



## Comparison Between Titanium and Zirconia Inserts in Oral Mucosa Tissue Healing in Rabbits

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### Abstract

**A**FTER THE INSERTION of a foreign material beneath a surgically prepared wound the body immune system, respond in an inflammatory reaction, which is followed by healing if the inserted material is biocompatible with the tissue. This study we aimed to evaluate the healing process of a surgically prepared wound in lab rabbits' oral mucosa following the insertion of different set of biomaterials these were Titanium and Zirconia. Using histological examination of collected samples. The measuring parameters were the inflammatory cells infiltration, granulation tissue formation, reepithelization and two immunohistochemical tests using cluster of differentiation 31 and matrix metalloproteinase 3 expression in the collected samples to Determine the best material that allow for mucosal healing in contact with from the examined two types and monitor any complications that may arise during the healing of the soft tissue that is in contact with the mentioned materials. In conclusion, Oral mucosal reaction to Titanium and Zirconia sounds similar based on the recorded results in term of healing process with a slight advantage for the latter. The immunohistochemical analysis of the healing process sounds like an effective way to measure the monitored process since both the CD 31 and MMP 3 showed a tuned result with the reepithelization which is considered as the hallmark of healing. Zirconia implants exhibited slight faster resolution of inflammation and enhanced tissue healing compared to Titanium implants, suggesting potential advantages in clinical applications.

**Keywords:** Titanium, Zirconia, Oral mucosa, Healing, Rabbits.

### Introduction

The mechanisms of the wound healing process under goes through 4 stages: include the hemostasis, the inflammation, the proliferation, and remodeling. Mouth wounds are usually studied in animals. They are an ideal model for studying wound healing because they heal quickly and without causing scarring [1].

Titanium is widely used in dental treatments as it is a biologically inert element, but its use may have long-term effects [2].

Zirconium is a white, crystalline element used in the manufacture and decoration of jewelry. It has recently been used in the dental industry, as it is more durable, resistant to bacteria, and more aesthetic. It has recently been used as a substitute for titanium, and now its effects in the living environment are still under study [3] [4].

The proteins found on the surfaces of cells are called the differentiation group. Each unique is given a different number, enabling us to identify the phenotypes of those cells. Surface expression

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is useful for characterizing phenotypes in cells [5].

The Platelet endothelial cells adhesive molecules (PECAM-1) are termed cluster of differentiation 31 (CD31) [6] and are cell adhesion proteins that interact with another PECAM-1 molecule via homotypic or with molecules other than PECAM-1 through heterotypic interactions [7]. It is present within endothelial cell, platelet, macrophage, Kupffer cell, granulocyte, lymphocyte (T cells, B cells, and natural killer cells), giant cell, and bone cells. CD-31 is a membrane glycoprotein expressed in the endothelium, and is used as a marker to measure angiogenesis by calculating microvascular density (MVD) [8].

Matrix metalloproteinases (MMPs, also called metalloproteinases, are calcium- and zinc-dependent metalloproteinases [9]. The biological function of MMPs is to degrade the extracellular ECM proteins, glycoproteins, the membrane receptor, and cytokine, as well as the Growth factor: They participate in many life processes, such as tissue repair, cellular differentiation, morphogenesis, angiogenesis, cell division and migration, wound healing and apoptosis [10].

Stromelysin-1 known as the matrix metalloproteinase-3 (MMP-3) is the enzymes encoded by the MMP3 gene. Which is one of the parts of the MMP group in chromosome 11. (NIH 2023) MMP-3 enzymes degrade collagen, proteoglycans, fibronectin, and laminin, (Docherty AJ and Murphy G [11]. MMP-3 works to activate other types of MMPs such as MMP-1 and MMP-7, and MMP-9, which affects the remodeling of connective tissue [12]. These enzymes contribute to the repair of wounds, the development of atherosclerosis, and tumors [13].

For the purpose of studying and comparing effect of the titanium and the zirconium on the wound curative process in the mouth of rabbits, this study was conducted.

### **Material Methods**

**Ethical approval:** This study was accepted by the Ethical committee of College of Dentistry, University of Mosul, Department of the Oral & Maxillofacial Surgery under Ethical Approval No. (Uom.Dent.29/23) in (2/4/2023).

### **Experimental design:**

Thirty-six male New Zealand rabbits,

approximately six months old and weighing between  $1.3 \text{ kg} \pm 200 \text{ grams}$ , were used in our study. They were Randomly allocated into three groups of receiver site for the experimental materials.

- First group received titanium implants in the mucogingival fold lateral to the upper central incisor using a small surgical incision (4 mm) that was closed with a 5.0 m long secured silk suture in a primary closure.
- The second group received custom zirconia implants on the same side of the rabbits.
- A third group received no material, rendering them as the (control negative) group with incision and suturing only.

Samples from each group were collected at intervals of three, seven, and fourteen days after insertion.

Then using histological examination for the collected samples. The measuring parameters were the inflammatory cells infiltration, granulation tissue formation, reepithelization [14] and two immunohistochemical tests using cluster of differentiation (CD 31) and Matrix Metalloproteinase (MMP3) expressions.

Scoring criteria for the above measurements are shown in tables 1, 2, 3 & 4

As for the scoring system for the expression of CD31 and MMP3 it was converted to numerical values to be suitable for the statistical analysis in tables (3-5):

### **Results**

The samples collected from the animals were examined blindly by the histopathologists. Each slide was examined under the light microscope that aims to evaluate the inflammatory cells infiltration (I.C.I), granulation tissue formation (G.T.F), re-epithelialization (Re-Ep), cluster of differentiation 31 (CD31) and matrix metalloproteinase 3 (MMP3). With the three, seven and fourteen days period, samples from four specimens. Table 5 shows the mean score of each group while table 6 gives the Mann-Whitney U test results significance levels of the tested groups at the 3 different periods with ( $P \leq 0.05$ ).

The Mann-Whitney U test results presented in Table 6 indicate the significance levels ( $P \leq 0.05$ ) of the tested groups at three different time periods (3 days, 7 days, and 14 days). The table compares

the following groups: Zirconia versus Titanium versus control negative group.

At the 3-day period, the Mann-Whitney U test did not find any statistically significant differences ( $P > 0.05$ ) between the Zirconia and Titanium groups in terms of Inflammatory cells infiltration (I.C.I.), Granulation tissue formation (G.T.F.), Re-epithelization (Re-ep.), CD31, and MMP3. The Zirconia group was slightly advantageous in Re-epithelization and CD31 results. they both shows no statistical significant difference with the controlled negative group. Both Titanium and Zirconia showed no statistical significant difference in comparison to the control negative group.

Similarly, at the 7-day period, there were no statistically significant differences ( $P > 0.05$ ) between the Zirconia and Titanium groups in terms of I.C.I., Re-ep., CD31, and MMP3. Furthermore, no significant difference ( $P \leq 0.05$ ) was found between the groups in Granulation Tissue Formation (G.T.R.) , Yet , the Zirconia group shows slight advantaged scores in (G.T.R.), (Re-ep) and CD 31. And again the Titanium and Zirconia groups were not at any significant scores compared to the control negative group.

