WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 5, 1435-1446. Research Article ISSN 2277– 7105

COMPARITIVE EVALUATION OF CURCUMIN GEL VERSUS ANTIOXIDANTS FOR TREATMENT OF HOMOGENOUS LEUKOPLAKIA: A CLINICAL STUDY

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Article Received on
06 March 2022,

Revised on 26 March 2022,
Accepted on 16 April 2022

DOI: 10.20959/wjpr20225-23827

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ABSTRACT

Background: Leukoplakia is the most common oral white lesion that is classified under potentially malignant disorder affecting oral mucosa. It is significant as it has a high risk of malignant transformation. There is no single treatment available which is uniformly effective in leukoplakia, it is important to explore a spectrum of therapies to validate a definitive treatment strategy. **Aim:** To assess the effectiveness of Curcumin gel versus Antioxidants in the treatment of homogenous leukoplakia. **Objectives:** 1) To assess the effectiveness of Curcumin gel in the treatment of homogenous leukoplakia. 2) To compare the effectiveness of Curcumin gel versus Antioxidants in the treatment of homogenous leukoplakia. **Materials and Methods:** 30 patients with clinically diagnosed homogenous leukoplakia were recruited for the study and randomly divided into Group 1(Curenext gel group-15) and Group 2 (Antioxidant SM Fibro Capsule group- 15). Group 1 patients were instructed to apply the gel thrice daily for a period of 1 month and Group 2 patients were given SM Fibro Capsule once daily for 1 month. Evaluation of treatment was assessed by quantitative bi-dimensional measurement using clinical photographs of the lesion and measuring the size of the lesion using photoshop software. **Results:** In both Group 1 and Group 2, marked improvement was observed in size (length and breadth). Mean percentage reduction in lesion length and lesion breadth shows statistically significant improvement result with SM Fibro capsule compared to curenext gel group with p value of <0.001*. **Conclusion:** The treatment of homogenous

leukoplakia with curenext gel and SM Fibro capsule was found to be effective in reduction of size. Antioxidant SM Fibro capsule when compared with curenext gel showed significant reduction in size.

KEYWORDS: Homogenous leukoplakia; Curenext gel; Antioxidant SM Fibro capsule.

INTRODUCTION

Oral Leukoplakia (OL) is the most common potential malignant disorder of the oral cavity.[1] The precise etiology of oral leukoplakia is unknown but several factors have been associated for their occurrence such as Tobacco, Alcohol, candida albicans, Herpes, Dietary Deficiency, Trauma, Galvanism, UV-Radiation. The risk of malignant transformation in oral leukoplakia varies from 0.3% to 25%.[1] Free radical scavengers should be the requisite part of the treatment regimen to prevent the progression of pre-cancerous lesions into malignancies.[2] Antioxidants acts as radical scavengers that block the process of oxidation by neutralizing free radicals.[3]

In recent years herbal medicines gained importance in treatment of oral diseases including premalignant disorders.[4] Curcumin commonly known as turmeric belongs to ginger family (zingiberaceae). It is a yellow pigment in curry powder derived from curcuma longa plant. The components are known as curcuminoids, which include mainly curcumin, demethoxycurcumin, bisdemethoxycurcumin.[5] By inhibiting free radical it suppress or prevent the oral pre-cancerous and cancerous lesions.[6] Hence the aim of the present study is to assess and compare the effectiveness of curcumin gel versus antioxidants for the treatment of homogenous leukoplakia.

