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**An Evaluation of the Effect of Curcumin and Natural
Avocado Oil on Induced Traumatic Oral Ulceration in
Rabbits; (Clinical, Histological and Immunohistochemical
Study)**

A thesis

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Doctor of Philosophy in Oral Medicine

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Abstract

Back ground: Traumatic oral ulcer is well-circumscribed, depressed lesion with an epithelial defect that is covered by a fibrin clot, resulting in a yellow-white appearance, occurs due to chemical, mechanical or thermal injury to oral mucosal end with painful erosion. Curcumin is safe and nontoxic herbal medicine with antioxidant, anti-inflammatory and immunomodulating effect that accelerated mucosal healing process. Avocado oil extracted from the pulp of the fruit is rich in polyunsaturated fatty acids and the monounsaturated fatty acid. Natural avocado oil was a novel potent herbal medicine enhance wound healing through quenching reactive oxygen species, inhibited inflammatory process and accelerated proliferating phase.

Aims of the study: Evaluation of the effects of topical application of natural avocado oil, curcumin gel and mixed curcumin and avocado oil in treatment of traumatic oral ulceration by: Clinical analysis of oral ulceration during treatment periods, histological and histomorphometric assessment of soft tissue healing and immunohistochemical expression of transforming growth factor beta II receptors and interleukin 6 in healed oral ulcer.

Subjects, materials and methods: Seventy-two male white New Zealand rabbits of 1000-1400 gm weight, 2-8 months age. All animals were subjected to traumatic ulcer on the buccal muosa with 8mm diameter, and 2mm depth by punch biopsy. The animals were divided into the following:

- Control Group: consisted of eighteen rabbits, the ulcer was rinsed once daily with single topical dose of 10 μ L sterilized distilled water.
- Study groups: divided into three main groups:
 - a) Group A: Eighteen rabbits, traumatic oral ulceration treated once daily with topical application of natural avocado oil.
 - b) Group B: Eighteen rabbits, traumatic oral ulceration treated once daily with topical curcumin gel.
 - c) Group C: Eighteen rabbits, traumatic oral ulceration treated once daily with mixed curcumin and natural avocado oil.

The animals were scarified at the end of three healing intervals: 3,7, and 14 days, 18 rabbits, 6 rabbits from each group for each period. At the day of scarification, final ulcer

sizes were measured to analyze ulcer size and percentage of ulcer healing between groups. After that, the specimens were taken and prepared for histological section (hematoxylin and eosin stain) for assessment of the number of inflammatory cells and blood vessels in addition to epithelial thickness in ulcer area. Also, immunohistochemical investigation for expression of transforming growth factor beta II receptors and interleukin 6 were performed, for all groups over all periods.

Results: Clinical findings of the present study showed significantly ($p < 0.001$) reduced ulcer size and significantly ($p < 0.001$) increased percentage of ulcer healing in all study groups and at all periods of healing than in control group.

Histological and histomorphometric findings of the present study showed decreased inflammation, accelerated surface reepithelization, enhanced angiogenesis, and promoted remodeling of the extracellular matrix resulting with fast maturation of tissue healing in all study groups than in the control group. All study groups showed significantly decreased ($p < 0.001$) the inflammatory intensity than in control group at all healing periods. Also all study groups showed highly significantly higher ($p < 0.001$) epithelial thickness at the 3rd day in groups B and C, at the 7th and 14th days in the groups A and C, in addition to significantly higher ($p < 0.05$) at the 3rd day in group A, at the 7th and 14th days in group B than in control group. The blood vessels count showed highly significantly higher ($p < 0.001$) in all study groups than in control group at all healing periods.

Immunohistochemical examination of the study groups revealed increase transforming growth factor beta II receptors positive expression and decrease interleukin 6 expression in the ulcer area with the time. Transforming growth factor beta II receptors expression was strong in epithelium and moderate in lamina propria at the 3rd and 7th days in all study groups and expression was strong in epithelium and strong in lamina propria at the 14th day in all study groups, control group showed strong expression in epithelium and lamina propria at the 3rd, 14th days and weak expression in epithelium and strong in lamina propria at the 7th day. The mean of transforming growth factor beta II receptors expression in epithelium was increased and showed highly significantly higher ($p < 0.001$) in all study groups than in control group at all healing periods, in lamina propria the expression was

highly significantly higher ($p < 0.001$) at the 3rd day in group A and B, at the 7th day in group A and at the 14th day in all groups and showed significantly higher ($p < 0.05$) at the 3rd day in group C, while showed non-significant ($p > 0.05$) at the 7th day in groups B and C than in control group. While interleukin 6 expression at the 3rd day showed negative immunostaining in epithelium in study groups A, C and moderate positive immunostaining in epithelium in study group B, and in lamina propria showed negative immunostaining in study group A and moderate positive immunostaining in study groups B and C. Control group showed strong positive immunostaining expression in epithelium and lamina propria. At the 7th day interleukin 6 expression showed negative immunostaining in epithelium in study groups A and B, while weak positive immunostaining in study group C and in lamina propria showed moderate positive immunostaining in study groups A, C and weak positive immunostaining in study group B. Control group showed moderate positive immunostaining expression in epithelium and strong positive immunostaining in lamina propria. At the 14th day interleukin 6 expression showed weak positive immunostaining in epithelium and lamina propria in all study groups. Control group showed weak positive immunostaining expression in epithelium and moderate positive immunostaining in lamina propria, which means that the mean of IL6 expression was significantly reduced ($p < 0.001$) in all study groups than in control group at all periods in both epithelium and lamina propria.

Conclusions: Topical application of avocado oil, curcumin and mixed curcumin and avocado oil reduced ulcer size and accelerated oral ulcer healing through increase transforming growth factor beta II receptors expression and decreased interleukin 6 expression in ulcer area. Mixed curcumin and avocado oil showed better results than the use of avocado oil or curcumin alone and the effects approximately similar between avocado oil and curcumin in the all result findings.