

## Efficacy of *Punica granatum* L. peel extract in the treatment of Oral Lichen planus in comparison with Triamcinolone Acetonide 0.1%

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### Abstract

Oral lichen planus (OLP) is a relatively common chronic inflammatory disease affecting oral mucosa. *Punica granatum* L. is the herb. It has antioxidant, anti-inflammatory, anticarcinogenic, antiviral, antifungal properties etc. The aim of the present study is to evaluate the efficacy of Punica granatum peel extract in the treatment of oral lichen planus in comparison with triamcinolone acetonide 0.1%. A sample of 40 patients who were clinically and histopathologically diagnosed with OLP were included and randomly assigned into two groups. Test group was given *Punica granatum* peel extract and control group was given triamcinolone acetonide 0.1%. Subjective symptoms and objective signs were recorded on weekly basis until the remission of symptoms. Results depicted that Punica have shown comparable results with that of topical corticosteroids. So, it can be used as an effective alternative for topical corticosteroids.

**Key words :** Lichen planus, herbal treatment, *Punica granatum* peel extract, Anti inflammatory effect.

**O**ral lichen planus (OLP) is a chronic inflammatory condition that affects the mucous membranes of oral cavity with a variety of clinical presentations i.e, reticular, papular, plaque-like, atrophic and ulcerative lesions. It affects from 0.1% to about 4% of the population. It is a disease of the middle-

aged, and is more common among women.<sup>12</sup>

OLP is usually a bilateral and symmetrical distribution. Reticular OLP, which is probably the most common presentation, is usually asymptomatic while the other types may cause pain or discomfort, either spontaneously or

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during meals, *e.g.* during the use of spicy food which lead to compromised food intake and reduced quality of life. The clinical course of OLP is characterized by remissions and exacerbations.<sup>23</sup>

According to the World Health Organization, OLP is categorized into the group of potentially malignant disorders, while its most severe complication is the progression into oral squamous cell carcinoma (OSCC). The reported rate of OLP malignant transformation ranges between 0 and 10%.<sup>22</sup>

The etiology of lichen planus is unknown, but there are several hypotheses. The disease is supposed to be the result of a cell mediated immune reaction in which Langerhans cells, keratinocytes and activated T lymphocytes are involved.<sup>19</sup> Treatment of symptomatic OLP is challenging. Up to now different therapies are described for OLP including drug therapy, psoralen with ultraviolet light A (PUVA) and laser.

Drug therapy is the most common method for treatment of OLP. Several drugs have been used with varying efficacy which include corticosteroids (topical, intralesional or systemic), retinoids, cyclosporines, griseofulvin, hydroxychloroquine and dapsone.<sup>14</sup> Though these drugs are effective, they have several adverse effects and contraindications. Corticosteroids though the main line of intervention for Lichen planus, fewer side effects like Abdominal pain, rashes, weight gain had been reported.<sup>3</sup> Hence alternative therapy using herbal medication has been investigated in the recent years, one such alternative is *Punica granatum*.<sup>24</sup>

*Punica granatum* has been introduced as a natural medicine for prevention and treatment of inflammation and cancer. *Punica granatum* fruit is rich in antioxidant of polyphenolic class which includes tannins and flavonoids. They are found higher in fruit peel among all the parts of the plant<sup>2,8</sup> and demonstrated antimicrobial activity, free radical scavenging ability, immune system activation and numerous antioxidant properties.<sup>4,13</sup>

Extracts of all parts of the fruit had enormous phytochemical compounds as phenols, flavonoids, quinones, saponin, tannins, organic acids amid of which peel has surpassing phytochemical compounds. appear to be a suitable replacement due to their medicinal qualities and low side effects. Pomegranates are regarded as “a pharmacy unto itself” in Ayurvedic medicine, where they are used as a “blood tonic,” an antiparasitic, and a remedy for ulcers, diarrhea, and pharyngitis. In the Middle East and India, the Unani medical system uses pomegranates as a treatment for diabetes, malignancies like Hepatocellular carcinoma as it has potent Anti-oxidant potential.<sup>6,7,15,16,17</sup>

The present research was conducted in the out patients attending Department of Oral Medicine and Radiology. After obtaining ethical clearance and informed consent, 40 patients diagnosed clinically and histopathologically with symptomatic reticular and erosive lichen planus were included in the study. Patients who were under steroids at the time of treatment or in last three months or treatment regimens such as chemotherapy and radiation therapy and who are with uncontrolled systemic illness were excluded from the study.