Moving to the 14-day period, the Mann-Whitney U test results showed no statistically significant differences ( $P > 0.05$ ) between the Zirconia and Titanium groups in terms of I.C.I., G.T.F., and CD31. However, slight differences were observed in CD 31. and MMP3, suggesting a minor distinctions in CD 31 and MMP3 expression between the two materials at this time point. The control negative group also showed no statistical significant difference.

In summary, the statistical analysis suggests that while there were no significant differences between Zirconia and Titanium groups in some parameters at the tested time points, slight variations were observed in other parameters, indicating potential differences in their biological responses (Table 6).

### **Discussion**

The original purpose of this study was to get more detailed information regarding the healing process taking place in the oral mucosa following the insertion of a certain types of biomaterials. Although Titanium and is considered as the (gold standard) in osseous tissue integration in dental implants [15] , there were questions regarding the

soft tissue healing around the implant and weather zirconia is a better option .

### **Three days' results**

At three days results the Titanium and Zirconia groups showed identical scores in the inflammatory cells infiltration , granulation tissue formation and the MMP3 expression . while the Zirconia's group was slightly advanced in re-epithelization since Zirconia shows favorable interaction with the soft tissue [16]. another slight advantage was shown by the Zirconia in CD 31 expression.

At the 3-days period, the absence of statistically significant differences between Zirconia and Titanium groups across all parameters suggests similar initial responses from surrounding tissues. This finding implies that both materials may elicit comparable early biological reactions, which could be advantageous in terms of initial tissue integration and healing processes.

These findings agreed with similar studies that also compared Titanium and Zirconia in the oral mucosa : Dong-Joon Lee *et al* cultured oral tissue cells on Zirconia and Titanium discs , these were Human periodontal ligament fibroblasts (HPLFs) , immortalized human cementoblasts (ihCEMs) and human gingival fibroblast cells (HGF-1) : The ihCEMs proliferated more on the Zirconia discs compared to the Titanium disc at 3–5 days, The HPLFs on zirconia showed similar patterns to ihCEMs. Among the two types of discs, Zirconia showed the highest proliferation rate, HGF-1 cells proliferated best on zirconia discs at day 3 and day 5 [17]

In another study related the behavior of human gingival fibroblasts to the of the surfaces on which they were placed. After 48 and 72 hours of the incubation process, the proliferation of human gingival fibroblasts was significantly faster on smooth zirconia disks than on smooth titanium ones, with the fibroblasts distributing more evenly on smooth zirconia. The expression of integrin (alpha 2) at 3 hours, and of integrin (alpha 5) and type I collagen at 48 hours, was up-regulated on zirconia compared with titanium.[18]

### **Seven days' results**

After 7 days, the inflammatory cells infiltration scores were lowered for both groups . The MMP3 expression was raised equally in both groups . The Zirconia group was slightly advantageous in granulation tissue formation which was raised in

comparison to the three days, in re-epithelization and in CD 31 expression. all the mentioned data hold no statistical significance. these findings come along with Sadowsky research which founded that with soft-tissue integration, the proliferation of gingival fibroblasts was significantly faster on zirconia disks than on titanium disks, he concluded that (wettability) of zirconia may enhance the adsorption of proteins and helps in better distribution of fibroblasts . Soft tissues surrounding abutments coated with zirconia demonstrated a lower expression of proinflammatory cytokines (tumor necrosis factor-alpha and interleukin-6) in comparison to Titanium abutments [19]. This conclusion was confirmed by Various in vivo and in vitro investigations of soft tissue response around zirconia revealed comparable or even better healing response, less inflammatory infiltrate and reduced plaque adhesion on zirconium oxide discs compared to conventionally pure titanium .[15]

#### **Fourteen days' results**

At this period, it is normal to observe a regression in the inflammatory process to allow the healing proliferation phase take place. so the inflammatory cells infiltration mean score was equal for both the titanium and zirconia groups. granulation tissue formation scores were lowered in both groups . re-epithelization was raised in both groups. the CD 31 expression was raised in both groups with slight advantage for the Zirconia . mean MMP3 expression was also raised in both materials and again with minor advantage for the Zirconia (2.75 vs 2.5) it is obvious that these results hold no statistical significance. There was again no significance in compare to the control negative group.

The 14-day period reveals further insights, particularly in Re-epithelization and MMP3 expression. The lack of significant differences in (I.C.I.), Gingival Tissue Fibroblasts (G.T.F.), and CD31 at this stage indicates a stabilization or convergence of responses between Zirconia and Titanium groups. However, the slight differences in CD 31 and MMP3 expression highlight ongoing divergent processes that may influence tissue integration and inflammatory responses over time [13].

Overall, these results suggest that while Zirconia and Titanium may initially evoke similar biological responses, subtle differences emerge as the healing process progresses. Differences

resulting from differences in the chemical composition of materials and surfaces usually require further studies to understand these changes.

The appearance of signs of inflammation 3 days after the titanium and zirconium implant is a natural response to the presence of a foreign body reaction inside the body. After 7 days had passed since the implantation, it was found that the severity of the inflammatory effects had subsided, the histopathological effects had decreased, and signs of healing had begun to appear. Various changes were recorded in the density of blood vessels in the tissues implanted with titanium and zirconium, which were detected by examining the expression of CD31.

After 14 days of treatment, the picture became much clearer, and the difference in the re-formation of blood vessels and the reduction of inflammation became clear in the Zirconia group compared to the Titanium group, which showed a little faster healing response. The prolonged presence of granulation tissue and moderate angiogenesis in the Titanium group at 14 days may suggest a little slower integration process compared to Zirconia, possibly due to differences in surface properties, biocompatibility or host immune response. these results agreed with several studies that aimed to compare Titanium against Zirconia in oral mucosa such as Norbert Enkling *et al* who compared the soft tissue response to implant abutments made of titanium, zirconia, zirconia veneers by various clinical, microbiological, histological and molecular biological markers within an experimental model : the results showed no significant difference in abutments in terms of clinical findings, bacterial counts, concentrations of pro-inflammatory cytokine, or morphological changes in soft tissue around these abutments [20]

In another study Healthy clinical conditions were seen around both Zirconia and Titanium abutments at all times, there was with no significant differences in most of the clinical parameters of the peri-implant soft tissue health. Mean probing depths around Titanium abutments were slightly deeper than around Zirconia ones after 3 months [21]

#### **Conclusion**

Oral mucosal reaction to Titanium and Zirconia sounds similar based on the recorded results in term of healing process with a slight advantage for the latter but with no statistical



significance. The immunohistochemical analysis of the healing process sounds like an effective way to measure the monitored process since both the CD 31 and MMP 3 showed a tuned result with the reepithelization which is considered as the hallmark of healing.

