Review Article

Mishamalaki Drug- An Ayurvedic Antioxidant Regimen for Periodontal Diseases and Diabetes Mellitus?

Ayurvedic Antioxidant Regimen

Nubesh Khan Syed Mohammed

ABSTRACT

Numerous epidemiological studies have suggested a link between diabetes and periodontitis, both of which are widespread chronic disorders in the world. It seems that diabetes increases the risk of periodontal disease, although treating periodontitis can also help improve glycemic control. Recently, research has focused on the significance of oxidative stress-inflammatory pathways in the etiology of diabetes and periodontitis. The use of antioxidants in the treatment of periodontal disease has gained importance. Research has indicated that addressing oxidative stress and hyperglycemia concurrently may yield better results than treating hyperglycemia exclusively with intensive care. Nishamalaki, an ayurvedic drug, has both antiglycemic and antioxidant property. This review investigated Nishamalaki's potential benefits as an antioxidant for treating both periodontal diseases and diabetes.

Key Words: Antioxidants, Chronic periodontitis, Diabetes, Reactive oxidative species.

Citation of article: Mohammed NKS. Nishamalaki Drug- An Ayurvedic Antioxidant Regimen for Periodontal Diseases and Diabetes Mellitus? Med Forum 2023;34(12):90-94. doi:10.60110/medforum.341221.

INTRODUCTION

Reactive oxygen species (ROS) have received increased attention in recent years for their potential role in the growth of a number of chronic inflammatory diseases, including type 2 diabetes, atherosclerosis, rheumatoid arthritis, and periodontitis.¹

The majority of tissues continuously create reactive oxygen species as part of normal cellular metabolism. When free radicals or other reactive nonradical species behave negatively, the antioxidant defense system can prevent or lessen the harm they cause. Antioxidants effectively combat ROS under physiological circumstances, preventing ROS-related tissue damage. When inflammation takes place, innate immune system cells, like neutrophils and macrophages, play a significant part in the substantial increase in ROS production, when phagocytosis occurs through the respiratory burst's metabolic route.² Tissue damage and oxidative stress come from the antioxidant defense system's incapacity to combat high ROS levels or activities.

Department of Preventive Dentistry, College of Dentistry in Ar Rass, Qassim University, Al-Qassim, Kingdom of Saudi Arabia.

Correspondence: Dr. Nubesh Khan Syed Mohammed, Assistant Professor of Preventive Dentistry, College of Dentistry in Ar Rass, Qassim University, Al-Qassim, Kingdom of Saudi Arabia.

Contact No: 966591506707 Email: n.race@qu.edu.sa

Received: July, 2023 Accepted: September, 2023 Printed: December, 2023 Dental plaque is the main cause of the inflammatory and contagious disease known as periodontitis. The majority of periodontal tissue deterioration is assumed to be caused by the homeostatic balance between reactive oxygen species and antioxidant defense mechanisms, which shield and repair vital tissue cells and molecular components. This response of the host to microorganisms and their products is what causes the most loss of periodontal tissue loss.³

There is a lot of evidence linking periodontitis to noncommunicable illnesses like diabetes, heart disease, and chronic kidney disease. It is recognized that type 2 diabetes and periodontal disease have a symbiotic relationship. Periodontal disease affects a substantial percentage of diabetic patients, and it is widely acknowledged that periodontal care significantly reduces HbA1c levels. Periodontal treatment relieves the bacterial infection that causes periodontal disease, which in turn reduces local inflammation in the periodontal tissue and insulin resistance.

Oxidative stress is increased by diabetes, which can disrupt insulin action and secretion and speed the disease's progression to an overt state.^{5,6} According to Koromantzos et al plasma levels of d-8-iso prostaglandin F2a were discovered in diabetic patients and Nox1, Nox2, Nox4, and p47 levels were greater in diabetes model rats.⁷ One of the key elements in the beginning and development of periodontitis may be elevated reactive oxygen species.⁸ By activating transcription factors for the forkhead box and reducing Wnt signaling, an increase in ROS results in a decrease in bone production and an increase in bone resorption.⁹ As shown by Vo et al in their clinical trial, using antioxidants topically or systemically during periodontal treatment causes reduction in local inflammation.¹⁰ Arora et al and Singh et al have conducted those analyses on the administration of lycopene and vitamin E for the treatment of periodontitis in people without underlying medical conditions.^{11,12}

Periodontal surgery or non-surgical therapy, such as SRP, are two commonly used methods to treat PPD. Systematic reviews by Mailoa et al and Smiley et al concluded that the main result of periodontal therapy is not improved by the use of several therapies in combination with SRP. ^{13,14} Individuals with type 2 diabetes, which is associated with poor recovery after surgery and the development of periodontal disease, however, may benefit from combined therapy. As a result, combining SRP with antioxidant supplements may have positive therapeutic effects. But there aren't many literature-based meta-analyses that look at how antioxidants and periodontal therapy are used together in diabetes individuals.

