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Original Research Article

Role of Curcumin and Aloevera in Oral Submucous Fibrosis

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Abstract:

Background: Oral Submucous fibrosis is a condition characterized by inflammatory changes in oral cavity and buccal mucosa. It is caused by excessive chewing of arecanut, tobacco and nutritional deficiencies. Steroids are the main treatment for it, but now Curcumin & Aloevera are considered as newer adjuvant modalities.

Materials and Methods: This is a prospective randomized trial aimed to compare the effectiveness of Curcumin & Aloevera gel in Oral Submucous Fibrosis conducted on 105 patients of OSMF. Patients were divided in 3 groups and given vehicle as control, Aloevera and Curcumin as test drugs.

Results: On intragroup comparison in Aloe Vera and curcumin groups there was statistically significant improvement in Interincisal Distance (IID) and Tongue Protrusion (TP) at 1, 2 and 3 months. On intergroup comparison for IID and TP between Control and Aloe Vera, Control and Curcumin and Aloe Vera with Curcumin the difference was not statistically significant.

On comparing Aloe Vera with Curcumin group for burning sensation in mouth, they were comparable for two visits, but Curcumin group showed statistically significant improvement at 3 months.

Conclusions: There was reduction in Burning Sensation and improvement in Interincisal distance and Tongue Protrusion with both the drugs after 3 months of treatment when compared to Day 0. Curcumin was found to be better than Aloe Vera and it improve all the three parameters but more effectively the Burning Sensation. Hence, Curcumin is more effective in improving the symptoms of OSMF.

Keywords: Oral Submucous fibrosis, Aloe Vera, Curcumin, Steroid, Burning Sensation.

Introduction

Oral submucous fibrosis is a chronic debilitating disease that is represented by changes in the epithelium and submucosal tissues. As the disease advances there is difficulty in mouth opening and alteration in taste patterns. [1] The term Oral Submucous Fibrosis was coined by Joshi in 1953. [2] The common sites involved are labial mucosa, buccal mucosa, retromolar pads, soft palate and floor of the mouth. Oral Submucous Fibrosis is a potentially malignant disorder attributed to areca nut (betel nut) chewing. [2] The other etiological factors include excessive chilly consumption, vitamin B & iron deficiency, autoimmunity, genetic and environmental factors. [3]

Treatment of OSMF

Glucocorticoids are the drug of choice in the management of OSMF by topical application (triamcinolone acetate) or intralesional injections because of their anti-inflammatory properties. They lead to apoptosis of the cell. [4] Other modalities for treatment are lycopene, spirulina, curcumin and aloevera gel. Treatment of OSMF is still arguable issue with no proven available cure & still a gap in the knowledge of its pathogenesis. As many herbal therapeutic modalities are available for the treatment in OSMF. Hence in this study we opted for Curcumin & Aloevera gel as test drug.

Curcumin in Oral Submucous Fibrosis

One new drug which is accepted now days is Curcumin in OSMF. Primary active constituent of turmeric is "diferuloyl methane" which had been identified in 1910. Since then it is widely used. The anti-inflammatory and antioxidant properties of curcumin are responsible for its chemopreventive action. [5] The anti-inflammatory and antioxidant activities of curcumin have been observed that showed the cessation of lipo-oxygenase (LOX) and cyclo-oxygenase (COX) activities that can induce inflammation. [6] Curcumin acts by proliferating the number of micronuclei in the circulating lymphocytes and act as an excellent scavenger of free radicals.

Keeping in mind the studies that have been done so far and the therapeutic effects of curcumin, our study was conducted with the aim of evaluating the topical efficacy curcumingel in patients with OSMF.

Aloevera in Oral Submucous Fibrosis

Aloevera (Aloe barbedensis) plant has many medicinal values. It is used in medicine as it has anti-inflammatory, immunomodulatory and antioxidant properties. [7,8] It reduces burning sensation and improves mouth opening thereby enhances patients compliance. It proves to be safe, can be applied topically, easily available, economical, non-invasive and efficacious in the management for "oral submucousfibrosis. "Aloe Vera is a mannoprotein containing many amino acids known as 'wound healing hormones'. The polysaccharides contained in the gel of the leaves, promote wound healing. [9]

Material And Methods

It is a prospective, randomized study which was carried out in our hospital over a period of 9 months in the Department of ENT. The study was conducted after obtaining informed consent from all the participants and institutional ethics committee clearance approval. Patient selection was based on Pindborg staging of the classification of OSMF.