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**TABLE 1. Scoring system of inflammatory cells infiltration**

| Score | Inflammatory cells infiltration                             |
|-------|---|
| 0     | From 13 to 15 inflammatory cells in each histological field |
| 1     | From 10 to 13 inflammatory cells in each histological field |
| 2     | From 7 to 10 inflammatory cells in each histological field  |
| 3     | From 4 to 7 inflammatory cells in each histological field   |
| 4     | From 1 to 4 inflammatory cells in each histological field   |

**TABLE 2. Scoring system of granulation tissue formation**

| Score | Granulation tissue formation  |
|-------|---|
| 0     | Inflammatory-immature tissue in $\geq 70\%$ of the tissue samples                             |
| 1     | Thin-immature tissue in $\geq 60\%$ of the tissue samples                                     |
| 2     | Moderate remodeling in $\geq 40\%$ of the tissue samples                                      |
| 3     | Thick granulation layer with well formed collagen matrix in $\geq 60\%$ of the tissue samples |
| 4     | Complete tissue organization in $\geq 80\%$ of the tissue samples                             |

**TABLE 3. scoring system of re-epithelization**

| Score | Re-epithelization   |
|-------|---|
| 0     | Lack of epithelial proliferation in $\geq 70\%$ of the tissue samples   |
| 1     | Poor epidermal proliferation in $\geq 60\%$ of the tissue samples       |
| 2     | Incomplete epidermal proliferation in $\geq 40\%$ of the tissue samples |
| 3     | Moderate epithelial proliferation in $\geq 60\%$ of the tissue samples  |
| 4     | Complete epidermal proliferation in $\geq 80\%$ of the tissue samples   |

**TABLE 4. Score system of CD31 & MMP3 with its numerical evaluation conversion (no source?)**

| Score | Numerical value | Expression level              |
|-------|-----------------|-------------------------------|
| -     | 0               | Lack of positive expression   |
| +     | 1               | Mild/weak positive expression |
| ++    | 2               | Moderate positive expression  |
| +++   | 3               | Intense positive expression   |

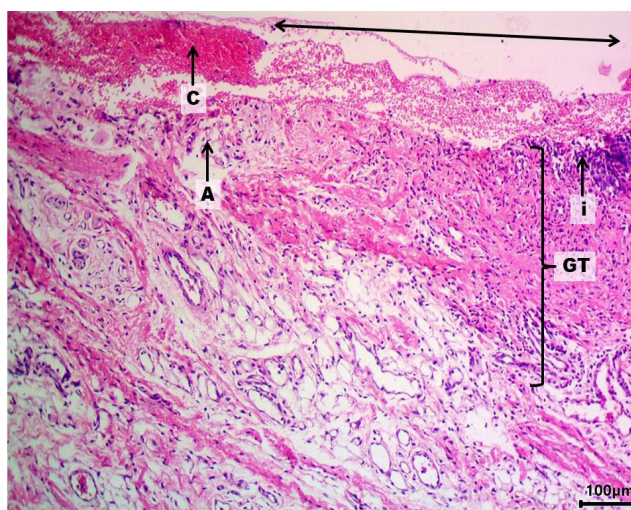
**TABLE 5. The mean score of the samples groups**

| Samples group                  | Mean I.C.I. | Mean G.T.F. | Mean Re-Ep. | Mean CD31 | Mean MMP3 |
|--------------------------------|-------------|-------------|-------------|-----------|-----------|
| 3 days Zirconia samples group  | 1.75        | 0.5         | 0.75        | 0.75      | 0         |
| 3 days Titanium samples group  | 1.75        | 0.5         | 0.5         | 0.5       | 0         |
| 3 days control samples group   | 1.75        | 0.5         | 0.5         | 0.5       | 0         |
| 7 days Zirconia samples group  | 1.25        | 1.75        | 1.75        | 1.75      | 0.75      |
| 7 days Titanium samples group  | 1.25        | 1.5         | 1.5         | 1.5       | 0.75      |
| 7 days control samples group   | 1.75        | 1.5         | 1.5         | 1.5       | 0.5       |
| 14 days Zirconia samples group | 0.25        | 1.25        | 2.5         | 2.75      | 2.75      |
| 14 days Titanium samples group | 0.25        | 1.25        | 2.5         | 2.5       | 2.5       |
| 14 days control samples group  | 0.75        | 1.5         | 2.5         | 2.5       | 2.5       |

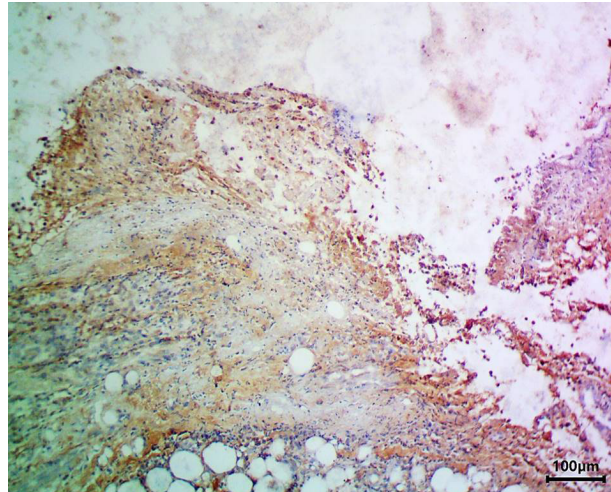
**TABLE 6. Mann-Whitney U test results significance levels of the tested groups at the 3 different periods with ( $P \leq 0.05$ )**

| Groups compared at periods            | I.C.I | G.T.F | Re-ep | CD 31 | MMP3  |
|---------------------------------------|-------|-------|-------|-------|-------|
| Zirconia - Titanium at 3 days Period  | 1.000 | 1.000 | 0.495 | 0.495 | 1.000 |
| Zirconia - control at 3 days period   | 1.000 | 1.000 | 0.495 | 0.495 | 1.000 |
| Titanium - control at 3 days period   | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| Zirconia - Titanium at 7 days period  | 1.000 | 0.495 | 0.495 | 0.495 | 1.000 |
| Zirconia - control at 7 days period   | 0.186 | 0.495 | 0.495 | 0.495 | 0.495 |
| Titanium - control at 7 days period   | 0.186 | 1.000 | 1.000 | 1.000 | 0.495 |
| Zirconia - Titanium at 14 days period | 1.000 | 1.000 | 1.000 | 0.495 | 0.495 |
| Zirconia - control at 14 days period  | 0.186 | 0.850 | 1.000 | 0.495 | 0.495 |
| Titanium - control at 14 days period  | 0.186 | 0.850 | 1.000 | 1.000 | 1.000 |

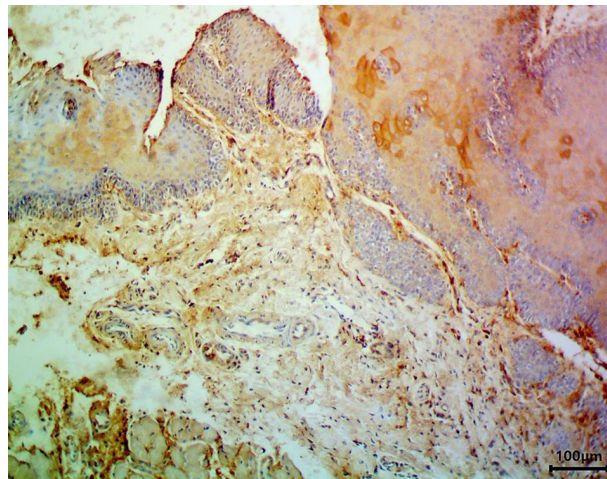
### Histopathological and immunohistochemical examination findings:



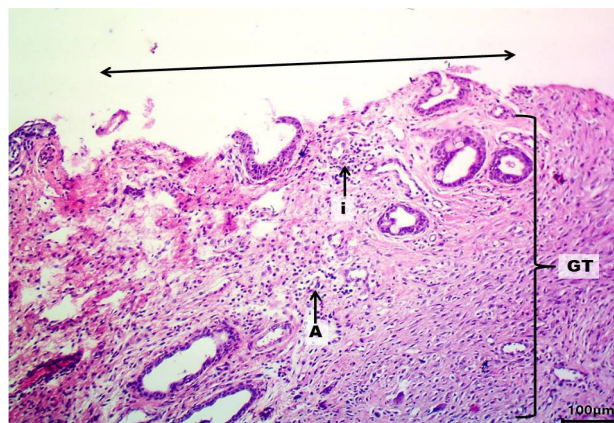
**Fig. 1. rabbit oral mucosa of Titanium treated group (3 days) showing the site of pin ( $\leftrightarrow$ ) with blood clot formation (C), inflammation cells infiltration (score 2) (i), high granulation tissues (score 1) (GT), with angiogenesis (A). H&E stain, 10X.**



**Fig. 2.** Immunohistochemistry the expression of CD31 in Titanium (3 days) showing moderate positive expression (score 2). H stain, 10X.

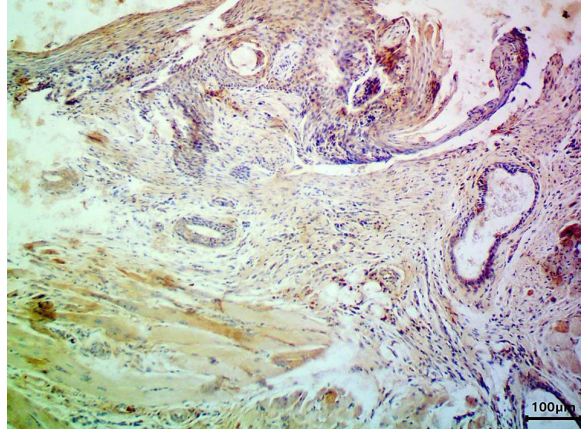


**Fig. 3.** Immunohistochemistry of the expression of MMP3 in Titanium (3 days) show moderate positive expression (score 2). H, 10X.

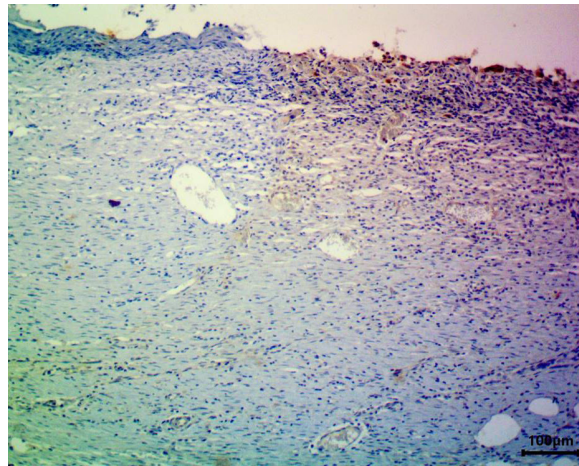


**Fig. 4.** rabbit oral mucosa of the Titanium treated group (7 days) showing the site of pin (↔) with inflammation cells infiltration (score 1) (i), granulation tissue (score 1) (GT), with angiogenesis (score 2) (A). H&E stain, 10X.

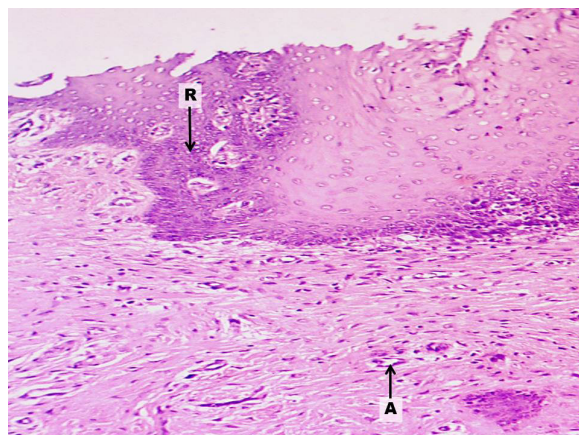




**Fig. 5.** Immunohistochemistry expression of CD31 in the Titanium (7 days) showing weak positive expression (score 1). H stain, 10X.

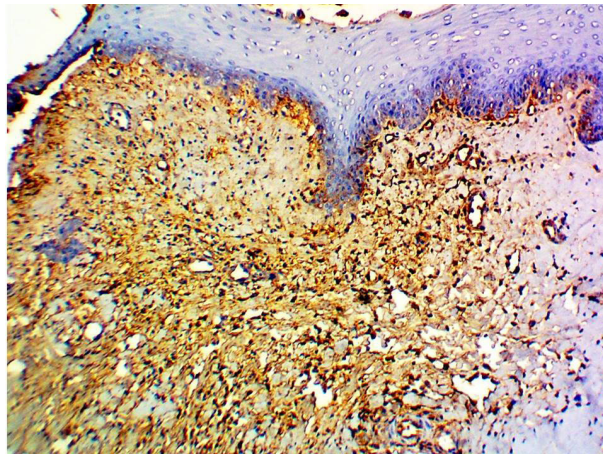


**Fig. 6.** Immunohistochemistry expression of the MMP3 in the Titanium (7 days) showing moderate positive expression (score 2). H stain, 10X.

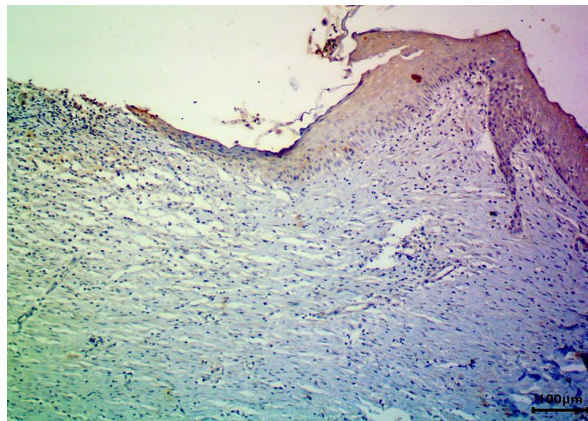


**Fig. 7.** rabbit oral mucosa of the Titanium (14 days) showing the site of pin without inflammatory (score 0), and granulation tissue (score 0), angiogenesis (score 3) (A) and well-developed re-epithelialization (score 3) (R). H&E stain, 10X.