Despite providing numerous effective treatment choices for diabetes mellitus, modern medications can have a number of side effects, including hypoglycemia. Due to these drawbacks, Due to the limitations of intensive hyperglycemia treatment in preventing diabetic complications, which are linked to oxidative stress, it has been suggested that simultaneous targeting of hyperglycemia and oxidative stress could be more effective than intensive hyperglycemia treatment alone in the management of diabetes mellitus. Antioxidant therapy has therefore drawn more interest. Plant products having hypoglycemic and antioxidant qualities would be highly helpful in the treatment of diabetes mellitus.

Herbal medicines cannot be considered scientifically authentic if the medicine being examined has not been confirmed and described to ensure consistency in the manufacturing process. Additionally, numerous deadly side effects, including direct toxic effects, allergic reactions, impacts from pollutants, and interactions with herbal medications, have lately been identified. As a result, research into herbal medicines is becoming more and more important in order to develop potent formulations using quick, accurate, and contemporary quality control methods.

Nishamalaki, a variety of combinations of Haridra and Amalaki that have been proven to be helpful and are often used in the management of diabetes mellitus, is recommended in Ayurvedic texts. Amalaki, also known as Indian gooseberry or Amla, is regarded as the most important medicinal plant by the ancient Indian medical system known as Ayurveda.

The current review discussed Nishamalaki's potential benefits as an antioxidant for treating both periodontal diseases and diabetes.

ROLE OF ANTIOXIDANTS ON PERIODONTAL HEALTH

Periodontal disease, which affects 10-15% of the world's population, is one of the leading causes of tooth loss. Periodontal disease has been related to the overabundance of free radicals that result from oxidative stress or an antioxidant deficit. An obvious oxidative process with elevated quantities of reactive oxygen and nitrogen species occurs early in the development of periodontal disease, particularly in periodontitis.

For the first time ever, the University at Buffalo School of Dental Medicine shown how the risk of periodontal disease may be increased by a diet deficient in antioxidant vitamins. The serum levels of antioxidant substances, including vitamins A, C, and E, selenium, a-carotene, bcryptoxanthin, lycopene, and lutein, were examined to see if they were related to periodontal disease. According to the findings, selenium has a strong link with periodontal disease. When antioxidant levels are low, gum tissue's capacity to combat oxidative stress, preserve healthy tissue, and limit bacterial damage appears to be reduced. 15

The results of Krol's study suggest that peripheral and gingival serum total antioxidant status was considerably lower in each subgroup compared to controls, which was connected with periodontal clinical status. He concluded that periodontal tissues may acquire lesions more quickly due to oxidative stress, as evidenced by a rise in ROS concentration and a fall in antioxidant activity in gingival blood. In a contradicting study, it was revealed that gingival tissues, erythrocyte membranes, and plasma of patients with periodontitis had significantly increased enzymatic antioxidant activity than healthy controls.

Two oxidative damage markers, malondialdehyde and 8-hydroxy-deoxygunosine, were shown to be more common in the saliva of those with periodontitis. 16,17 According to research by Canakci et al, periodontal inflammation is accompanied by an increase in oxygen radical formation or activity as well as a decrease in saliva's antioxidant capacity. 18 The degree of periodontal disease, however, was not associated with the elevated oxidative stress.

Root planing and scaling are shown to alter the activity of antioxidant enzymes, supporting the idea that oxidative stress plays a part in periodontal degeneration. Salivary antioxidants like SOD and GPx, according to Novakovic et al, accurately represented both the tissue response to therapy and the periodontal response. Previous research found a highly substantial inverse relationship between salivary antioxidant levels and the periodontal parameters examined. ^{20,21}

Waddington et al discussion of inflammatory periodontitis provided additional evidence that ROS

contributes to tissue degradation.²² Only after the antioxidant defense mechanism has failed to counteract the increased ROS generation does oxidative stress occur. Human gingival tissue's SOD and CAT activities were assessed, and it was discovered that these activities decreased as the depth of the periodontal pocket increased. Patients with periodontitis had lower levels of SOD and GPx in their saliva.