MATERIAL AND METHODS

30 patients with clinically diagnosed homogenous leukoplakia were selected reporting to the department of Oral Medicine and Radiology, The Oxford Dental College, Banglore. Prior to conducting the study, ethical clearance was obtained from the ethical board of The Oxford Dental College. Informed consent was obtained from all the patients. Individuals of age ranging from 18-50 years with clinically diagnosed homogenous leukoplakia, who have not undergone any treatment for leukoplakia for past 3 months and who are willing to quit smoking, tobacco and alcohol habits were included in the study. Those with potentially malignant disorders other than homogenous leukoplakia, any systemic illness or who are already diagnosed as cancer patients, allergy to zingiberaceae family were excluded from the

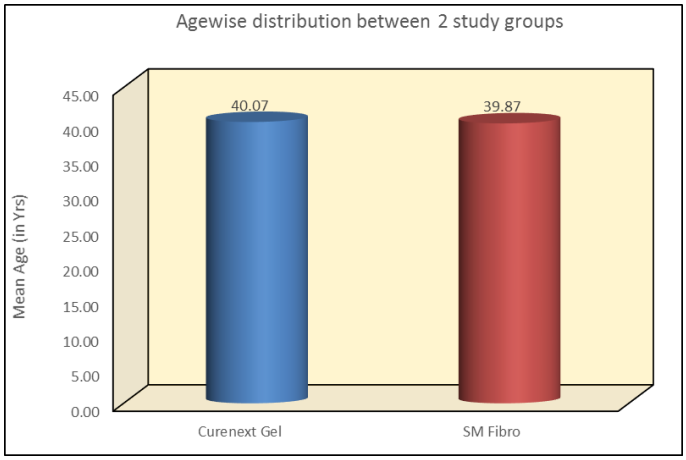
study. The patients were divided into 2 Groups- Group 1 and group 2. Each group consist of 15 patients. They were randomised by lottery method. Group 1patients were given Curcumin gel and group 2 patients were given Antioxidant SM Fibro Capsule.

Tobacco cessation counseling was done for all the patients at the very first appointment. Group 1 Patients were instructed to apply the gel thrice daily after breakfast, lunch and dinner for a period of 1 month. They were instructed to use sterile ear buds for gel application at the site of the lesion and were also demonstrated about the quantity and method of gel application on the lesion at the first appointment itself. Group 2 were given SM Fibro Capsule once daily for 1 month. The therapy was followed up for the next 30 days. Group 1 and Group 2 patients were examined on the 15^{th}, 30^{th} day to assess the change in the size of the lesion at the baseline and post treatment. The evaluation of the treatment was assessed by quantitative bidimensional measurement using clinical photographs of the lesion and measuring the size of the lesion by photoshop software. The two longest diameters calculated by the software were used to calculate the total size of the lesion. The measurements was done twice, first at the baseline (before application of the gel) for Group 1 and for group 2 (before giving capsule) and at the post treatment(end of 1 month). The data obtained was statistically analyzed.

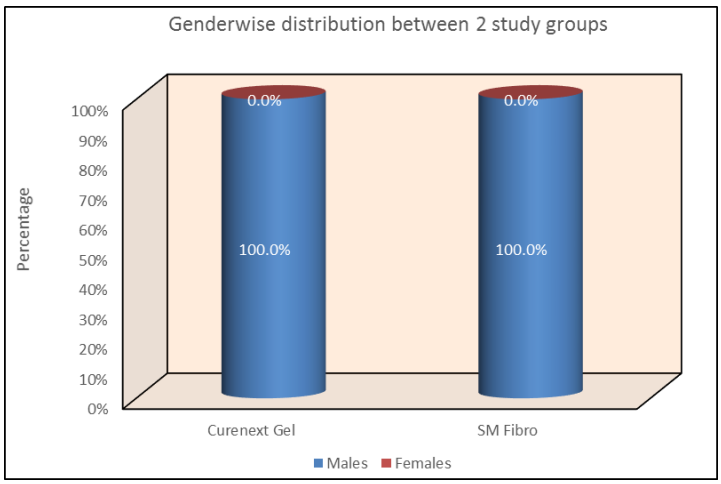
RESULTS

Table 1: Age and gender distribution between 2 study groups.