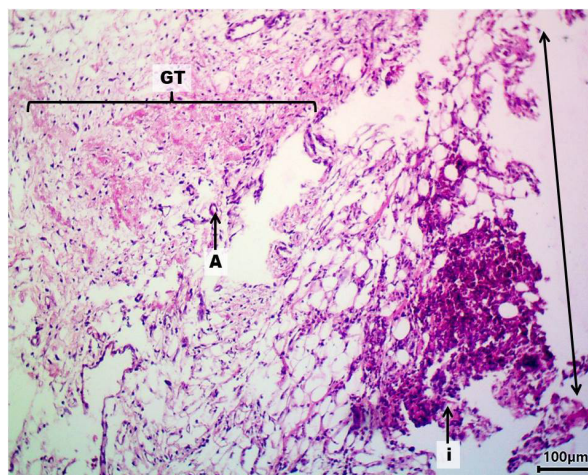




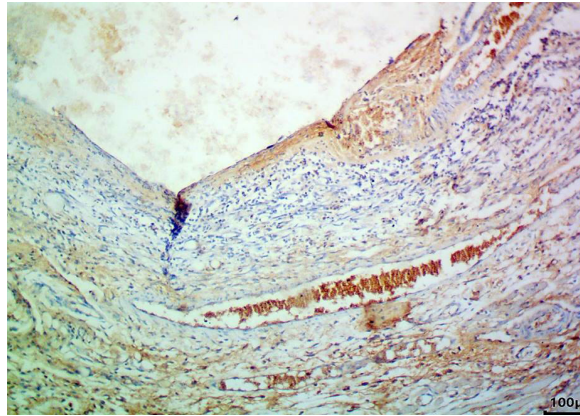
**Fig. 8.** Immunohistochemistry the expression of CD31 in Titanium (14 days) show the moderate positive expression (score 2). H stain, 10X.



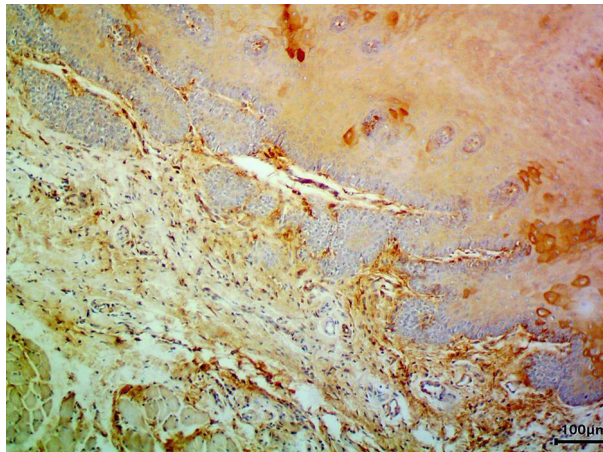
**Fig. 9.** Immunohistochemistry expression of MMP3 in Titanium (14 days) show moderate positive expression (score 2). H stain, 10X.



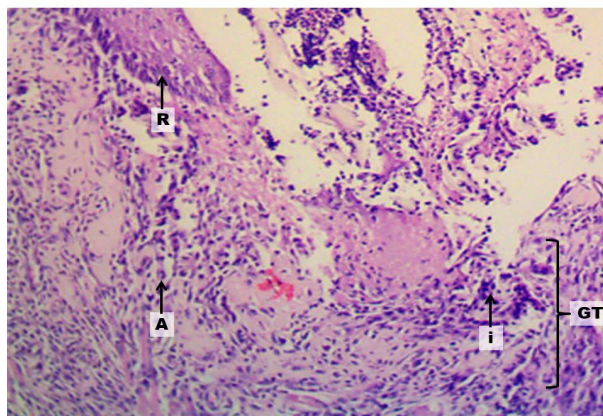
**Fig. 10.** photomicrograph of rabbit oral mucosa of the Zirconia treated group (3 days) showing the site of pin (↔) with inflammatory cells exudation (score 2) (i), high granulation tissue (score 1) (GT), with angiogenesis (A). H&E stain, 10X.



**Fig. 11.** Immunohistochemistry the expression of CD31 in Zirconia (3 days) showing moderate positive expression (score 2). Hematoxylin stain, 10X.

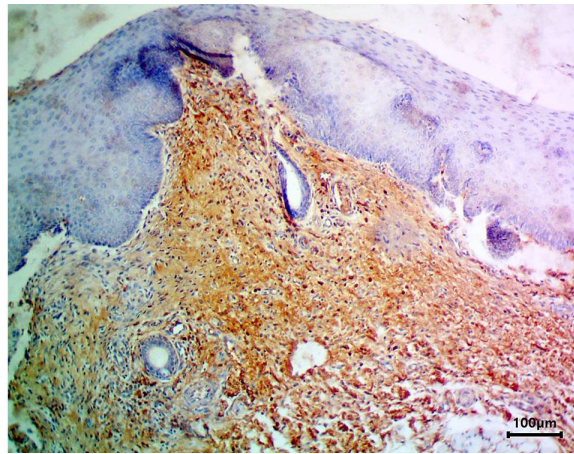


**Fig. 12.** Immunohistochemistry expression of the MMP3 in the Zirconia group (3 days) showing intense positive expression (score 3). Hematoxylin stain, 10X.

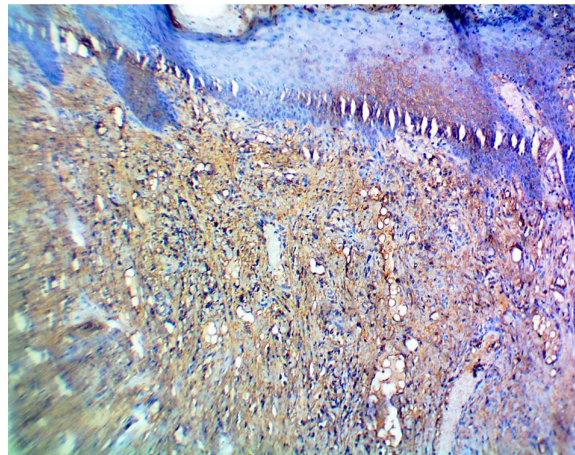


**Fig. 13.** rabbit oral mucosa of the Zirconia treated group (7 days) showing the site of pin (↔) with inflammation (score 1), granulation tissue (score 2) (GT), with angiogenesis (score 2) (A) and re-epithelialization (score 2) (R). H&E stain, 10X.