New patients of OSMF in conformity with Pindborg Staging and old patients of OSMF who have left treatment 6 weeks before were included in the study.

Patients with chronic diseases such as Tuberculosis, Diabetes Mellitus, AIDS and any other oral mucosal lesions along with OSMF, pregnant patients and lactating mothers were excluded from the study.

Triamcinolone gel and Curcumin gel were procured from Abott Pharmaceuticals and Aloevera Gel MAQs Herbal, Haridwar (Uttarakhand).

Study groups:

Patients of OSMF who satisfied the inclusion criteria were registered in the study

Group 1: Control Group: Were given 10mg Triamcinolone intra-lesional injection once a week along with 5mg of Topical vehicle which was applied thrice a day for 3 months.

Group 2: Aloevera Group: Were given 10mg Triamcinolone intra-lesional injection once a week along with 5mg of Aloe Vera gel which was applied thrice a day for 3 months.

Group 3: Curcumin Group: Were given 10mg Triamcinolone intra-lesional injection once a week along with 5mg of Curcumin gel which was applied thrice a day for 3 months.

The patients were explained how to apply for ointments.

Efficacy endpoint

Patients were assessed at 0,1,2,3 months for their endpoint parameters.

- Burning Sensation: Patients were explained to note their burning sensation on the visual ana-log scale(VAS)
- Interincisal Distance (IID): IID was measured with Vernier Callipers as the distance between upper and lower jaw central incisors on maxi-mum opening of mouth.
- Tongue Protrusion (TP): TP was measured with Vernier Callipers as the distance of movement of the tongue beyond the incisal tips of lower incisors.

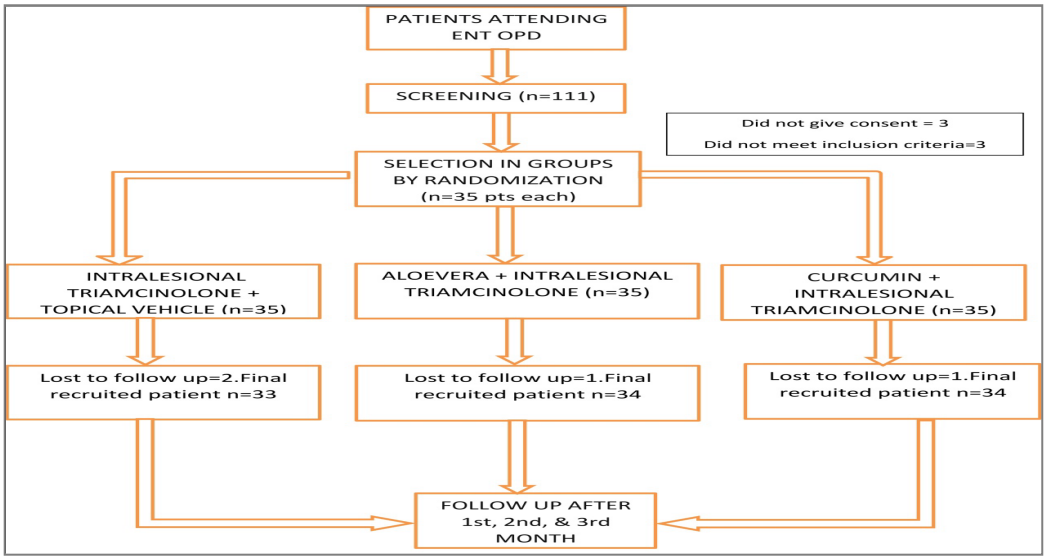

Figure 1: Timeline showing screening and selection of patients

Statistical Analysis: Statistical analysis was done by graph pad prism version 6.

IID and TP were assessed by ANOVA and post hoc Tuckey's test. And Burning Sensation was assessed using Krusal Wallis and Mann Whitney test.

'p'<0.05 was considered statistically significant.

'p'<0.001was considered statistically highly significant.

