monogr Eval Carcinog Risks Hum. 2010;96:3-1383.

[Google Scholar]

31. Dai Z, et al. Resveratrol enhances proliferation and osteoblastic differentiation in human mesenchymal stem cells *via* ER-dependent ERK1/2 activation. Phytomedicine. 2007;14:806-814.

[PubMed] [Google Scholar] [CrossRef]

32. He X, et al. Resveratrol prevents RANKL-induced osteoclast differentiation of murine osteoclast progenitor RAW 264.7 cells through inhibition of ROS production. Biochem Biophys Res Commun. 2010;401:356-362.

[PubMed] [Google Scholar] [CrossRef]

33. Zhou H, et al. Resveratrol augments the canonical Wnt signaling pathway in promoting osteoblastic differentiation of multipotent mesenchymal cells. Exp Cell Res.2009; 315:2953-2962.

[PubMed] [Google Scholar] [CrossRef]

34. Dal-Fabbro R, et al. Effect of red wine or its polyphenols on induced apical periodontitis in rats. Int Endod J. 2021;54:2276-2289.

[PubMed] [Google Scholar] [CrossRef]

35. Dal-Fabbro R, et al. Effects of different alcohol concentrations on the development of apical periodontitis in rats. Arch Oral Biol. 2019;108:104538.

[PubMed] [Google Scholar] [CrossRef]

36. Subramanian K, et al. Molecular analysis of persistent periradicular lesions and root ends reveals a diverse microbial profile. J Endod. 2009;35:950-957.

[PubMed] [Google Scholar] [CrossRef]

37. Kajiya M, et al. Role of periodontal pathogenic bacteria in RANKL-mediated bone destruction in periodontal disease. J Oral Microbiol. 2010;2:10.

[PubMed] [Google Scholar] [CrossRef]

38. Chen LL, et al. Effect of catch-up growth by various dietary patterns and resveratrol intervention on bone status. Exp Biol Med (Maywood).2012;237:297-304.

[PubMed] [Google Scholar] [CrossRef]

39. Xuzhu G, et al. Resveratrol modulates murine collagen-induced arthritis by inhibiting Th17 and B-cell function. Ann Rheum Dis. 2012;71:129-135.

[PubMed] [Google Scholar] [CrossRef]

40. Kongstad J, et al. Amount and type of alcohol and periodontitis in the Copenhagen City Heart Study. J Clin Periodontol. 2008;35:1032-1039.

[PubMed] [Google Scholar] [CrossRef]

41. Susin C, et al. The association between alcohol consumption and periodontitis in southern Brazilian adults. J Periodontal Res. 2015;50:622-628.
[PubMed] [Google Scholar] [CrossRef]
42. Casati MZ, et al. Resveratrol decreases periodontal breakdown and modulates local levels of cytokines during periodontitis in rats. J Periodontol.2013;84:e58-64.
[PubMed] [Google Scholar] [CrossRef]
43. Correa MG, et al. Systemic treatment with resveratrol and/or curcumin reduces the progression of experimental periodontitis in rats. J Periodontal Res.2017; 52:201-209.
[PubMed] [Google Scholar] [CrossRef]
44. Bhattarai G, et al. Resveratrol prevents alveolar bone loss in an experimental rat model of periodontitis. Acta Biomater.2016;29:398-408.
[PubMed] [Google Scholar] [CrossRef]
45. Tamaki N, et al. Resveratrol improves oxidative stress and prevents the progression of periodontitis *via* the activation of the Sirt1/AMPK and the Nrf2/antioxidant defense pathways in a rat periodontitis model. Free Radic Biol Med.2014;75:222-229.
[PubMed] [Google Scholar] [CrossRef]
47. Ribeiro FV, et al. Resveratrol Inhibits Periodontitis-Related Bone Loss in Rats Submitted to Cigarette Smoke Inhalation. J Periodontol.2017;88:1-16.
[PubMed] [Google Scholar] [CrossRef]
48. Napimoga MH, et al. Quercetin inhibits inflammatory bone resorption in a mouse periodontitis model. J Nat Prod.2013;76:2316-2321.
[PubMed] [Google Scholar] [CrossRef]
49. Taskan MM, et al. Quercetin Decreased Alveolar Bone Loss and Apoptosis in Experimentally Induced Periodontitis Model in Wistar Rats. Antiinflamm Antiallergy Agents Med Chem.2020;19:436-448.
[PubMed] [Google Scholar] [CrossRef]
50. Wattel A, et al. Flavonoid quercetin decreases osteoclastic differentiation induced by RANKL *via* a mechanism involving NF kappa B and AP-1. J Cell Biochem.2004;92:285-295.
[PubMed] [Google Scholar] [CrossRef]
51. Wattel A, et al. Potent inhibitory effect of naturally occurring flavonoids quercetin and kaempferol on in vitro osteoclastic bone resorption. Biochem Pharmacol.2003;65:35-42.
[PubMed] [Google Scholar] [CrossRef]
52. Robaszkiewicz A, et al. Antioxidative and prooxidative effects of quercetin on A549 cells. Cell Biol Int.2007;31:1245-1250.
[PubMed] [Google Scholar] [CrossRef]
53. Liang W, et al. Oral administration of quercetin inhibits bone loss in rat model of diabetic osteopenia. Eur J Pharmacol.2011;670:317-324.
[PubMed] [Google Scholar] [CrossRef]
54. Tsuji M, et al. Dietary quercetin inhibits bone loss without effect on the uterus in ovariectomized mice. J Bone Miner Metab.2009;27:673-681.
[PubMed] [Google Scholar] [CrossRef]