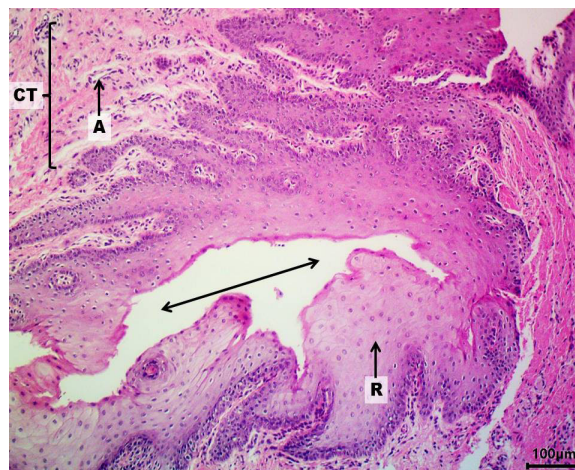




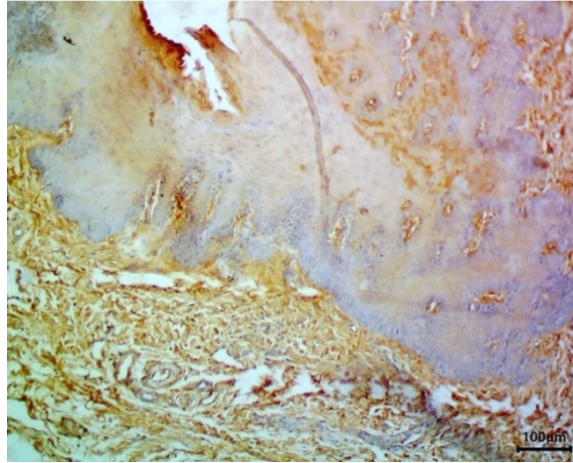
**Fig. 14.** Immunohistochemistry the expression of CD31 in the Zirconia group (7 days) show intense positive expression (score 3). H stain, 10X.



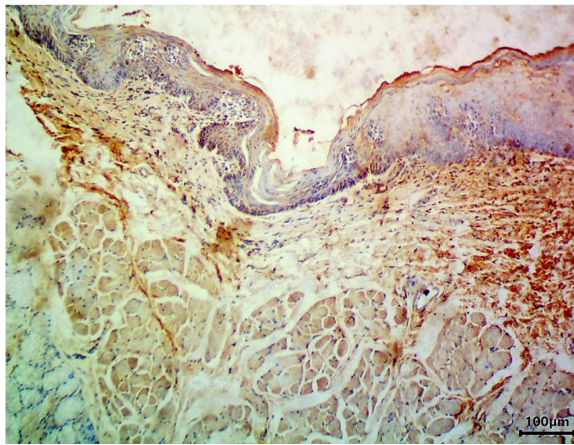
**Fig. 15.** Immunohistochemistry the expression of MMP3 in Zirconia group (7 days) show the moderate positive expression (score 2). H stain, 10X.



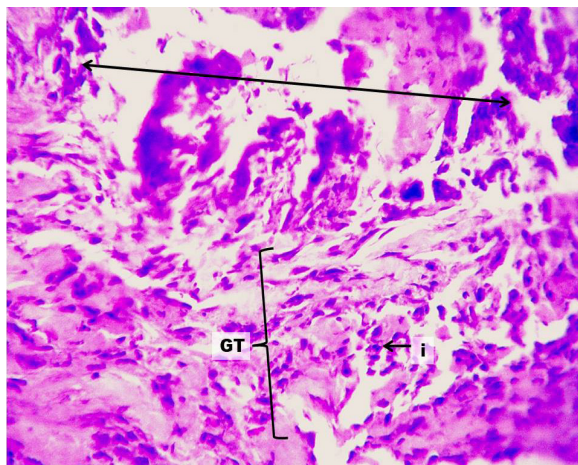
**Fig. 16.** rabbit oral mucosa of the Zirconia treated group (14 days) showing the site of pin (↔) without inflammatory (score 0), granulation tissue (score 1) (CT), angiogenesis (score 3) (A) and well-developed re-epithelialization (score 3) (R). H&E stain, 10X.



**Fig. 17.** Immunohistochemistry the expression of CD31 in the Zirconia group (14 days) showing intense positive expression (score 3). Hematoxylin stain, 10X.

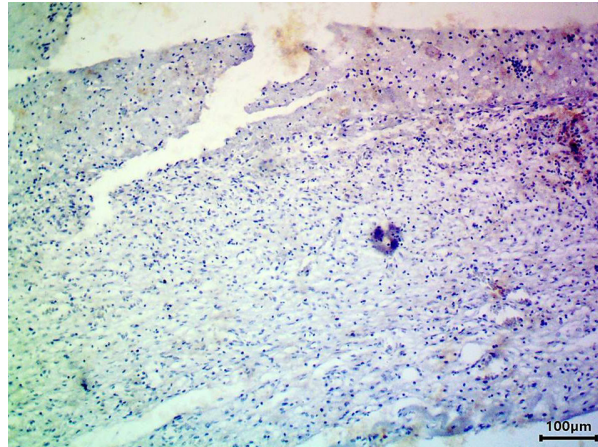


**Fig. 18.** Immunohistochemistry expression of MMP3 in Zirconia (14 days) show intense positive expression (score 3). H stain, 10X.

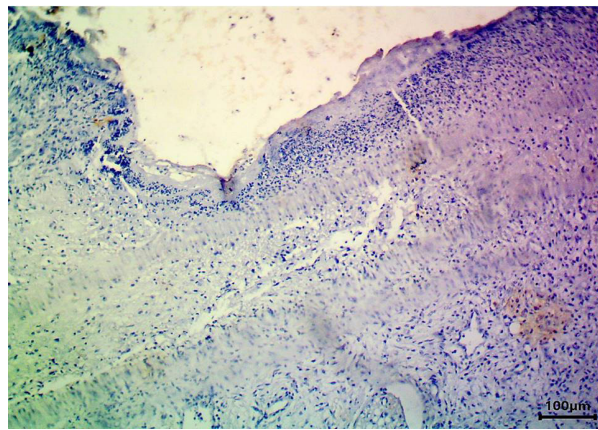


**Fig. 19.** photomicrograph of rabbit oral mucosa of the Control group (3 days) showing the site of wound ( $\leftrightarrow$ ) with inflammatory cells infiltration (score 3) (i), granulation tissue (score 1) (GT). H&E stain, 10X.

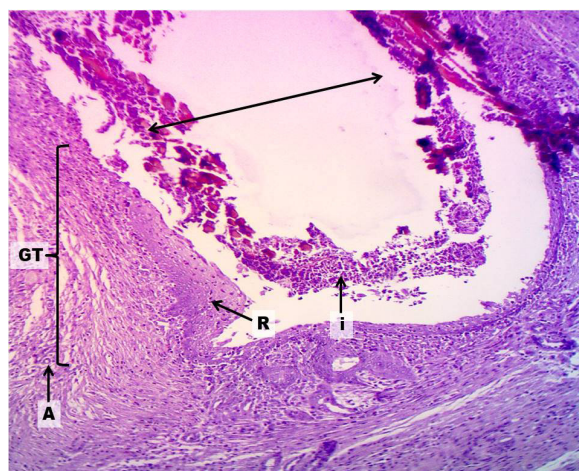




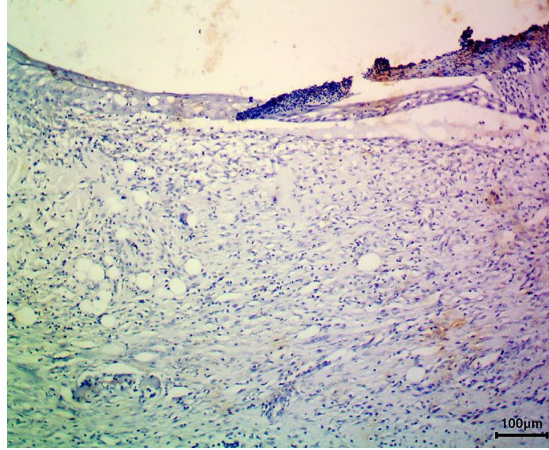
**Fig. 20.** Immunohistochemistry expression of the CD31 in the Control group (3 days) showing weak positive expression (score 1). Hematoxylin stain, 10X.