*Preparation of plant extract :*

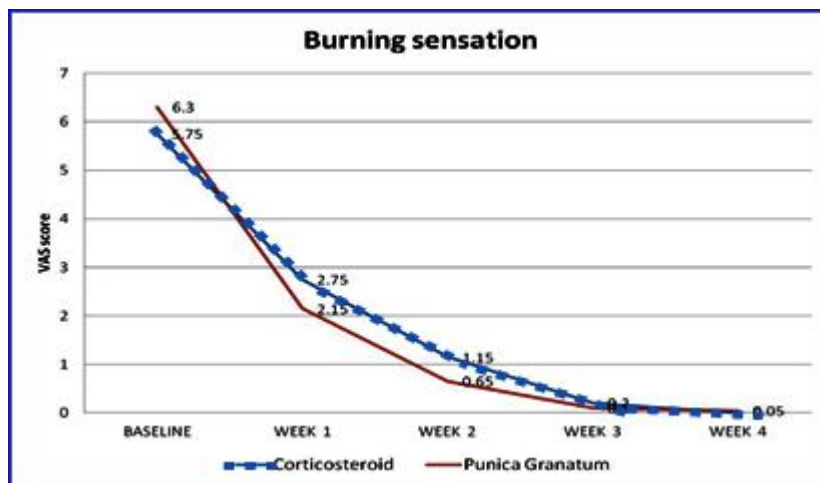
Pomegranate peels were dried and powdered. This powder was soaked in 99% ethyl alcohol for about 3 days and stirred two times a day. Later this was filtered by using Whatman filter paper. The obtained filtrate was subjected to rotary evaporator at a temperature of 70°C and 120 rpm to obtain a crude extract. The weight of crude extract was calculated by measuring the weight of beaker before and after the collection of extract and it was converted into the gel by adding suitable ingredients under GRAS limitations.<sup>19</sup>

The details of the study were explained to the patients and they were given Punica granatum peel extract gel and triamcinolone acetonide 0.1% randomly. Patients were advised to apply the medication on the lesion thrice a day for 7 days. Subjective symptoms and objective signs were recorded on weekly basis until the remission of the symptoms. All the recorded data was subjected to statistical