Results

This study was done for the duration of 9 months. In this study 111 patients were examined, out of which 3 did not give consent and 3 did not meet inclusion criteria. So a total of 105 patients were taken and 4 patients were lost in follow up (2 in Control group and 1 each in the Aloe Vera and Curcumin groups). Hence data of 101 patients was analyzed. They were given Triamcinolone gel as standard treatment in addition to curcumin and aloevera in their respective groups.

The Burning Sensation, TP and IID were measured at baseline (0), 1, 2, 3 months. No side effects were reported with any of the drugs given during the course of the treatment.

In this study the mean age was found to be 35.27 ± 12.21 years in the Control group, 40.94± 9.87 years in the Aloe Vera group and 37.82 ± 10.37 in the Curcumin group.

There was clinical improvement in IID (intragroup) by ANOVA with all three groups, but it was statistically significant with Aloevera and Curcumin groups. There was no statistically significant difference when intergroup comparison was done using the Posthoc Tuckey's test. (Tables 1)

On comparing Aloevera with Curcumin group by Mann Whitney U Test both showed improvement but it was highly significant with Curcumin after 3 months.(Table 2)

On taking the second parameter Burning Sensation and applying Kruskal – Wallis Test, there was high statistically significant difference in each of the three groups at 1 month, 2 month and 3 months of treatment. (Table 3) On comparison of Control with Aloe Vera group by Mann Whitney Test there was very highly significant difference at 1, 2 and 3 months. (Table 4)

Similarly on comparing Control with Curcumin group by Mann Whitney Test there was statistically significant difference at 1 month and very high statistically significant difference after 2 and 3 months. (Table 4)

Next we compared Aloe Vera with Curcumin group also by Mann Whitney Test and these two groups were comparable at 1 and 2 months. The Curcumin group showed better improvement at 3 months in Burning Sensation parameter and it was statistically significant. (Table 4)

There was clinical improvement in Tongue Protrusion (intragroup) by ANOVA with all the three groups but it was statistically significant with Aloevera and Curcumin groups. There was no statistically significant difference when intergroup comparison was done using the Posthoc Tuckey's test. (Table 5)