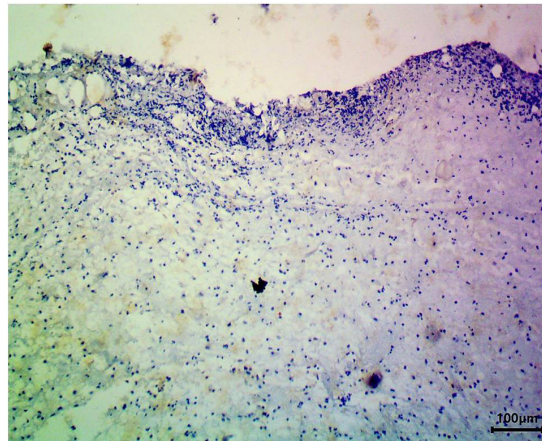
**Fig. 21.** Immunohistochemistry expression of the MMP3 in the Control group (3 days) showing weak positive expression (score 1). Hematoxylin stain, 10X



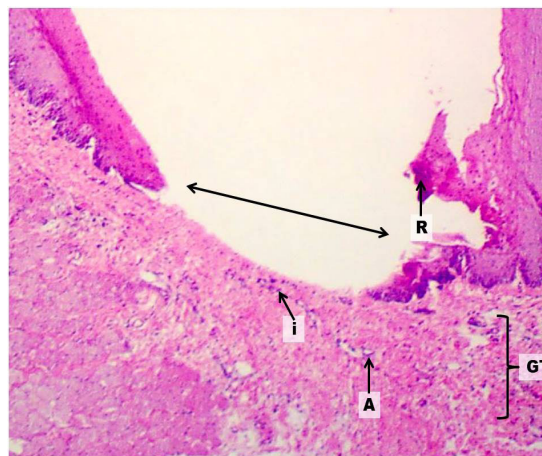
**Fig. 22.** photomicrograph of rabbit oral mucosa of the Control group (7 days) showing the site of wound (↔) with inflammatory cells (score 2) (i), granulation tissue (score 2) (GT), with angiogenesis (score 1) (A) and re-epithelialization (score 1) (R). H&E stain, 10X.



**Fig. 23.** Immunohistochemistry expression of the CD31 in the Control group (7 days) showing weak positive expression (score 1). Hematoxylin stain, 10X.

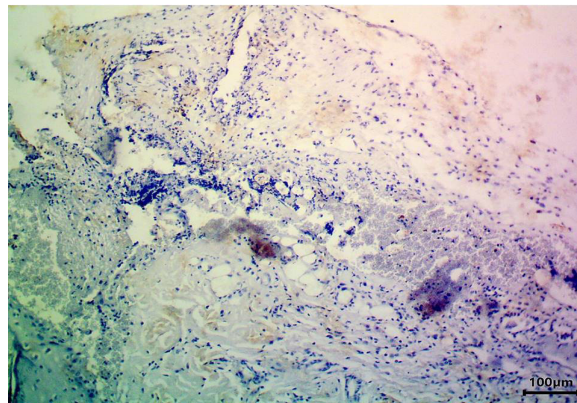


**Fig. 24.** Immunohistochemistry expression of the MMP3 in the Control group (7 days) showing weak positive expression (score 1). Hematoxylin stain, 10X.

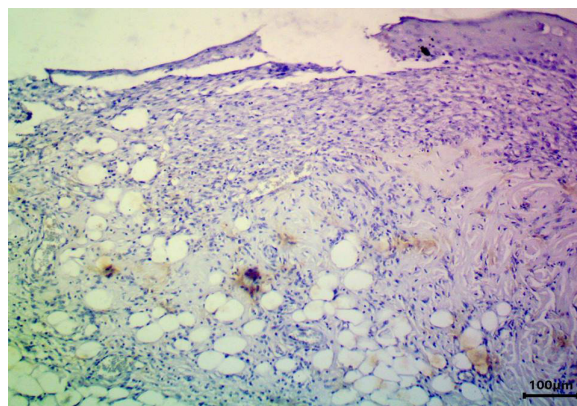


**Fig. 25.** photomicrograph of rabbit oral mucosa of the Control group (14 days) showing the site of wound (↔) with inflammation (score 1), granulation tissue (score 1) (GT), angiogenesis (score 2) (A) and re-epithelialization (score 2) (R). H&E stain, 10X.





**Fig. 26. Immunohistochemistry expression of the CD31 in the CD31 in the Control group (14 days) showing weak positive expression (score 1). Hematoxylin stain, 10X.**



**Fig. 27. Immunohistochemistry expression of the MMP3 in the N group (14 days) showing weak positive expression (score 1). Hematoxylin stain, 10X.**

### References

- Overmiller, A.M., Sawaya, A.P., Hope, E.D. and Morasso, M.I. Intrinsic Networks Regulating Tissue Repair: Comparative Studies of Oral and Skin Wound Healing. *Cold Spring Harb Perspect Biol.*, **14**(11), a041244(2022). doi: 10.1101/cshperspect.a041244. PMID: 36041785; PMCID: PMC9620853.
- Guo, T., Gulati, K., Arora, H., Han, P., Fournier, B. and Ivanovski, S. Race to invade: Understanding soft tissue integration at the transmucosal region of titanium dental implants. *Dent. Mater.*, **37**(5), 816-831(2021). doi: 10.1016/j.dental.2021.02.005. Epub 2021 Mar 4. PMID: 33676764.
- Wang, S. F., Zhang, J., Luo, D. W., Gu, F., Tang, D. Y., Dong, Z. L., Tan, G. E. B., Que, W. X., Zhang, T. S., Li, S. and Kong, L. B. Transparent ceramics: Processing, materials and applications. *Progress in Solid State Chemistry*, **41** (1), 20–54 (2013). doi:10.1016/j.progsolidstchem.2012.12.002. ISSN 0079-6786.
- Lee, D.J., Ryu, J.S., Shimono, M., Lee, K.W., Lee, J.M. and Jung, H.S. Differential Healing Patterns of Mucosal Seal on Zirconia and Titanium Implant. *Front. Physiol.*, **10**, 796 (2019). doi: 10.3389/fphys.2019.00796. PMID: 31333481; PMCID: PMC6616312.
- Jeffrey, K. A. (2019). *Introductory Immunology Basic Concepts for Interdisciplinary Applications* (Second Edition) academic press
- Gumina, R.J., Kirschbaum, N.E., Rao, P.N., vanTuinen, P. and Newman, P.J. The human PECAM1 gene maps to 17q23. *Genomics*, **34** (2), 229–232 (1996). doi:10.1006/geno.1996.0272. PMID 8661055.
- DeLisser, H.M., Newman, P.J. and Albelda, S.M. Molecular and functional aspects of PECAM-1/CD31. *Immunology Today*, **15** (10), 490–495. (1994). doi:10.1016/0167-5699(94)90195-3. PMID 7945775.

