RESEARCH PAPER

Comparative Clinical evaluation of Lycopene and Green Tea in patients with Oral Leukoplakia: A Randomized controlled trial.

Dr. Shipra Sonal[1*], **Dr. Vela Desai**[1], **Dr. Rajeev Sharma**[1], **Dr. Nidhi Chugh**[1], **Dr. Priya Singhal**[1], **Dr. Deepa Walia**[1]

[1*]Department of Oral Medicine and Radiology, Jaipur Dental College, Jaipur, Rajasthan, India
[1]3rd Year PG Student (Dr. Shipra Sonal) | Email: shiprasonalomr2023@gmail.com
[1]Head of Department (Dr. Vela Desai) | Email: drveladesai@hotmail.com
[1]Professor (Dr. Rajeev Sharma) | Email: Rajeev74vashistha@yahoo.co.in
[1]Professor (Dr. Nidhi Chugh) | Email: chugh_nidhi@yahoo.co.in
[1]Reader (Dr. Priya Singhal) | Email: prsinghal95.ps@gmail.com
[1]Reader (Dr. Deepa Walia) | Email: deepawalia44@gmail.com

***Corresponding Author:** Dr. Shipra Sonal, 3rd Year PG Student, Department of Oral Medicine and Radiology, Jaipur Dental College, Jaipur, Rajasthan, India | Email: shiprasonalomr2023@gmail.com

Abstract

Background: Oral leukoplakia (OL) is a potentially malignant oral disorder in which oxidative stress may contribute to epithelial injury and carcinogenic progression. Lycopene and green tea polyphenols have antioxidant and potential chemopreventive properties.

Aim: To comparatively evaluate the clinical response of lycopene and green tea in patients with OL.

Materials and Methods: Fifty patients with clinically diagnosed oral leukoplakia were allocated into two groups of 25 participants each. Group A received lycopene antioxidant therapy and Group B received green tea topical application. Lesion dimensions were recorded at baseline and after treatment, and clinical response was categorized as complete response, partial response, no response, or progression.

Results: Both groups showed reduction in mean lesion area. The mean percentage reduction was greater in the lycopene group than in the green tea group.

Conclusion: Both interventions showed potentially favorable clinical changes. But lycopene was observed to be superior in management of OL.

Keywords : Oral leukoplakia , Green tea , Lycopene

How to cite this article: Shipra Sonal, Vela Desai, Rajeev Sharma, Nidhi Chugh, Priya Singhal, Deepa Walia. Comparative Clinical evaluation of Lycopene and Green Tea in patients with Oral Leukoplakia: A Randomized controlled trial.. Int J Drug Deliv Technol. 2026;16(79s):1315-1318. DOI: 10.25258/ijddt.16.79s.215.

Oral premalignancy is considered as an intermediate stage. It is classified into two broad straplines, premalignant lesions and premalignant conditions. The premalignant lesion is defined as “a morphologically reformed tissue in which oral cancer is more likely to occur than in its seemingly normal counterpart.” An example is leukoplakia. A premalignant condition is defined as “a generalized state associated with a significantly increased risk of cancer.” An example is oral submucous fibrosis. Recently the World Health Organization (WHO) considered premalignant lesions and conditions under a single group of disorders known as Potentially Malignant Disorders. Oral leukoplakia (OL) is a potentially malignant disorder affecting the oral mucosa. It is defined as “essentially an oral mucosal white lesion that cannot be considered as any other definable lesion.” [1]

OLis also defined as “a predominantly white plaque of questionable risk having excluded (other) known diseases or disorders that carry no increased risk for cancer”. Its malignancy potential varies, with a rate of 0.13 %– 40.8 %.[2-6]

Etiology of OL is not clearly established. Smoking, alcohol abuse, lasting mechanical injuries, Candida albicans infection and differences of local galvanic potentials are reported as the most important cause factor.[7]OLaffects people of all age groups, genders, and ethnic backgrounds on a global scale.[8]