Another study found a substantial inverse relationship between periodontal characteristics and the antioxidant enzyme activity SOD, CAT, and glutathione reductase in patients with periodontitis. In saliva, individuals with periodontitis exhibited lower quantities of non-enzymatic antioxidants and greater concentrations of enzymatic antioxidants such as SOD and GPx, according to research by Novakovic et al.²³

Numerous research has attempted to focus on the role that antioxidants can be used in the management of periodontitis, because of its protective effect against ROS. The results of supplemental periodontal therapies with antioxidants such vitamin E, taurine, and lycopene have been found to be superior to standard periodontal therapy in terms of clinical periodontal parameters, systemic and local antioxidant activity, and levels of local and systemic ROS.

Vitamin C helps older people maintain their periodontal health, according to recent studies. ²⁴ Another recent study looked at the impact of dietary treatments, in addition to periodontal therapy, including lycopene, vitamin C, vitamin E, capsules with fruits, vegetables, and berries. ²⁵ It has been established that lycopene and vitamin E are the only dietary supplements linked to better clinical markers. These results suggest that antioxidants may be used to treat periodontitis, which may be beneficial for both periodontal health and general oxidative state.

REVIEW OF THE LITERATURE ON NISHAMALAKI'S PHARMA-CODYNAMIC EFFECTS

One of the components of Nishamalaki, Amalaki (Indian Goose Berry), is regarded as the best ayurvedic rejuvenation herb. In addition to stimulating the brain to replenish the body's three fundamental elements—water, fire, and air—which are necessary for all physiological activities, it is distinctive in that it includes a natural balance of flavors in a single fruit. It was proposed that the more potent and consistent antioxidant action of tannins, rather than the mistaken "vitamin C" component, offers the better benefit. It contains calcium, phosphorus, iron, carotene, thiamine, riboflavin, and niacin among other minerals and vitamins.

An in vitro study conducted by Nampoothiri et al. on the antioxidant and inhibitory potential of Terminalia bellerica and Emblica officinalis fruits against LDL oxidation and key enzymes linked to type 2 diabetes revealed that the methanolic extract of Emblica officinalis exhibited scavenging activity against hydroxyl, superoxide, and nitric oxide radicals. This in vitro investigation demonstrated the antioxidant efficacy of Emblica officinalis' active tannoid principles.

Turmeric, another essential component of Nishamalaki, is one of the greatest ayurvedic treatments for all metabolic diseases, including diabetes. It is well renowned for its abilities to improve skin tone, fight bacteria, and promote healing. In addition to these advantages, it provides a scratching action that helps with eliminating extra body fat. It also corrects metabolism and is helpful for anemia, diabetes, and liver issues.

Numerous studies in the scientific community proved the antioxidant, anti-inflammatory, antidiabetic, and lipid-lowering properties of turmeric.²⁷ Turmeric's hypoglycemic impact has been attributed to increased peripheral glucose consumption, increased insulin secretion, and decreased hepatic glucose synthesis. The consumption of 6 grams of turmeric enhanced postprandial serum insulin levels in healthy subjects, according to Wickenberg J, et al investigation on the turmeric's effects on post-meal plasma glucose and insulin in healthy individuals.²⁸ Curcumin's effects on human protein glycosylation, lipid peroxidation, and oxygen radical production were studied by Jain et al.²⁹

RESEARCH REVIEW ON THE ANTIOXIDANT PROPERTY OF NISHAMALAKI

Since Nishamalaki is more effective, it is likely that it uses additional or combined processes, maybe working through several systems, and exerting protective benefits. In a rat model of diabetes brought on by streptozotocin, Suryanarayana P. et al. investigated the effects of turmeric and curcumin on antioxidant enzymes and oxidative stress. ³⁰ Their research revealed that Amla and Curcuma each have antioxidant activity and reduced lipid peroxidation on their own.

Jayshree et al found that Nishamalaki had decreased MDA activity, thereby preventing the development of oxidative stress and lipid peroxidation.³¹ There has also been a reported rise in the levels of SOD and catalase, which has had the combined effect of reducing superoxide radical generation.