Age and gender distribution between 2 groups						
Variable	**Category**	**Curenext Gel**		**SM Fibro**		**P-Value**
		Mean	**SD**	**Mean**	**SD**	
Age	Mean	40.07	6.90	39.87	5.15	0.93[a]
	Range	29 - 50		31 - 48		
		n	%	n	%	
Sex	Males	15	100%	15	100%	1.00[b]
	Females	0	0%	0	0%	



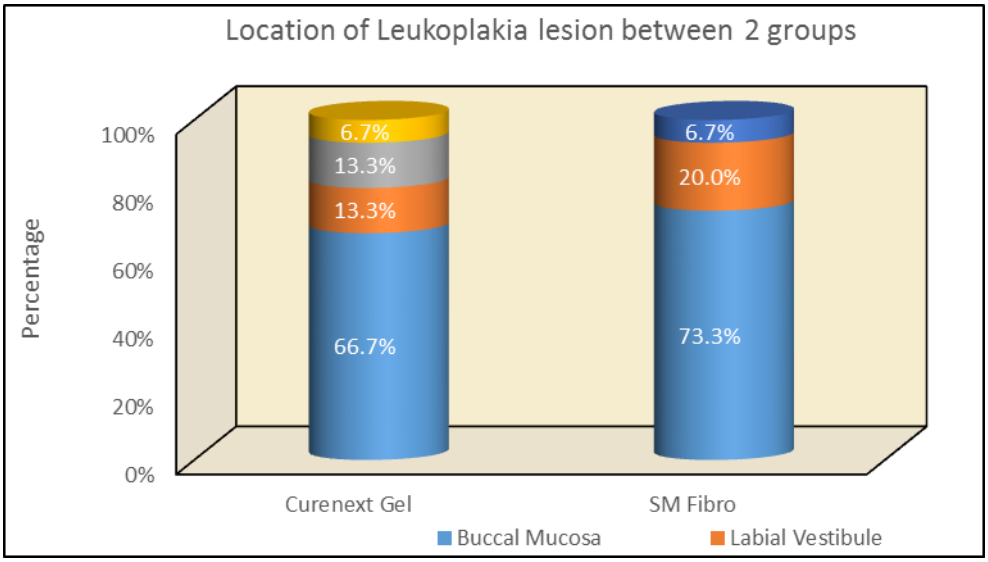
Graph 1: Agewise distribution between 2 study groups.



Graph 2: Genderwise distribution between 2 study groups.

Table 2: Comparison of Location of Lesion between 2 study groups using Chi Square Test.

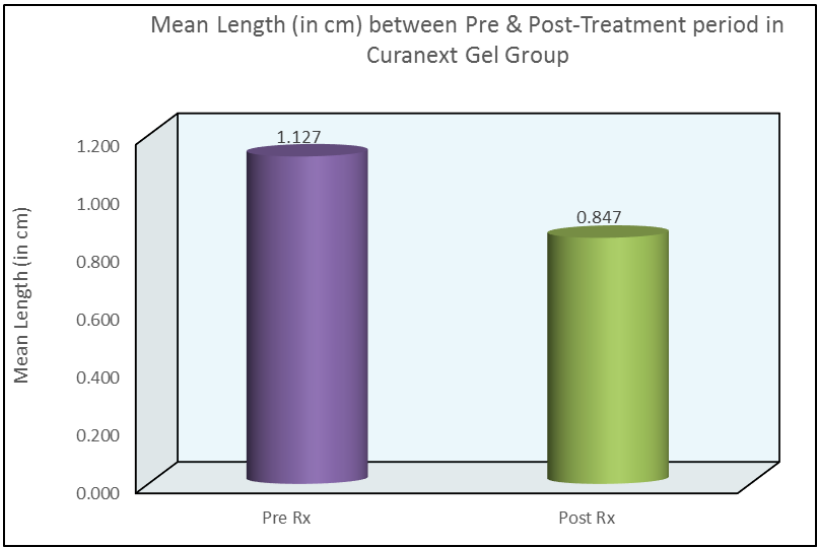
Comparison of Location of Lesion between 2 groups using Chi Square Test						
Variable	**Category**	**Curenext Gel**		**SM Fibro**		**P-Value**
		n	**%**	**n**	**%**	
Location	Buccal Mucosa	10	66.7%	11	73.3%	0.37
	Labial Vestibule	2	13.3%	3	20.0%	
	Gingiva	2	13.3%	0	0.0%	
	Lower Lip	1	6.7%	0	0.0%	
	Ventral surface of Tongue	0	0.0%	1	6.7%	



Graph 3: Location of leukoplakia lesion between 2 groups.

