

# **A Comparative Clinical and Immunohistochemical Study between Topical Pimecrolimus and Corticosteroid in Treatment of Oral Lichen Planus**

**Thesis**

*Submitted in partial fulfillment for the Doctor Degree in Oral Medicine,  
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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



(المجادلة: 11)

*To My Beloved Parents and Sisters*  
*for their continuous support and*  
*encouragement*

*To My Husband & Kids*  
*for their understanding & endless love*

*AND*

*To The Memory of My Beloved Brother*  
*Wael*

*With his words and kindness I have been*  
*always inspired*

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# *List of Abbreviations*

**OLP:** Oral Lichen Planus  
**CD8<sup>+</sup>:** Cluster of differentiation 8 positive  
**CD4<sup>+</sup>:** Cluster of differentiation 4 positive  
**IL-2:** Interleukin-2  
**INF- $\gamma$ :** Interferon- gamma  
**MMP:** matrix metalloproteinase  
**IgA:** Immunoglobulin A  
**IgG:** Immunoglobulin G  
**IgM:** Immunoglobulin M  
**C3:** Complement component 3  
**HLA:** human leukocyte antigen  
**LCs:** Langerhans Cells  
**Th1:** T helper-1 cells  
**TNF- $\alpha$ :** Tumor-necrosis factor- alpha  
**OLL:** Oral Lichenoid Lesions  
**OLCL:** Oral Lichenoid Contact Lesions  
**OLDR:** Oral Lichenoid Drug Reaction  
**GVHD:** Graft-versus host disease  
**miHAs:** Minor histocompatibility antigens  
**HSV-1:** Herpes simplex virus type 1  
**EBV:** Epstein-Barr virus  
**CMV:** Cytomegalovirus  
**HHV-6:** Human Herpes virus type 6  
**HHV-7:** Human Herpes virus type 7  
**HPV:** Human Papilloma Virus  
**HCV:** Hepatitis C virus  
**Ag:** Antigen  
**IL-4:** Interleukin-4  
**IL-5:** Interleukin-5

**IL-6:** Interleukin-6

**IL-10:** Interleukin-10

**IL-13:** Interleukin-13

**IL-12:** Interleukin-12

**Th2:** T helper-2 cells

**MIG:** Monokine induced by interferon gamma

**IP-10:** Interferon gamma-inducible protein-10

**MCP-1:** Monocyte chemotactic protein

**IL-1:** Interleukin-1

**IL-8:** Interleukin-8

**MHC:** major histocompatibility complex

**Tc:** T Cytotoxic Cells

**RCA:** Request cytotoxic activity

**RCA-R:** Request cytotoxic activity receptor

**TNF R1:** Tumor-necrosis factor- alpha receptor-1

**RANTES:** Regulated on Activation, Normal T-cell Expressed and Secreted

**CCR:** Chemokine Cell Receptor

**TGF- $\beta$ -1:** Transforming growth factor- beta-1

**APCs:** Antigen presenting cells

**HSP:** Heat Shock Proteins

**SCC:** Squamous cell carcinoma

**MIF:** Macrophage migration inhibitory factor

**GCs:** Glucocorticoids

**GRs:** Glucocorticoid receptors

**GREs:** Glucocorticoid responsive elements

**AP-1:** Activator protein-1

**NFATc:** nuclear factor of activated T cells

**NF-KB:** nuclear factor kappa B

**ICAM:** Intercellular adhesion molecule

**VCAM:** Molecular mechanism of corticosteroid action.

**GM-CSF:** Granulocyte monocyte colony stimulating factor

**TCR:** T cell receptors

**PUVA:** Photochemotherapy with 8-methoxypsoralen and long-wave ultraviolet light

**CO2:** Carbone dioxide

**CsA:** Cyclosporine A

**TCL:** Tacrolimus

**PCL:** Pimecrolimus

**SRL:** Sirolimus

**EVL:** Everolimus

**NFATn:** nuclear component of NFAT

**FDA:** Food and Drug Administration

**CS:** Clinical Scoring

**VAS:** Visual Analog Scale

**CIG:** Clinical Improvement Grading

**PBS:** Phosphate-buffered saline

**HRP:** horseradish peroxidase

**SPSS:** Statistical Package for Social Sciences

**ANOVA:** Repeated-measures analysis of variance

**TUA:** Total Ulcerative Area

**TAA:** Total Atrophic Area

**TRA:** Total Reticular Area

**TLA:** Total Lesion Area

**H/E:** Hematoxyline and Eosin staining

**LP:** Lamina Propria

**PV:** Paravascular

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# INTRODUCTION

Lichen planus is a chronic, immunological, mucocutaneous disease, characterized by periods of remission and relapse (*Sahebjamee M & Arbabi-Kalati F. 2005*). Oral lichen planus (OLP) is one of the most common mucocutaneous diseases manifesting in the oral cavity, and the oral mucosa may be the only site of involvement (*Lehman JS, et al. 2009*).

Lichen planus is worldwide in distribution, with variable incidence between 0.5% and 4% (*Silverman S, et al. 1991*). There are many published reports from the middle-east that evaluated various aspects of lichen planus. However, studies concerned with the clinical and epidemiological pattern are few (*Anbar TE et al. 2005*).

Lesions of OLP usually have recognizable and distinctive clinical features. Three major clinical forms of OLP (reticular, erosive/ ulcerative, and erythematous/atrophic) have been recognized, which could alternate and overlap in a dynamic state as disease progresses. Ulceration is the most severe form and always painful in that it interferes with eating, speech, and swallowing. Erosive OLP lasts for years, sometimes resistance to treatment and spontaneous remissions are rare (*Eisen D. 2002; Eisen D et al. 2005*).

Oral lichen planus is a T-cell-mediated chronic inflammatory oral mucosal disease. T-cell accumulation in the superficial lamina propria, basement membrane disruption, intra-epithelial T-cell