



## CLINICAL EVALUATION OF PROPOLIS AND LYCOPENE IN THE MANAGEMENT OF ORAL LEUKOPLAKIA IN ADULT POPULATION- A COMPARATIVE STUDY

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**ABSTRACT** **INTRODUCTION:** Oral leukoplakia is premalignant mucosal condition with probability of transforming into oral carcinoma. A number of studies have proven the use of antioxidants in the management of Oral leukoplakia. Recently, use of natural drugs, such as propolis having anti-inflammatory and antioxidant properties has gained considerable interest. **AIMS:** To compare the clinical efficacy of propolis with that of Lycopene in management of oral leukoplakia **SETTINGS AND DESIGN:** Total number of 50 clinically diagnosed leukoplakia cases was included in the study. These patients were divided randomly into 2 groups. **METHODS AND MATERIAL:** Group 1 (N=25) was received capsule Lycopene 2 times daily for 15 days and group 2 (N=25) was received capsule propolis 2 times daily for 15 days. Both the groups were evaluated for size of lesion at baseline (1st visit), first follow-up (7th day), and second follow-up (14th day) and after 6 months. **STATISTICAL ANALYSIS USED:** P value < 0.005 considered to be statistically significant. The paired t test and unpaired t test were used. **RESULTS:** The results revealed that the greatest significant percentage of change and subsequent improvement in size of lesion were recorded in the both the group. **CONCLUSIONS:** Reported data in this study using propolis could provide a new promising safe and effective therapy

**KEYWORDS :** Propolis, Lycopene, Antioxidant, Oral Leukoplakia

### INTRODUCTION

Oral cancer is progressive disease which manifests as a series of recognizable stages. Tobacco use in any form is an important preventable risk factor for development of oral cancer. The occurrence of premalignant lesions or premalignant condition takes place in between the initiation of carcinogenic tobacco habits and the development of invasive oral cancer. Leukoplakia is one of the most common oral premalignant lesions representing 85% of such lesions.<sup>1</sup>

The prevalence of leukoplakia varies among scientific studies. Also in the population studies it is more common in men than the female.<sup>2</sup> The use of tobacco is considered to be most common risk factor for the oral leukoplakia. It may be found at all sites of oral mucosa. Early identification of leukoplakia may prevent its malignant transformation by early interception and management.<sup>1</sup> Over 1-30 years, the malignant transformation rate has been reported in the range of 1-20%.<sup>2</sup>

Various diagnostic modalities are available for this lesion which includes vital staining. Based on the diagnosis various treatment modalities can be used which includes both conservative and surgical aspect. In the conservative management various pharmacological agents such as antioxidants like retinoid, carotenoids, retinol, ascorbic acid and alpha-tocopherol (vitamin E) had been used as effective chemo preventive agents in the treatment of leukoplakia. Lycopene, a carotenoid which gives red color to tomatoes, other vegetables and fruits. It is considered as a potent antioxidant with a single oxygen quenching ability.<sup>1</sup>

Also there are certain natural products such as propolis. It is made by honey bees from the shoots and exudates of different plants. It is useful in certain dermatological preparations which is useful in treatment of herpes simplex, burns, wound healing, acne, and neurodermatitis. Commercially it is available in the form of powder, capsules, creams,

mouthwash solutions, throat lozenges. The mouthwashes and toothpastes containing propolis were found to be an effective modality in the prevention of caries and also in the treatment of stomatitis and gingivitis. It also finds use in health foods, beverages and in cosmetic. Propolis has several medicinal properties, like anti-tumor capacity, anesthetic, antioxidant, anti-inflammatory, anti-fungal and anti-viral, antibacterial, vasoprotective and cicatrizing.<sup>3,4</sup>

Numerous studies have evaluated the use of propolis in general health but very few studies have assessed its role in management of oral diseases. Also it was found to be effective in the management of oral lichen planus. Recently its role in the management of oral leukoplakia has not been investigated. Thus there is need of further investigation in this era.