Table 3: Comparison of Mean Length (in cm) of lesion between Pre & Post-Treatment period in Curenext Gel group using Student Paired t Test.

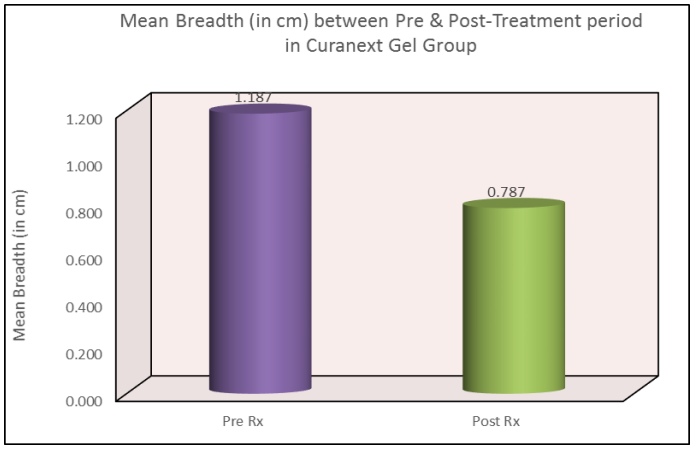
Comparison of mean Length (in cm) of lesion between Pre & Post-Treatment period in Curenext Gel group using Student Paired t Test						
Parameter	**Time**	**N**	**Mean**	**SD**	**Mean Diff**	**P-Value**
Length	Pre Rx	15	1.127	0.488	0.280	<0.001*
	Post Rx	15	0.847	0.318		



Graph 4: Mean length (in cm) between Pre & Post-Treatment period in curenext Gel Group.

Table 4: Comparison of Mean Breadth (in cm) of lesion between Pre & Post-Treatment period in Curenext Gel group using Student Paired t Test.

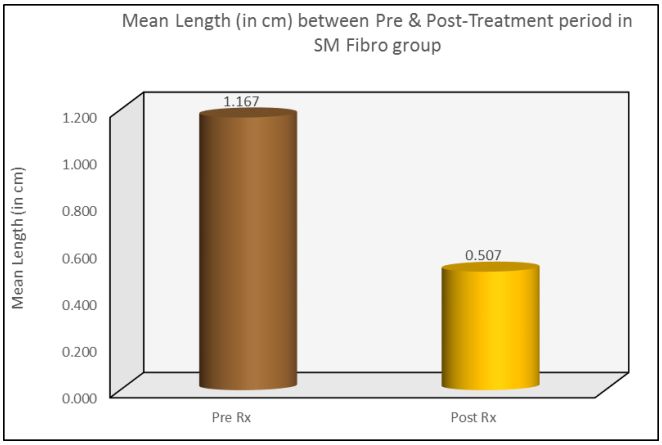
Comparison of mean Breadth (in cm) of lesion between Pre & Post-Treatment period in Curenext Gel group using Student Paired t Test						
Parameter	**Groups**	**N**	**Mean**	**SD**	**Mean Diff**	**P-Value**
Breadth	Pre Rx	15	1.187	0.494	0.400	<0.001*
	Post Rx	15	0.787	0.344		



Graph 5: Mean Breadth (in cm) between Pre & Post-Treatment period in curenext Gel Group.

Table 5: Comparison of Mean Length (in cm) of lesion between Pre & Post-Treatment period in SM Fibro group using Student Paired t Test.