CONCLUSION

This investigation explored the potential periodontitis relationship to oxidative stress and related systemic variables. The main cause of periodontal tissue damage brought on by host-microbe interactions is oxidative stress. Reactive oxidative species would seem to have a crucial part in the pathology of periodontal disease, despite the fact that there are a variety of potential

mechanisms that could result in the destruction of periodontal tissue. Reactive oxygen species are dangerous oxidants that should be eliminated as soon as they form or repaired in vivo. The standard periodontal therapy has been supplemented with a range of antioxidants, and positive results have been observed. This opens up new opportunities for periodontal therapy. According to studies, the anti-diabetic medication Nishamalaki has antioxidant properties and also lessens oxidative stress. We can improve clinical outcomes by combining novel antioxidant and anti-inflammatory therapies with conventional periodontal care. Nishamalaki, an antioxidant supplement, may relieve the burden of periodontal disease without any additional effort.

Author's Contribution:

Concept & Design of Study: Nubesh Khan Syed

Mohammed

Drafting: Nubesh Khan Syed

Mohammed

Data Analysis: Nubesh Khan Syed

Mohammed

Revisiting Critically: Nubesh Khan Syed

Mohammed

Final Approval of version: Nubesh Khan Syed

Mohammed

Conflict of Interest: The study has no conflict of interest to declare by any author.

Source of Funding: None

REFERENCES

- 1. Allen EM, Matthews JB, O'Halloran DJ, Griffiths HR, Chapple IL. Oxidative and inflammatory status in type 2 diabetes patients with periodontitis. J Clin Periodontol 2011;38(10):894-901.
- Chapple IL, Brock GR, Milward MR, Ling N, Matthews JB. Compromised GCF total antioxidant capacity in periodontitis: cause or effect? J Clin Periodontol 2007a;34:103–110.
- 3. Brock GR, Butterworth CJ, Matthews JB, Chapple IL. Local and systemic total antioxidant capacity in periodontitis and health. J Clin Periodontol 2004;31:515-21.
- Fisher MA, Taylor GW, West BT, McCarthy ET. Bidirectional relationship between chronic kidney and periodontal disease: A study using structural equation modeling. Kidney Int 2011;79:347–355.
- Ceriello A, Motz E. Is oxidative stress the pathogenic mechanism underlying insulin resistance, diabetes, and cardiovascular disease? The common soil hypothesis revisited. Arterioscler Thromb Vasc Biol 2004;24:816–823.
- Mizutani K, Park K, Mima A, Katagiri S, King GL. Obesity-associated gingival vascular inflammation,

- and insulin resistance. J Dent Res 2014;93: 596–601.
- 7. Koromantzos PA, Makrilakis K, Dereka X, Offenbacher S, Katsilambros N, Vrotsos IA, et al. Effect of nonsurgical periodontal therapy on Creactive protein, oxidative stress, and matrix metalloproteinase (MMP)-9 and MMP-2 levels in patients with type 2 diabetes: A randomized controlled study. J Periodontol 2012;83:3–10.
- 8. Sczepanik FSC, Grossi ML, Casati M, Goldberg M, Glogauer M, Fine N, et al. Periodontitis is an inflammatory disease of oxidative stress: We should treat it that way. Periodontol 2000;84: 45–68.
- Galli C, Passeri G, Macaluso GM. FoxOs, Wnts and oxidative stress-induced bone loss: new players in the periodontitis arena? J Periodontal Res 2011;46:397–406.
- 10. Vo TTT, Chu PM, Tuan VP, Te JS, Lee IT. The Promising Role of Antioxidant Phytochemicals in the Prevention and Treatment of Periodontal Disease via the Inhibition of Oxidative Stress Pathways: Updated Insights. Antioxidants 2020; 9:1211.
- 11. Arora N, Avula H, Avula JK. The adjunctive use of systemic antioxidant therapy (lycopene) in nonsurgical treatment of chronic periodontitis: A short-term evaluation. Quintessence Int 2013;44: 395–405.
- 12. Singh N, Chander Narula S, Kumar Sharma R, Tewari S, Kumar Sehgal P. Vitamin E supplementation, superoxide dismutase status, and outcome of scaling and root planing in patients with chronic periodontitis: A randomized clinical trial. J Periodontol 2014;85:242–249.
- Mailoa J, Lin GH, Khoshkam V, MacEachern M, Chan HL, Wang HL. Long-Term Effect of Four Surgical Periodontal Therapies and One Non-Surgical Therapy: A Systematic Review and Meta-Analysis. J Periodontol 2015;86:1150–1158.
- 14. Smiley CJ, Tracy SL, Abt E, Michalowicz BS, John MT, Gunsolley J, et al. Systematic review and meta-analysis on the nonsurgical treatment of chronic periodontitis by means of scaling and root planing with or without adjuncts. J Am Dent Assoc 2015;146:508–524.
- 15. Tsai CC, Chen HS, Chen SL, Ho YP, Ho KY, Wu YM, et al. Lipid peroxidation: a possible role in the induction and progression of chronic periodontitis. J Periodont Res 2005;40:378–384.
- 16. Khalili J, Biloklytska HF. Slivary manodialdehyde levels in clinically healthy and periodontal disease individuals. Oral Dis 2008;14(8):754-760.
- 17. Takane M, Sugano N, Iwaski H, Iwano Y, Shimizu N, Ito K. New biomarker evidence of oxidative DNA damage in whole saliva from clinically