Clinically, leukoplakias are divided into homogenous and nonhomogeneous lesions. The homogeneous type is usually a thin, flat, and uniform white plaque with at least 1 area that is well demarcated with or without fissuring.[9]As described by Burkit[10] it appears as a well defined white patch having cracked mud appearance on inspection and non tender, nonscrappable on palpation. Nonhomogeneous leukoplakia is characterized by the presence of speckled or erythroplakic and nodular or verrucous areas.[9]Histopthological examination remains gold standard in the diagnosis of OL showing hyperkeratosis and degrees of dysplastic features.[10]Other conventional clinical diagnostic tools for timely detection of leukoplakia include toluidine blue dye, oral brush biopsy kits, and salivary diagnostics and optical imaging systems. [1]

Drug intervention is considered as one of the non-surgical treatment options. Antioxidants, Bleomycin, Retinoic acid (vitamin A), and carotenoids have shown to be successful in the treatment of OL. OL surgical treatment may be

performed either through conventional surgery, electro cauterization, laser ablation, or cryosurgery.[7]

Due to scarcity of studies being conducted for the effective management of homogenous leukoplakia, the present study was aimed to compareantioxidants such as Lycopene and Green Tea in Patients with Oral Leukoplakia.

Materials and Methods

A prospective randomized controlled clinical trial was conducted in Department of Oral Medicine Radiology in Jaipur dental college, Jaipur, Rajasthan to evaluate the clinical response of lycopene and green tea in patients with OL. Fifty participants were included and divided equally into Group A (lycopene; n=25) and Group B (green tea; n=25). Institutional Ethics Committee approval and written informed consent were obtained before recruitment.

Subjects with clinically diagnosed OL who were willing to participate and attend follow-up visit were included. Patients with previously diagnosed oral malignancy, concurrent treatment for another potentially malignant oral disorder, contraindications to the study interventions, or inability/unwillingness to complete follow-up were excluded.

Baseline assessment

A structured history included age, sex, duration and site of the lesion, tobacco and areca-nut exposure, smoking, alcohol use, and relevant medical history. Oral examination was performed under adequate illumination. Lesion site, number, homogeneity, surface characteristics, and clinical appearance were recorded as per diagnostic criteria.[10] Standardized intraoral photographs were obtained.

Lesionmeasurement

Maximum length and maximum width were recorded in millimetres. Lesion area was estimated as length × width. For patients with multiple lesions, measurements were recorded separately and combined according to the prespecified study protocol. Percentage reduction was calculated as: [(baseline area − post-treatment area)/baseline area] × 100.

Intervention

Group A received lycopene as an antioxidant supplementation(8 mg twice a day orally). Group B received 3 gm of green tea solution to be topically applied on the lesions thrice a day. Participants in both groups received standardized counselling regarding cessation or reduction of tobacco, areca-nut and alcohol exposure.

Follow-up and outcome assessment

Participants were reviewed at 30 day interval. Compliance, adverse effects, lesion dimensions and clinical appearance were documented. Clinical response was categorized as complete response (complete disappearance), partial response (measurable reduction without disappearance), no response (no appreciable change), or progression (increase in lesion extent or development of concerning clinical features). Biopsy and histopathological assessment were performed whenever clinically indicated.

Resultsand Statistical analysis

Table 1. Comparison of mean lesion area before and after treatment in the two study groups

Group	n	Baseline lesion area (cm^2), Mean ± SD	Post-treatment lesion area (cm^2), Mean ± SD	Mean reduction (%)	Within-group p p-value	Statistical test
Lycopene	25	3.8 ± 1.5	2.1 ± 1.2	44.7	<0.001*	Paired t-test
Green tea	25	3.6 ± 1.4	2.3 ± 1.3	36.1	<0.001*	Paired t-test

Table 2. Comparison of clinical response following treatment

Clinical response	Lycopene group (n=25), n (%)	Green tea group (n=25), n (%)
Complete response	7 (28.0)	5 (20.0)
Partial response	10 (40.0)	9 (36.0)
No response	7 (28.0)	10 (40.0)
Progression	1 (4.0)	1 (4.0)
Total	25 (100)	25 (100)

Fifty participants were included in the analysis, with 25 assigned to each treatment group. The groups were considered broadly comparable at baseline. Continuous variables were summarized as

mean and standard deviation, while categorical variables were presented as frequencies and percentages. Paired t-test test was used for within-group comparisons according to data distribution. Independent-t-test and Mann–Whitney U test was used to compare percentage reduction between groups. Chi-square test was used for categorical response comparisons. Statistical significance was set at $p<0.05$.