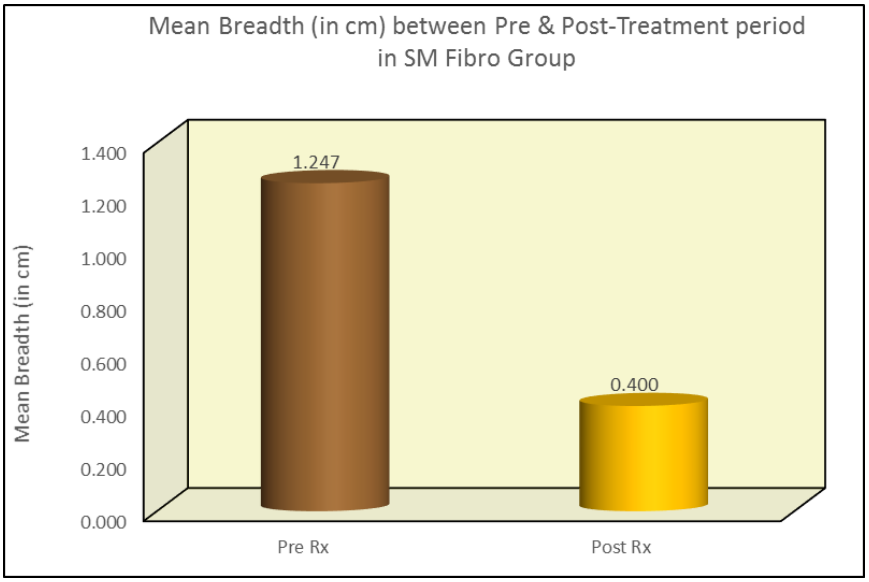
Comparison of mean Length (in cm) of lesion between Pre & Post-Treatment period in SM Fibro group using Student Paired t Test						
Parameter	**Groups**	**N**	**Mean**	**SD**	**Mean Diff**	**P-Value**
Length	Pre Rx	15	1.167	0.437	0.660	<0.001*
	Post Rx	15	0.507	0.296		



Graph 6: Mean Length (in cm) between Pre & Post-Treatment period in SM Fibro Group.

Table 6: Comparison of Mean Breadth (in cm) of lesion between Pre & Post-Treatment period in SM Fibro group using Student Paired t Test.

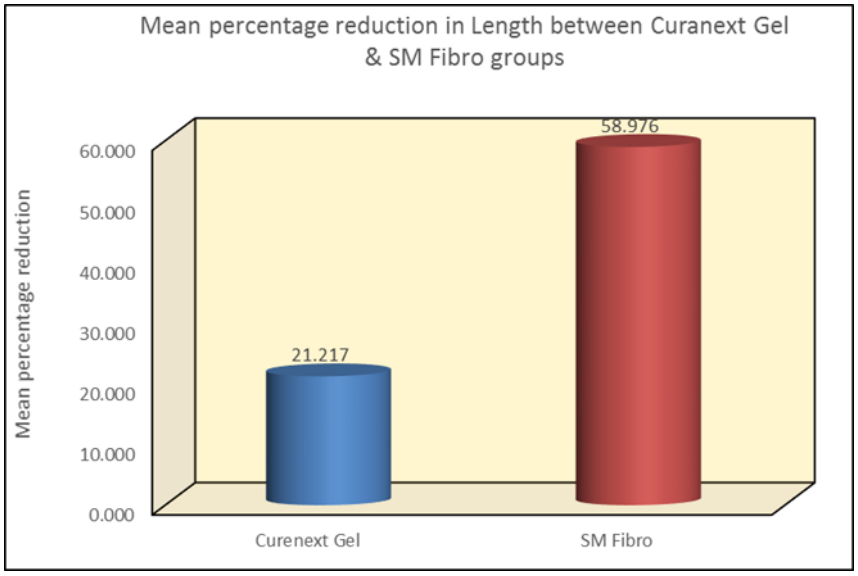
Comparison of mean Breadth (in cm) of lesion between Pre & Post-Treatment period in SM Fibro group using Student Paired t Test						
Parameter	**Time**	**N**	**Mean**	**SD**	**Mean Diff**	**P-Value**
Breadth	Pre Rx	15	1.247	0.461	0.847	<0.001*
	Post Rx	15	0.400	0.251		



Graph 7: Mean Breadth (in cm) between Pre & Post-Treatment period in SM Fibro Group.