With this background in the mind, this study was designed with aim to evaluate the effectiveness of propolis and lycopene in the management of oral leukoplakia patients.

### SUBJECTS AND METHODS:

The current prospective, randomized and single blind study included 50 oral leukoplakia patients reporting to the Department of Oral Medicine and Radiology, MGV's Dental College Hospital, Nashik. The study was conducted after obtaining the approval from institutional ethical committee. Subjects fulfilling the inclusion criteria's and; rendering signed written informed consent for participation were enrolled in the study. The patients were diagnosed clinically for Oral homogenous leukoplakia with unilateral involvement. Both male and female patients with oral leukoplakia were included in the study.

### Inclusion criteria

- Patients with age group 18-60yrs.
- Clinically diagnosed cases of oral leukoplakia.

- Patient willing to participate in the study.
- Patients with leukoplakia who have not received any treatment in last 3month.

**Exclusion criteria**

- Patients not willing to complete the study.
- Patients with known systemic medical condition.
- Patients who are currently receiving any other treatment for the management of leukoplakia.
- Patients with any other oral lesions.
- Patients allergic to propolis/ Lycopene.

Detailed family and medical history was recorded. Also habit history and the course of the disease was recorded. A thorough clinical examination was carried and relevant findings were recorded. Patient was encourage to quit-implies life time commitment, was asked to stop all habit during treatment and study duration.

The subjects were randomly divided in 2 equal groups using simple random sampling, Group a [Lycopene group] and Group B [propolis group]. Group 1 (N=25) received capsules lycans (400mg)(John lee product with composition of Lycopene, multivitamin, multimineral) 2 times daily for 15 days and Group 2 (N=25) received capsules Bee Propolis (500mg) (hawaiian bee propolis) 2 times daily for 15 days . Both the groups will be evaluated for size of lesion at baseline (1st visit), first follow-up (7th day), and second follow-up (14th day). In case of any reaction such as rash, allergy, etc., the patients were asked to report immediately. During each visit of the patient, the clinical response was evaluated by bi- dimensional measurement of the lesions. The clinical response was noted down carefully.

To know the effectiveness of medicine in reduction in lesion size the patients were treated with two different medicines and the size of the lesion was recorded after 1<sup>st</sup> day, 7<sup>th</sup> day, and 15<sup>th</sup> day. The reduction in size of lesion was obtained by finding the difference between the reading of day 1<sup>st</sup> & 15<sup>th</sup>.

To evaluate if there is any significant difference between the average reduction in size of lesion treated with 2 different medicines. Statistical analysis was done using unpaired't' test was applied at 95% confidence of level and 4 degree of freedom. P value less than 0.005 was considered to be the statistical significant.

**RESULTS:**

A total of 50 patients were enrolled in this study, out of that 6 were females and 44 were males(table 1). The most common age group was between 18-40 years( table 2). A total of 50 lesions were diagnosed and treated.

**Table 1 Sex distribution of patients**

Groups	MALE	FEMALE
Group A	21	4
Group B	23	2

**Table 2 Age-wise distribution of patients**

Age range	Number of patients
18-40	27
40-55	14
Above 55	9

Risk factors were predominantly found in males: 12 were smokers and alcohol drinkers, 15 were tobacco chewers, 16 were smokers, 2 were only alcohol drinker, and 5 were neither smoker nor alcohol drinkers.

The sites most commonly involved are buccal mucosa followed by tongue, gingival, alveolar ridge then palate and lip as mentioned in table no.3. Also the majority of lesions had homogeneous surface involvement.

**Table no. 3 Site distribution of the lesions**

Site	No. of patients
Buccal mucosa	22
Tongue	9
Gingiva	8
Alveolar ridge	6
Palate	3
Lip	2

**Within Group Comparison**

To compare the reduction in size of leukoplakia two groups of 25 patients each were treated with propolis and Lycopene respectively. The lesion size is measured at the beginning i.e. day 0 and thereafter on 7<sup>th</sup> and 15<sup>th</sup> day.