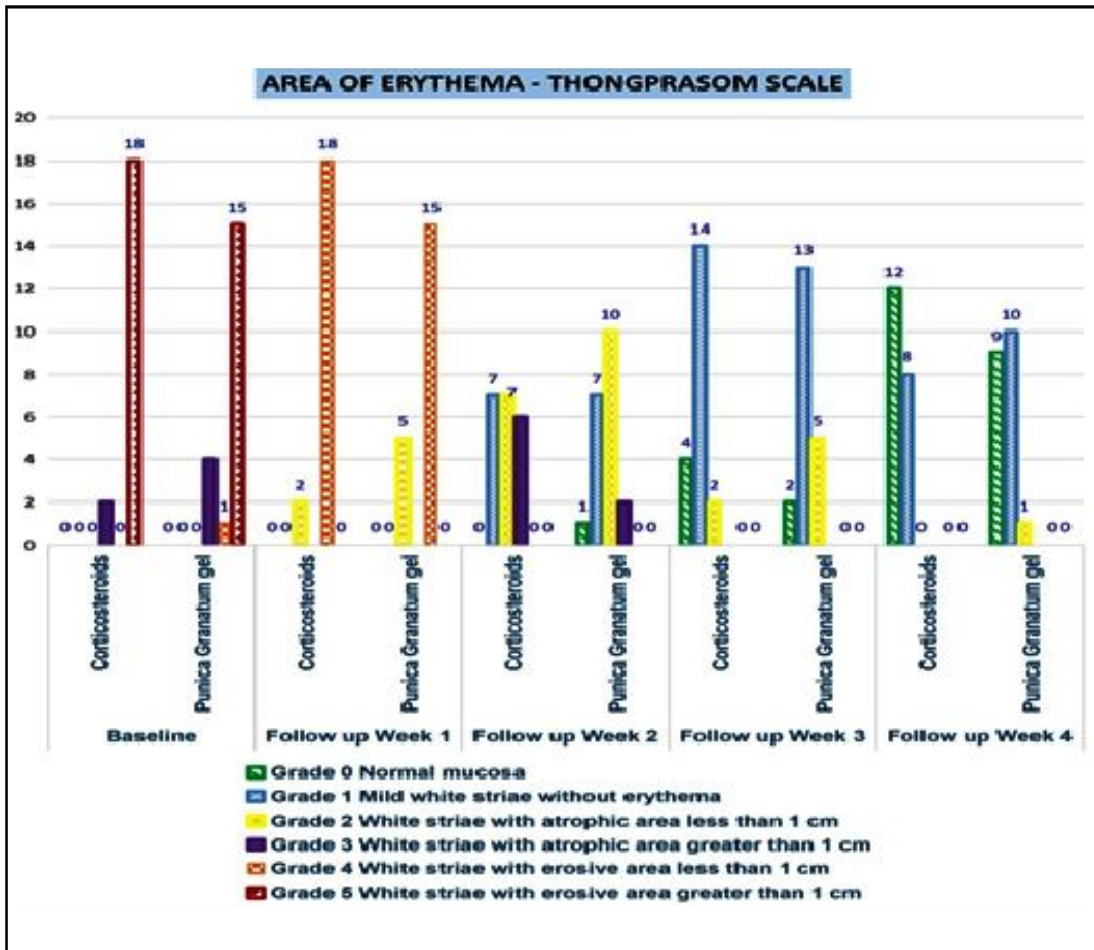
analysis to assess intra group and inter group differences by using SPSS version 20.

There was a significant reduction in burning sensation in the Corticosteroid and *Punica granatum* groups. At the baseline, mean of VAS score in corticosteroid group and Punica granatum group was 5.75 and 6.30 respectively. After initiation of the intervention at the end of first week, VAS score reduced to 2.75 and 2.15 respectively. At the end of second week, the mean of VAS score further reduced to 1.15 and 0.65 respectively. At the end of third week, the mean of VAS score further reduced to 0.20 and 0.10 respectively and at end of fourth week, the mean of VAS score was reduced to 0.00 and 0.00 respectively as mentioned in graph 1.

At baseline in corticosteroid group the area of erythema was recorded using Thongprasom scale. Among 20 patients, 18 patients were noticed with grade 5 and 2 patients were noticed with grade 3. At the end



Graph 1. Graphical representation of the VAS scores of burning sensation from Baseline to week 4.



Graph: 2. Graphical representation of the Thongprasom score area of erythema from Baseline to week 4.

of fourth week, 8 patients were noticed with grade 1 and 12 patients were noticed with grade 0. At baseline in Punica granatum peel group among 20 patients, 4 patients were noticed with grade 3, 1 patient was noticed with grade 4 and 15 patients were noticed with grade 5. At the end of fourth week, 1 patient was noticed with grade 2, 10 patients were

noticed with grade 1 and 9 patients were noticed with grade 0 which was plotted in the graph 2.

The following are the clinical pictures depicting the alterations in erythema in Corticosteroids and *Punica granatum* peel extract gel in LichenPlanus Patients.