- healthy and periodontally diseased individuals. J Periodontal 2002; 73(5): 551-4.
- 18. Canakci CF, Cicek Y, Yildrim A, Sezer U, Canakci V. Increased level of 8-hydroxydeoxyguanosine and malondialdehyde and its relationship with antioxidant enzymes in saliva of periodontitis patients. Eur J Dent 2009;3:100–106.
- Kim SC, Kim OS, Kim OJ, Kim YJ, Chung HJ. Antioxidant profile of whole saliva after scaling and root planing in periodontal disease. J Periodontal Implant Sci 2010;40(4):164–171.
- 20. Novakovic N, Todorovic T, Rakic M, et al. Salivary antioxidants as periodontal biomarkers in evaluation of tissue status and treatment outcome. J Periodontal Res 2014;49:129–136.
- 21. Trivedi S, Lal N, Mahdi AA, Singh B, Pandey S. Association of salivary lipid peroxidation levels, antioxidant enzymes and chronic periodontitis. Int J Periodontics Restor Dent 2015;35: e14–e19.
- 22. Waddington RJ, Moseley R, Embery G. Reactive oxygen species: a potential role in the pathogenesis of periodontal diseases. Oral Dis 2000;6:136-51.
- 23. Novakovic N, Todorovic T, Rakic M, Milinkovic I, Dozic I, Jankovic S, et al. Salivary antioxidants as periodontal biomarkers in evaluation of tissue status and treatment outcome. J Periodont Res 2014;49:129–136.
- 24. Alagl AS, Bhat SG. Ascorbic acid: new role of an age-old micronutrient in the management of periodontal disease in older adults. Geriatr Gerontol Int 2015;15:241–254.
- 25. Muniz FW, Nogueira SB, Mendes FL, Rosing CK, Moreira MM, de Andrade GM, et al. The impact of

- antioxidant agents complimentary to periodontal therapy on oxidative stress and periodontal outcomes: a systematic review. Arch Oral Biol 2015;60:1203–1214.
- 26. Nampoothiri SV, Prathapan A, Cherian OL, Raghu KG, Venugopalan VV, Sundaresan A. In vitro antioxidant and inhibitory potential of Terminalia bellerica and Emblica officinalis fruits against LDL oxidation and key enzymes linked to type 2 diabetes. Food Chem Toxicol 2011;49(1):125-31.
- 27. Luthra PM, Singh R, Chandra R. Therapeutic uses of Curcuma longa (turmeric). Ind J Clin Biochem 2001; 16(2):153-60.
- 28. Wickenberg J, Ingemansson SL, Hlebowicz J. Effects of Curcuma longa (turmeric) on postprandial plasma glucose and insulin in healthy subjects. Nutr J 2010;9:43.
- 29. Jain Sushil K. Justin Rains, Kimberly Jones. Effect of curcumin on protein glycosylation, lipid peroxidation, and oxygen radical generation in human red blood cells exposed to high glucose levels. Free Radical Biol Med 2006;41(1):92-96.
- 30. Suryanarayana P, Satyanarayana A, Balakrishna N, Kumar PU, Reddy GB. Effect of turmeric and curcumin on oxidative stress and antioxidant enzymes in streptozotocin-induced diabetic rat. Med Science Monitor 2007;13(12):BR286-92.
- 31. Jayshree SD, Vijaya AP et al. Evaluation of Effect of Nishamalaki on STZ and HFHF Diet Induced Diabetic Neuropathy in Wistar Rats. J Clin Diagn Res 2016;10(10):FF01-FF05.