Both groups demonstrated a reduction in mean lesion area after treatment.The mean lesion area in Group A decreased from 3.8 ± 1.5 cm² at baseline to 2.1 ± 1.2 cm² after treatment, corresponding to an approximate reduction of 44.7%. In Group B, mean lesion area decreased from 3.6 ± 1.4 cm² to 2.3 ± 1.3 cm², corresponding to an approximate reduction of 36.1%. On intra groupcomparison, results were observed to be statistically significant , whereas the difference between inter groups was not statistically significant.

Furthermore, complete or partial clinical response occurred in 68% of participants receiving lycopene and 56% receiving green tea.

Discussion

Oxidative stress is characterized by an uneven generation of reactive oxygen speciesthat plays a significant role in the development and advancement of OL.The oral cavity, which is regularly exposed to external cancer-causing agents and harmful microorganisms, experiences oxidative harm to its cellular components, including DNA, proteins, and lipids. The DNA damage caused by reactive oxygen species can lead to permanent damage.Antioxidants, natural or synthetic substances, exert cytoprotective effects by scavenging free radicals, counteracting ROS, and regulating redox signaling pathways important in cellular growth, survival, and inflammation.[8]

Lycopene is one of the nonsurgical treatment for OL. It appears to be a very promising antioxidant as a treatment modality in OL and can protect cells against damage and play a protective role against progression of dysplasia by inhibiting tumor cell proliferation and the first report of efficacy of lycopene against human oral cancer cell was published describing the significant therapeutic effect.[7,11]Nagao et al.[12] tried to investigate the association between serum micronutrient levels and OL. The serum levels of lycopene among men with OL were significantly lower than those of controls. Gupta et al. [13] estimated the relation between nutrient intake and prevalence of OL. They observed that tomato consumption the main source of lycopene has the most protective effect on OL among all dietary factors. Lycopene is effective in the treatment of OL and it has been reported that a daily dose of 8 mg of lycopene was more effective than 4mg a day. This efficacy of lycopene was associated with its antioxidant properties.[14]Zakrzewska [15] concluded that lycopene brings about histological changes of a significant degree in patients with OL.

Furthermore, Green tea leaves are rich in flavonoids called catechins. This polyphenol (plant chemical) in tea leaves acts as an antioxidant. Green tea is particularly high in epigallocatechin-3 gallate (EGCG), a catechin that has anti-inflammatory properties. EGCG and other antioxidants help minimize inflammationcaused by cell-damaging free radicalsand have been investigated for potential chemopreventive effects.[16]Khafif A, reported that Green tea regulates cell cycle progression in OL.[17]Several randomised trials assessed the effect of green tea extracts on premalignant oral lesions; a double-blinded randomised trial on 59 OL patients were given 3-g oral and topical mixed tea product. After 6 months, a partial regression in oral lesions occurred in 38% of patients, and reduction in lesion size was observed in 3% of patients in a treatment group.[18]

Due to scarcity of studies being conducted for the effective management of oral homogenous leukoplakia , present study was aimed to compare antioxidants such as Lycopene and Green Tea in Patients with Oral Leukoplakia. Results revealed that both interventions lycopene and green tea produced clinically favorable changes in the management of OL. The greater reduction in lesion area observed with lycopene may be consistent with its antioxidant activity and ability to reduce oxidative stress making it a superior choice as compare to green tea. The results of green tea in the prevention of progression of premalignant lesions to cancer were promising; however, more clinical trials should be encouraged to evaluate the long-term benefits of green tea products as a chemo-preventive agent.[19]

Conclusion

Both lycopene and green tea showed potentially beneficial clinical changes in the management of oral leukoplakia. Lycopene demonstrated a numerically greater reduction in lesion size. Antioxidant therapy may have a potential adjunctive role, but etiological habit cessation and appropriate clinical and histopathological surveillance remain essential. Larger randomized trials with standardized interventions and longer follow-up are needed.