Fig. 1A Lichenplanus Preoperative



Fig. 1B Lichenplanus Postoperative- after Steroid therapy

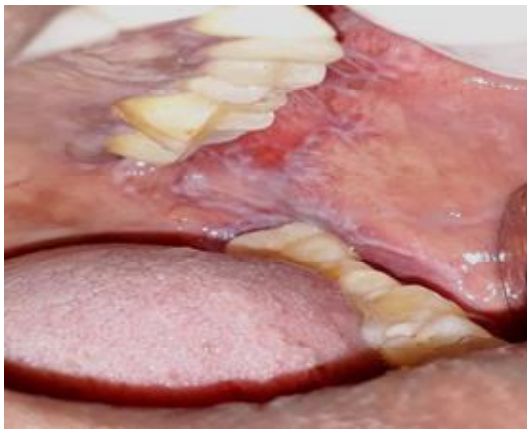


Fig. 2A Lichenplanus Preoperative



Fig. 2. AB Lichenplanus Postoperative- After Punica therapy

Corticosteroids are considered as gold standard treatment for oral lichen planus.<sup>11</sup> Chronic and recurrent nature of the disease poses an additional challenge which likely need for prolonged treatment and follow-up. It was reported that the hypothalamic-pituitary-adrenal axis was inhibited in most of the patient's receiving treatment with topical corticosteroids.<sup>5</sup>

Basal plasma cortisol levels were measured in the study conducted by Gonzalez and

Scully<sup>5</sup> on the patients requiring prolonged maintenance of topical corticosteroid treatment to remain symptom free, so that the small percentage with hypothalamic-pituitary-adrenal axis inhibition can be identified and informed.

*Punica granatum* extracts due to its constituents such as estrogenic flavonols, ellagic acid, ellagitannins, anthocyanins, punicic acid, flavonoids (quercetin, kaempferol, and luteolin glycosides), anthocyanidins, flavones,

imparts anti-inflammatory, antibacterial, anti-oxidant, anticancer, anti-angiogenesis, inhibitory effect on apoptosis, and stimulation of cell differentiation to it.<sup>7,18</sup>

Punicalagin is abundant in the peel of the fruit.<sup>20</sup> Polyphenolic phytochemicals in the pomegranate can play an important role in the modulation of inflammatory cell signaling in colon cancer cells.<sup>1</sup> In the present study, *Punica granatum* has shown a significant reduction in the erythema and burning sensation which is comparable to that of corticosteroids. Reduction in the burning sensation was prominent than the erythema with in the *Punica granatum* group during first week of the treatment. Erythema was significantly reduced by the end of fourth week in both the groups. In autoimmune diseases, Naive T cells (Th0) activation initiates an adaptive immune response which plays a central role in the development of the disease.

Punicalagin was identified as a potent immunosuppressant in activated murine splenic CD4+Tcells. Indeed, a 24 hour exposure of these cells to punicalagin (5 $\mu$ M) decreased the secretion of IL-2, IL-17, a protein stimulating growth and differentiation of T cells. A reduction of IL-2 mRNA levels was also observed with 5  $\mu$ M punicalagin (S.I. Lee et al., 2008).<sup>10</sup>

The anti-inflammatory, antioxidant, and antimicrobial characteristics of *Punica granatum* could be advantageous in the treatment of immune mediated disease such as aphthous ulcers and Lichen planus. Antioxidant activity of *Punica granatum* neutralizes the oxygen free radicals, which play an important role in the inflammatory process. This property may

accelerate the healing process by reducing the inflammation.<sup>9</sup> Current study was aimed at alleviating pain and remission the lesions during the study period. In our study *Punica granatum* has shown significant reduction in the clinical signs and symptoms of oral lichen planus which is comparable to that of Topical corticosteroids.

As oral lichen planus does not have complete remission, it usually has periods of exacerbations which requires long term symptomatic management. Although the corticosteroids are the main stay of the therapy, they have some constraints. *Punica granatum* was found to be equally effective in the management of oral lichen planus, so it can be used as an alternative medication.

#### Conflicts of interest nil

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