To know if the treatment is effective in reducing lesion size paired t test is applied at 95% confidence level and 24 degrees of freedom separately for both the groups and pre and post treatment average lesions size is compared. The results obtained are shown in Table 4.

**Table 4 Difference between size of lesion before and after treatment for both groups**

Group	Mean lesion size		S.D.		S.E.	t value	p Value & remark
	BT	AT	BT	AT			
Lycopene	3.3096	0.5733	1.2829	0.2731	0.2236	-12.395	0.0000 Significant
Propolis	3.1796	0.6475	1.3299	0.3322	0.2236	-11.482	0.0000 Significant

From the table it can be concluded that the average size of lesion has reduced significantly for both Lycopene and Propolis after the treatment. Thus both treatments are effective in reducing lesion size.

**Between Group Comparison**

To compare the two medicines first the difference between the lesion size before and after treatment is calculated separately for both the groups. Then the average reduction for both the groups is compared using unpaired t test at 95% confidence level and 48 degrees of freedom the results obtained are shown in Table 5.

**Table 5 Average reduction in size of lesion in both groups**

Group	Mean reduction in lesion size	S.D.	S.E.	t value	p value	Remark
A: Lycopene	-2.7363	1.05873	0.3162	-0.6543	0.2581	Not Significant
B: Propolis	-2.5321	1.05759				

From the table it can be concluded that there is no significant difference in average reduction of lesion size due to two different medicines. Thus both medicines are equally effective in reducing lesion size. If the average reduction in size is observed little more in case of medicine Propolis as compared to Lycopene even though not significant.

**DISCUSSION:**

Leukoplakia was defined by the World Health Organization(WHO) in 1978 as a white patch or plaque which cannot otherwise be characterized clinically or pathologically as any other disease.<sup>2</sup> Tobacco is considered as risk factor in cancerous or precancerous lesion as it plays essential role through genetic alterations. Tobacco cessation along with the consumption of antioxidant agents have been suggested to cure precancerous lesions like leukoplakia.<sup>5</sup>

The lycopene is a potent inhibitor used in the management of cancerous and precancerous lesions.<sup>6,7</sup> It exerts singlet oxygen quenching via physical and chemical quenching of free radicals.<sup>8</sup>

The propolis is natural powerful product collected by honey bees.<sup>9,10</sup> It has medicinal properties mainly including antioxidant, anti inflammatory, antitumor, and immunomodulatory effect.<sup>11</sup> It is useful in dentistry for the treatment of periodontal diseases, apthous stomatitis, denture stomatitis, oral candidiasis, viral infections.<sup>12</sup> Studies on the usage of propolis concluded that it is a product of great interest for medicine and dentistry.<sup>13</sup>

The study conducted by Joshy et al<sup>14</sup> and zyada et al<sup>15</sup> obtained favorable results in the management of oral lichen planus as it has anti-inflammatory, antioxidant and antitumoral properties. Also the study done by Zenouz et al<sup>16</sup> shows that there is significant decrease in size of lesion in the case of oral lichen planus using propolis. Thus this study conducted with aim to evaluate the efficacy of topical propolis in the management of oral leukoplakia.

In the present study, out of 50 cases studied, 44 were females and 6 were males where as in study conducted by Singh et al<sup>17</sup> shows out of 58 cases studied, 44 (76%) were males and 14 (24%) were women. Also common age of occurrence is between 18-40 where as in study conducted by Singh et al it was 31 to 60.

In the present study, it has been observed that the buccal mucosa is more frequently involved than other region of oral cavity which is in accordance with study conducted by Singh et al.

This study denotes that after starting the therapy, there is gradual decrease in lesion size in both groups. In the present study we have found that there is significant reduction in size of lesion using Lycopene which is in accordance with study done by Singh et al.

In the present study, propolis showed significant decrease in the size of lesion which is in accordance with study done by Joshy et al in which propolis was used in the treatment of oral lichen planus and it was found effective because of antioxidative and anti-inflammatory properties.