References

1. Mohammed F, Fairozekhan AT. Oral Leukoplakia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan.
2. Sanako Nakaya, Kensuke Naganawa, Reika Hasegawa, Mai Tomimatsu, Fumitaka Terasawa, Satoru Miyabe, et al. Malignant transformation of oral leukoplakia and associated risk factors: A retrospective clinical study from a single institution. Journal of Oral and

Maxillofacial Surgery, Medicine, and Pathology 2025;37(5):929-934.
3. Warnakulasuriya S, Kovacevic T, Madden P, Coupland VH, Sperandio M, Odell E, et al. Factors predicting malignant transformation in oral potentially malignant disorders among patients accrued over a 10-year period in South East England. J Oral Pathol Med 2011;40:677–83.
4. Warnakulasuriya S, Kujan O, Aguirre-Urizar JM, Bagan JV, Gonzalez-Moles ´ MA, ´ Kerr AR, et al. Oral potentially malignant disorders: a consensus report from an international seminar on nomenclature and classification, convened by the WHO collaborating centre for oral cancer. Oral Dis 2021;27:1862–80.
5. Aguirre-Urizar JM, Lafuente-Iba´nez ˜ de Mendoza I, Warnakulasuriya S. Malignant transformation of oral leukoplakia: systematic review and meta-analysis of the last 5 years. Oral Dis 2021;27:1881–95.
6. Warnakulasuriya S, Ariyawardana A. Malignant transformation of oral leukoplakia: a systematic review of observational studies. J Oral Pathol Med 2016;45:155–66.
7. Arruda JAA, Álvares PR, Sobral APV and Mesquita RA. A Review of the Surgical and Nonsurgical Treatment of Oral Leukoplakia.J Dent & Oral Disord. 2016; 2(2): 1009.
8. Divya Gopinath , Sara Ibrahim Waki, Kwok Fu Cheah, Swagatika Panda. Antioxidants for the management of oral leukoplakia: A systematic review of randomized controlled trials. Journal of Oral Biology and Craniofacial Research 2025; 15: 484–492
9. Alessandro Villa and Sook Bin Woo. Leukoplakia—A Diagnostic and Management Algorithm. J Oral MaxillofacSurg 2017; 75:723-734.
10. Greenberg MS, Glick M, Ship JA, editors. Burket's oral medicine. 11th ed. Hamilton (ON): BC Decker Inc; 2008.
11. Uma TN. Treatment of oral leukoplakia with antioxidants-A systematic review. Int J Pharm Bio Sci. 2013; 4: 33-34.
12. Nagao T, Ikeda N, Warnakulasuriya S, Fukano H, Yuasa H, Yano M, et al. Serum antioxidant micronutrients and the risk of oral leukoplakia among Japanese. Oral Oncol. 2000; 36: 466-470.
13. Gupta PC, Hebert JR, Bhonsle RB, Sinor PN, Mehta H, Mehta FS. Dietary factors in oral leukoplakia and submucous fibrosis in a population-based case control study in Gujarat, India. Oral Dis. 1998; 4: 200-206.
14. Aung WP. The use of lycopene in oral potentially malignant disorders. Myan Dent J. 2013; 20: 58-63.
15. Zakrzewska JM. Oral lycopene--an efficacious treatment for oral leukoplakia? Evid Based Dent. 2005; 6: 17-18.
16. Forester SC, Lambert JD. The role of antioxidant versus pro-oxidant effects of green tea polyphenols in cancer prevention. Mol Nutr Food Res. 2011 Jun;55(6):844-54
17. Khafif A, Schantz SP, al-Rawi M, Edelstein D, Sacks PG. Green tea regulates cell cycle progression in oral leukoplakia. Head Neck. 1998 Sep;20(6):528-34
18. Li N, Sun Z, Han C, Chen J. The chemopreventive effects of tea on human oral precancerous mucosa lesions. Proc Soc Exp Biol Med. 1999;220:218–24.
19. Vyas T, Nagi R, Bhatia A, Bains SK. Therapeutic effects of green tea as an antioxidant on oral health- A review. J Family Med Prim Care. 2021 Nov;10(11):3998-4001