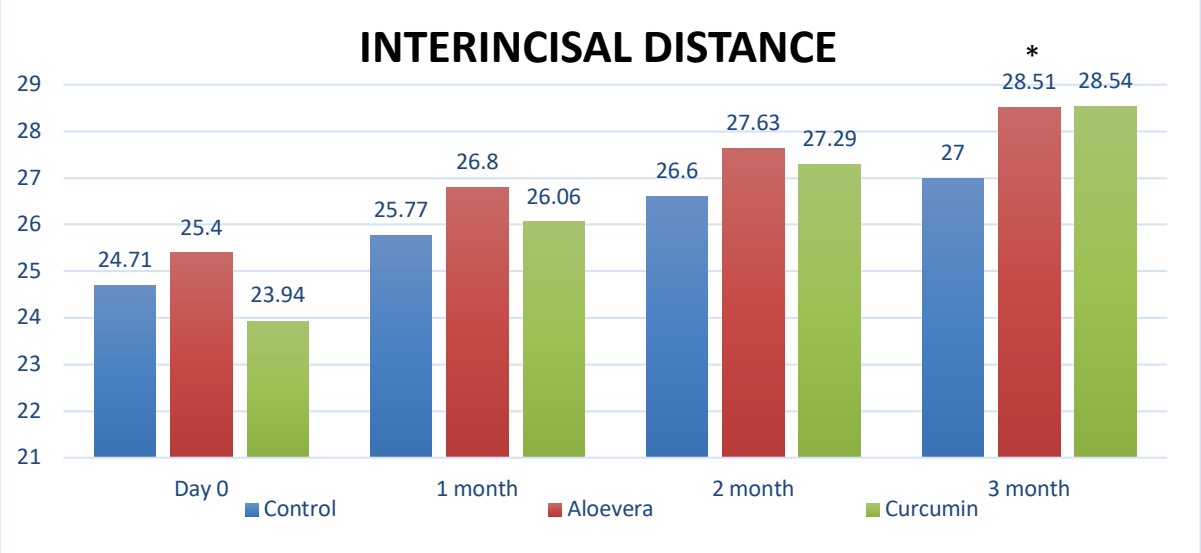

Figure 2: Comparison of average Interincisal Distance at different visits

Table 1: Comparison of average Interincisal Distance at different visits

Interincisal distance (visits)	Control group (n=33)	AloeVera group (n=34)	Curcumin group (n=34)	ANOVA	
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	F	P– value
Day 0	24.71 ± 4.799	25.40 ± 4.888	23.94 ± 5.352	0.738	0.480
1 month	25.77 ± 4.440	26.80 ± 4.745	26.06 ± 4.627	0.465	0.629
2 months	26.60 ± 4.414	27.63 ± 4.339	27.29 ± 4.376	0.501	0.607
3 months	27.00 ± 3.978	28.51 ± 4.224*	28.54±4.075#	1.627	0.202
ANOVA	F value=1.832 P value=0.1443	F value= 2.954 p value=0.0349*	F value= 6.264 p value= 0.0005#		
* p < 0.05 significant when compared to Day 0 # p < 0.001 very highly significant when compared to Day 0					

Table 2: Inter group comparison of average Interincisal Distance at different visits

Visits	Control vs Aloe Vera		Control vs Curcumin		Aloe Vera vs Curcumin	
	Mean difference	p value	Mean difference	p value	Mean difference	p value
Day 0	0.686	0.866	0.771	0.731	1.457	0.409
1 month	1.029	0.526	0.286	0.950	0.743	0.756
2 months	1.029	0.502	0.686	0.748	0.343	0.937
3 months	1.514	0.235	1.543	0.201	0.029	0.999

Table 3: Comparison of average Burning Sensation at different visits

Burning sensation (visits)	Control group n=33	Aloe Vera group n=34	Curcumin group n=34	Kruskal Wallis Test	
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation	Chi-Square	p– value
Day 0	5.314 ± 0.76	5.37 ± 1.31	5.86 ± 1.46	5.76	0.064
1 month	5.086 ± 0.85	4.06 ± 1.14	4.00 ± 1.45	16.53	0.0001*
2 months	5.057 ± 0.87	3.46 ± 1.09	2.97 ± 1.12	45.64	0.0001*
3 months	4.771 ± 0.84++	2.89 ± 0.90#	2.17 ± 1.17#	59.26	0.0001*
Friedman Test	Chi square=37.655 p value = <0.005+	Chisquare=86.175 pvalue =<0.0001#	Chi square = 94.7 p value = <0.0001#		
+ p<0.05 significant when compared to Day 0 # p<0.001 very highly significant when compared to Day 0 *P<0.001 very highly significant when compared with Control					