8. Ayuningtyas, N.F., Hendarti, H.T., Soebadi, B., Condro Surboyo, M.D., Hadi, P., Ganesha, R., Ernawati, D.S. and Marsetyo, R.I. Expression of VEGF and CD-31 in traumatic ulcer of diabetic Wistar rats after application of Citrus limon peel essential oil. *J. Oral Biol. Craniofac. Res.*, **13**(3), 380-385(2023). doi: 10.1016/j.jobcr.2023.03.009. Epub 2023 Mar 29. PMID: 37025967; PMCID: PMC10070900.
9. Verma, R.P. and Hansch, C. Matrix metalloproteinases (MMPs): chemical-biological functions and (Q)SARs” (PDF). *Bioorg. Med. Chem.*, **15** (6), 2223–2268. (2007). doi:10.1016/j.bmc.2007.01.011. PMID 17275314.
10. Laronha, H. and Caldeira, J. Structure and Function of Human Matrix Metalloproteinases. *Cells*, **9**(5),1076(2020). doi:10.3390/cells9051076. PMID: 32357580; PMCID: PMC7290392.
11. Docherty, A.J. and Murphy, G. The tissue metalloproteinase family and the inhibitor TIMP: a study using cDNAs and recombinant proteins. *Annals of the Rheumatic Diseases*, **49** (Suppl 1), 469–479. (1990). PMID 2197998.
12. Ye, S., Eriksson, P., Hamsten, A., Kurkinen, M., Humphries, S.E. and Henney, A.M. Progression of coronary atherosclerosis is associated with a common genetic variant of the human stromelysin-1 promoter which results in reduced gene expression. *The Journal of Biological Chemistry*, **271** (22), 13055–13060(1996). doi:10.1074/jbc.271.22.13055.
13. Eguchi, T., Kubota, S., Kawata, K., Mukudai, Y., Uehara, J., Ohgawara, T., Ibaragi, S., Sasaki, A., Kuboki, T., Takigawa, M. Novel transcription-factor-like function of human matrix metalloproteinase 3 regulating the CTGF/CCN2 gene. *Molecular and Cellular Biology*, **28** (7), 2391–413(2008). doi:10.1128/MCB.01288-07. PMC 2268440. PMID 18172013.
14. Toma, A.I., Fuller, J.M., Willett, N.J. and Goudy, S.L. Oral wound healing models and emerging regenerative therapies. *Transl. Res.*, **236**,17-34(2021). doi: 10.1016/j.trsl.2021.06.003.
15. Osman, R.B. and Swain, M.V. A Critical Review of Dental Implant Materials with an Emphasis on Titanium versus Zirconia. *Materials (Basel)*, **8**(3), 932-958 (2015). doi: 10.3390/ma8030932. PMID: 28787980.
16. Apratim, A., Eachempati, P., Krishnappa Salian K.K., Singh, V., Chhabra, S. and Shah, S. Zirconia in dental implantology: A review. *J. Int. Soc. Prev. Community Dent.*, **5**(3),147-56(2015). doi: 10.4103/2231-0762.158014. PMID: 26236672;
17. Lee, D.J., Ryu, J.S., Shimono, M., Lee, K.W., Lee, J.M. and Jung, H.S. Differential Healing Patterns of Mucosal Seal on Zirconia and Titanium Implant. *Front. Physiol.*, **10**, 796 (2019). doi: 10.3389/fphys.2019.00796.
18. Cionca, N., Hashim, D. and Mombelli, A. Zirconia dental implants: Where are we now, and where are we heading? *Periodontol.*, **73**, 241-258(2000).
19. Sadowsky, Steven J. Zirconia Implants: A Mapping Review. *Oral*, **4**(1), 9-22 (2024). <https://doi.org/10.3390/oral4010002>
20. Enkling, N., Marder, M., Bayer, S., Götz, W., Stoilov, M. and Kraus, D. Soft tissue response to different abutment materials: A controlled and randomized human study using an experimental model. *Clin. Oral Implants Res.*, **33**(6), 667-679 (2022). doi: 10.1111/clr.13932. Epub 2022 May 2.
21. van Brakel, R., Cune, M.S., van Winkelhoff, A.J., de Putter, C., Verhoeven, J.W. and van der Reijden, W. Early bacterial colonization and soft tissue health around zirconia and titanium abutments: an *in vivo* study in man *Clin. Oral Impl. Res.*, **22**, 571–577(2011). doi: 10.1111/j.1600-0501.2010.02005.x



## المقارنة بين خشوة التيتانيوم والزركون في استشفاء النسيج المخاطي الفموي في الأرانب

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### الملخص:

بعد ادخال جسم غريب تحت جرح مهياً جراحياً سيستجيب الجهاز المناعي بتفاعل التهابي الذي يكون متبوعاً بالاستشفاء اذا كان ذلك الجسم ذو مطابقة حيوية مع النسيج المضيف , تهدف هذه الدراسة الى مقارنة عملية الاستشفاء لجروح مهياً جراحياً لانسجة الفم الضامة المخاطية لارانب مختبرية بعد ادخال مجموعات مختلفة من المواد المتوافقة حيويًا و المتمثلة بكل من التيتانيوم و اوكسيد الزركون . و باستخدام الفحوصات الخلوية للعينات المجمعة . المراجع القياسية مثلت كل من تسرب الخلايا الالتهابية, تكوين النسيج الضام, اعادة بناء النسيج الظهارة بالإضافة الى فحصين للكيمياء المناعية هما فحص كتلة التمايز ٣١ و فحص انزيم المذيب لبروتين التمدن البين خلوي ٣ . لتحديد افضل مادة تسمح باستشفاء النسيج الضام المخاطي الفموي و الذي يكون بتماس معها و تحديد اي مضاعفات يمكن ان تنتج من التماس مع المواد المذكورة. الاستنتاج يشير الى ان النسيج الضام المخاطي الفموي يتفاعل بشكل متمثل مع كل من التيتانيوم و اوكسيد الزركون بناء على النتائج المسجلة مع افضلية طفيفة للزركون. قياسات فحوص الكيمياء المناعية لعملية الاستشفاء تبدو كطريقة فعالة لقياس الاستشفاء على اعتبار ان كل من فحص كتلة التمايز ٣١ و فحص انزيم المذيب لبروتين التمدن البين خلوي ٣ قد اظهرا نتائج متوافقة مع نتائج اعادة نسيج الظهارة و التي تمثل العلامة الفارقة للاستشفاء. قطع اوكسيد الزركون اظهرت تراجع الالتهاب بصورة اسرع قليلاً من التيتانيوم. و اعدا بافضليات محتملة في التطبيقات الطبية.

**الكلمات المفتاحية:** تيتانيوم، اوكسيد الزركون، النسيج الضام المخاطي الفموي ، الاستشفاء ، ارانب.