Table 7: Comparison of Mean percentage reduction in Lesion Length between Curenext Gel & SM Fibro groups using Mann Whitney Test.

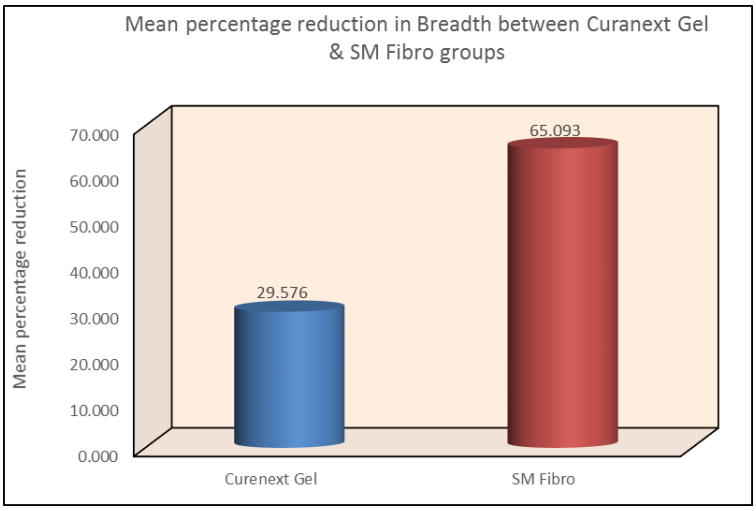
Comparison of mean percentage reduction in Lesion Length between Curenext Gel & SM Fibro groups using Mann Whitney Test						
Parameter	**Groups**	**N**	**Mean**	**SD**	**Mean Diff**	**P-Value**
Length	Curenext Gel	15	21.217	14.555	-37.758	<0.001*
	SM Fibro	15	58.976	22.690		



Graph 8: Mean percentage reduction in length between curenext Gel &SM Fibro groups.

Table 8: Comparison of Mean percentage reduction in Lesion Breadth between Curenext Gel & SM Fibro groups using Student Paired t Test.

Comparison of mean percentage reduction in Lesion Breadth between Curenext Gel & SM Fibro groups using Student Paired t Test						
Parameter	**Groups**	**N**	**Mean**	**SD**	**Mean Diff**	**P-Value**
Breadth	Curenext Gel	15	29.576	19.597	-35.517	<0.001*
	SM Fibro	15	65.093	19.920		



Graph 9: Mean percentage reduction in Breadth between curenext Gel & SM Fibro groups.

DISCUSSION

Oral leukoplakia is a potential malignant disorder of oral cavity. It is a white patch or plaque, that cannot be scrapped off easily and cannot be characterized clinically or pathologically as any other disease.[1] It is commonly seen among older and elderly men and its prevalence increases with age. The early identification of leukoplakia help in early intervention and management in order to prevent its malignant transformation.[7]

In our study male predominance were noted in both groups which accounts for 100%. This is in accordance with Bhagat et al study where majority of patients were males.[6] Age range of Group 1(Curenext gel) was 29-50years and Group2(SM Fibro capsule) was 31-48 years which was in accordance with the study conducted by Patel JS et al where most of the patients were in middle age group of 31-50 years.[7] Both the groups were comparable in terms of age and gender.