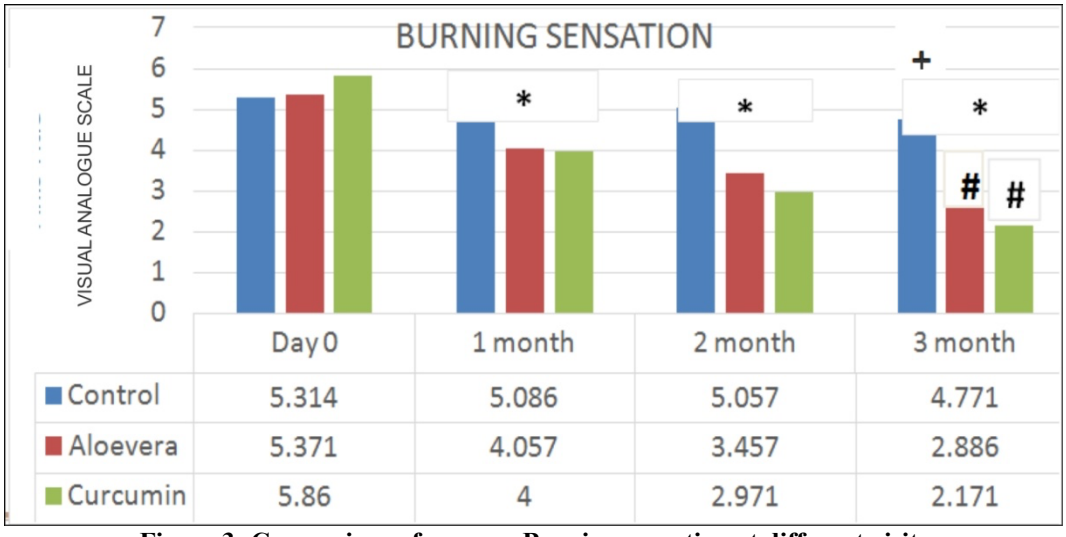

Figure 3: Comparison of average Burning sensation at different visits

Table 4: Intergroup comparison of average Burning Sensation at different visits

Visits	Control vs Aloe Vera		Control vs Curcumin		Aloe Vera vs Curcumin	
	Mann-Whitney U	p value	Mann-Whitney U	p value	Mann-Whitney U	p value
Day 0	601.5	0.892	470	0.06	451.5	0.0501
1 month	304	0.000+	342	0.001#	599	0.87
2 months	175	0.000+	97	0.000+	486	0.12
3 months	98	0.000+	56.5	0.000+	391.5	0.006+
# p<0.05 significant when compared with Control + p<0.001 very highly significant when compared with Control						

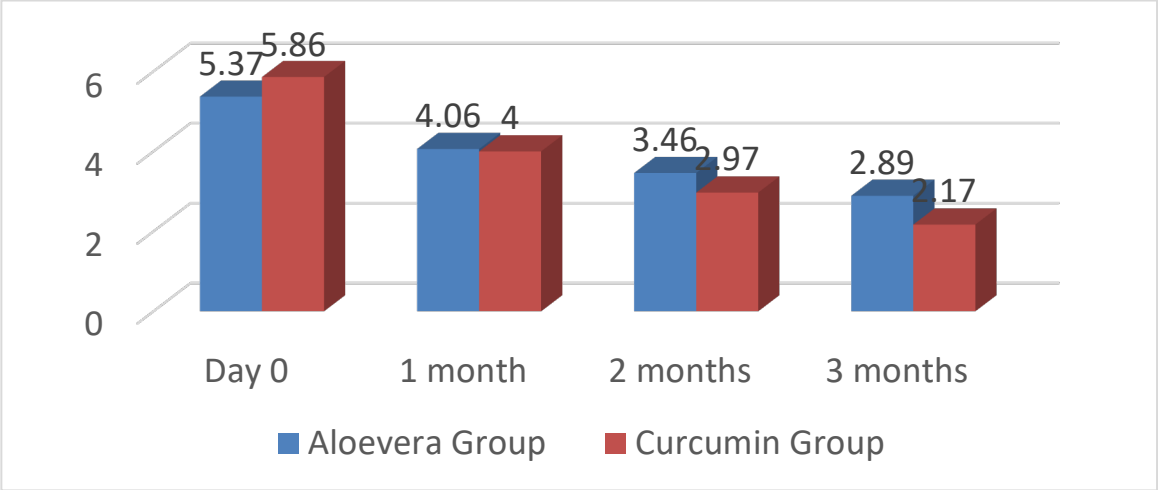

Figure 4: Intergroup comparison of average Burning Sensation between Aloe Vera and Curcumin groups at different visits

Table 5: Comparison of average Tongue Protrusion at different visits

Tongue Protrusion (visits)	Control group n=33	AloeVera group n=34	Curcumin group n=34	ANOVA	
	Mean±Std.Deviation	Mean±Std. Deviation	Mean±Std. Deviation	F	pvalue
Day 0	23.71 ± 5.306	24.43 ± 4.925	22.89 ± 5.810	0.727	0.486
1 month	24.57 ± 5.315	25.94 ± 4.671	25.11 ± 5.378	0.634	0.533
2 months	25.11 ± 5.109	26.66 ± 4.465	26.23 ± 4.959	0.943	0.393
3 months	25.54 ± 5.084	27.63 ± 4.609#	27.20 ± 4.425*	1.911	0.153
ANOVA	F value=0.8033 P value=0.4941	F value=2.914 P value=0.0367#	F value=4.596 P value=0.0043*		
# p<0.05 significant when compared to Day 0 * p< 0.05significant when compared to Day 0					