Based on all the clinical finding in the present study propolis is considered to be the effective treatment modality for reducing size of lesion and for decreasing the chances of malignant transformation rate of oral leukoplakia patients. Also in the present study period, no patients reported with undesirable side effects proving the safety of drug in the management of leukoplakia.

There are certain limitations as along with clinical evaluation histological response should also have been calculated. In the present study the long term effect of treatment did not evaluated and there is need to design a study with longer follow-ups.

## CONCLUSION

It is concluded that both Lycopene and propolis are equally effective treatment modalities. The favorable clinical response, anti-inflammatory, antioxidant property and safety profile of the propolis in treating oral leukoplakia confirm its potential to be used as a therapeutic alternative.

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## REFERENCES

- Patel, J.S., Umarji, H.R., Dhokar, A.A., Sapkal, R.B., Patel, S.G. and Panda, A.K., 2014. Randomized controlled trial to evaluate the efficacy of oral Lycopene in combination with vitamin E and selenium in the treatment of oral leukoplakia. *Journal of Indian Academy of Oral Medicine and Radiology*, 26(4).
- Glick Michael, Feagans WM. *Burket's Oral Medicine*. Shelton, Connecticut: People's Medical Publishing House-USA; 2015
- G.A.Burdock, "Review of the biological properties and toxicity of bee propolis (propolis)," *Food and Chemical Toxicology*, 1998.
- J. W. Dobrowolski, S. B. Vohora, K. Sharma, S. A. Shah, S. A. H. Naqvi, and P. C. Dandiya, "Antibacterial, antifungal, anti-moebic, anti-inflammatory and antipyretic studies on propolis bee products," *Journal of Ethno pharmacology*, vol. 35, 1991
- Shahi S, Ahmadian E. The protective role of Lycopene in the treatment of oral disease. *Journal of advanced chemical and pharmaceutical materials (JACPM)*. 2018
- Saawarn N, Shashikanth MC, Saawarn S, Jirge V, Chaitanya NC, Pinakapani R. Lycopene in the management of oral lichen planus: A placebo-controlled study. *Indian Journal of Dental Research*. 2011
- Levy J, Sharoni Y. functions of tomato Lycopene and its role in human health. *Herbal Gram*. 2004.
- Stahl W, Sies H. Lycopene: biologically important carotenoids for humans? *Archives of biochemistry and biophysics*. 1996
- M. Marcucci, "Propolis: chemical composition, biological properties and therapeutic activity," *Apidologie*, 1995.
- S. L. De Castro, "Propolis: biological and pharmacological activities. Therapeutic uses of this bee-product," *Annual Review of Biomedical Sciences*, 2001.
- E.L.Ghisalberti, "Propolis: are view," *BeeWorld*, 1979.
- LS VK. Propolis in dentistry and oral cancer management. *North American journal of medical sciences*. 2014
- Ahuja V, Ahuja A. Apitherapy-A sweet approach to dental diseases. Part II: Propolis. *Journal of Advanced Oral Research*. 2011
- Joshy A, Doggalli N, Patil K, Kulkarni PK. To evaluate the efficacy of topical propolis in the management of symptomatic oral lichen planus: A randomized controlled trial. *Contemp Clin Dent* 2018
- Zyada MM, El-Said Elewa M, El-Meadawy S, El-Sharkawy H. Effectiveness of topical mucoadhesive gel containing propolis in management of patients with atrophic and erosive oral lichen planus: Clinical and immunohistochemical study. *Egypt Dent Assoc* 2012
- Zenouz AT, Mehdipour M, Abadi RT, Shokri J, Rajaee M, Aghazadeh M, Golizadeh N. Effect of use of propolis on serum levels of il-17 and clinical symptoms and signs in patients with ulcerative oral lichen planus. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*. 2015
- Singh M, Krishanappa R, Bagewadi A, Keluskar V. Efficacy of oral Lycopene in the treatment of oral leukoplakia. *Oral oncology*. 2004