The site involved in the majority of patients in group 1 (Curenext gel) (66.7%) and group 2(SM Fibro capsule) (73.3%) was buccal mucosa. According to literature leukoplakia associated with smoking favoured anterior part of buccal mucosa and those associated with tobacco chewing involved posterior part of buccal mucosa.[8] The results was consistent with the study conducted by Kaugar et al where majority of leukoplakia lesion noted in buccal mucosa.[9] But this was contradictory to study conducted by Nagao et al where in 13 patients out of 23, lesion noted on gum/sulcus.[10]

There was marked improvement in mean length and mean breadth of Group1 (Curenext gel) before and after treatment with curenext gel with statistically significant p value of <0.001*. which was in accordance with the study conducted by Rai et al where curcumin reduced the lesion size in leukoplakia patients with p value less than 0.5.[11] Shiv Kumar et al. in 2016 conducted a study on 20 patients, where comparison is done between lycopene and curcumin. The results suggested that curcumin can be used for treating leukoplakia as p-value was less than 0.0001 for both the groups which was highly significant.[11] S.kapoor et al conducted a study on 60 patients (20 oral leukoplakia, 20 oral lichen planus, 20 OSMF) to evaluate effect of curcumin in management of potentially malignant disorders. Study showed highly significant results in all groups. P value was less than 0.0001 which is highly significant.[11] Kuriakose et al conducted a study to evaluate the effectiveness of curcumin in oral leukoplakia, results showed 74.5% clinical response rate.[12] Bhagat et al conducted a study on 60 oral leukoplakia patients, study showed that there was significant improvement in

lesion treated with curcumin.[6] According to literature curcumin exhibit anti-neoplastic, anti-proliferative, and anti-mutagenic activities by suppressing initiation, progression, and metastasis and interrupting cell cycle by disrupting mitotic structures and inducing apoptosis.[6]

The mean length and mean breadth of Group 2 (SM Fibro capsule) before and after treatment show statistically significant improvement with SM Fibro capsule of p value <0.001*. This was consistent with the study conducted by Mohitpal Singh *et al*., in 2004, where the efficiency of lycopene in 58 cases of leukoplakia was assessed. In their study, the patients were divided into three groups, and received 8 mg/day, 4 mg/day, and a placebo for a period of 3 months. Response of 8 mg lycopene as compared to placebo was highly significant with p value <0.001. The results suggested that lycopene could be effectively and safely used for the management of oral leukoplakia.[2,7] Possible mechanism could be lycopene exhibits the highest physical quenching rate constant with singlet oxygen. It protects DNA damage induced by 1-methyl-3-nitro-1-nitrosoguanidine and H2O2.[2]

In another study conducted by Stich HF, Rosin MP, and Hornby AP *et al*, where the authors evaluate the efficiency of combined beta‑carotene and vitamin A, beta‑carotene alone, and placebo, in oral leukoplakia, which produced complete response rates of 27.5%, 14.8% and 3.0%, respectively.[13] According to literature beta‑carotene has an antioxidant potential to scavenge free-radical species, immune enhancing effects, enhances cell-to-cell communication, induces programmed cell death, and has a positive influence on the activity of carcinogen detoxification enzymes.[10]

Nagao et al conducted a double-blind controlled trial (RCT) to evaluate low-dose beta-carotene combined with vitamin C supplements, the overall response rate was 17.4% which was lower compared with the outcomes reported in previous studies. Authors concluded that low response rate was due to the lower dose of beta-carotene used.[10]

Mean percentage reduction in lesion length and lesion breadth shows statistically significant improvement result with SM Fibro capsule compared to curenext gel group with p value of <0.001*. The reason could be due to short retention time of curenext gel to the oral mucosa, consequently, low therapeutic efficacy.[14] Curcumin has been previously reported to have a pH-dependant stability (Wang et al., 1997), where the study showed that 50% of curcumin in phosphate buffer of pH 6.8 degrades in 39.7 min which is similar to the salivary condition.[14]

CONCLUSION

The results of this study suggest that Curenext gel and SM Fibro capsule were found to be effective and showed marked reduction in size. However SM Fibro capsule when compared with curenext gel showed significant reduction in size. Long-term studies with large sample size in the form of randomized controlled trails are recommended in the future to determine the effect and potential of curenext gel in the management of homogenous leukoplakia. Also to understand the efficacy better along with its various mechanism of actions further studies are required.

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