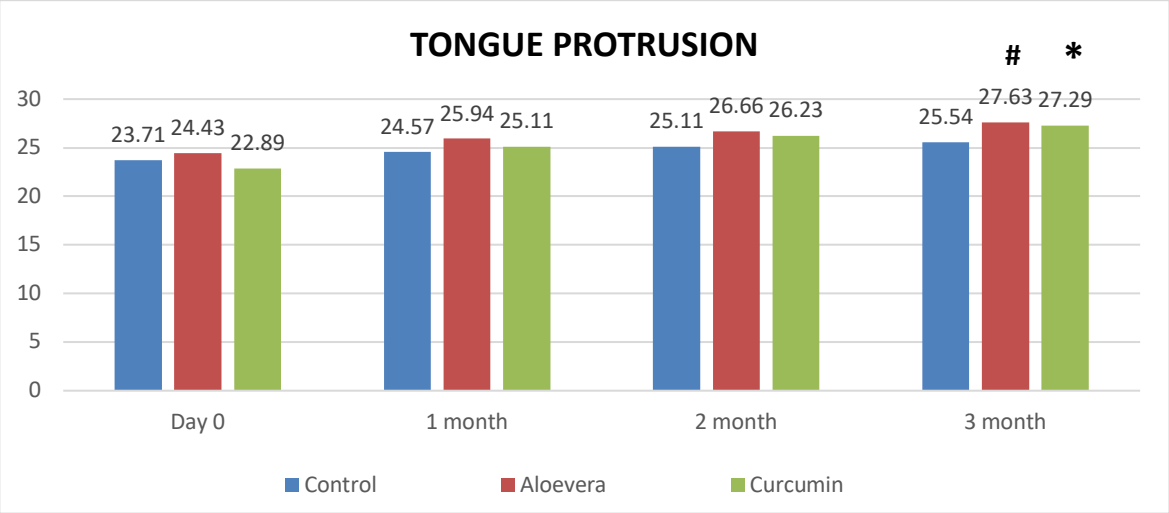

Figure 5: Comparison of average Tongue Protrusion at different visits

Discussion

OSMF is a premalignant condition that is associated with intake of tobacco products. In this study we have evaluated the role of Curcumin and Aloe Vera gel in improving the symptoms of the disease. Clinically there are various for OSMF. Mostly we are using combination strategies.

Patients included in the study had almost similar baseline demographic profiles between the groups. All the three groups showed improvement in IID and the difference in any of the group was not found statistically significant. On doing intragroup comparison, there was significant improvement in Aloevera and Curcumin group. The results of increase in the Interincisal distance obtained from Curcumin were in conformity with the study done by (Yadav et al., 2014) [10]. In a study done by (Hazarey et al., 2015) [11] to check the efficacy of Curcumin in treatment of Oral Submucous Fibrosis the results demonstrated increase in Interincisal Distance with Curcumin when compared with application of steroid ointment. This is in agreement to our present study. On comparing Burning Sensation between Aloevera and Curcumin they were comparable by 2 months but the results were better and highly significant with Curcumin after the end of 3 months. All the three groups showed improvement in Tongue Protrusion but the difference in any of the group was not statistically significant. On doing intragroup comparison, there was significant improvement in Aloevera and Curcumin group. Agarwal et al, in 2011 [12] evaluated the therapeutic potential of turmeric in the management of OSMF, and the results showed that curcumin is effective in improving the symptoms of OSMF by reduction in Burning Sensation and improvement in mouth opening. The results of our study were in concordance with this study. There are other studies also showing similar results, done by Singh, et al. 2017 [13], Hazarey, et al. 2015 [11] and Yadav, et al. 2014 [10].

In the intergroup comparison of Tongue Protrusion between two groups, post hoc Tukey's Test was applied. On comparison of Control with Curcumin group, there was improvement in Tongue Protrusion in the Curcumin group after 1 month, 2 months and 3 months of treatment but it was not statistically significant. This is in concordance with the study conducted by (Yadav et al., 2014) [10].Our study is also in concordance with Sagar Adhikari et al 2022 [14] showing similar results that curcumin shows promising results in treating OSMF.

Conclusion

Having discussed and interpreted the outcome of the present study, we can say that Aloe Vera gel and Curcumin gel are effective in reducing the symptoms of Oral Submucous Fibrosis. There was reduction in Burning Sensation and improvement in Interincisal distance and Tongue Protrusion with both the test drugs in all three parameters after 3 months of treatment when compared to Day 0. Curcumin was found to be better as compared to Aloe Vera group in improving more effectively the Burning Sensation. Longer and more specific human studies are required to further strengthen our conclusion and to unveil the related mechanism of actions of Aloe Vera and Curcumin in improving the course of disease.

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