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ORIGINAL ARTICLE

BONE HEALING EFFECT OF *ZIZIPHUS* HONEY ON HUMAN TOOTH EXTRACTION SOCKETS: A RADIOGRAPHIC EVALUATION

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ABSTRACT

Background: Tooth extractions are very common in Pakistan nowadays due to various causes such as dental caries, periodontitis, orthodontic purposes, and trauma due to accidents. The objective of the study is to radiographically assess the effect of *Ziziphus* honey on bone healing of the extracted tooth sockets in humans.

Materials & Methods: The study design was a randomized controlled trial using a Simple random sampling technique which was conducted in the Dental section of Lahore General Hospital, Lahore for the duration of 12 months from January 2020 to December 2020. A total number of 30 participants were divided randomly into an experimental group and a control group with 15 participants in each group. The tooth extractions were done in both groups, and *Ziziphus* honey was administered in the experimental group. Relative bone density (RBD) was measured on periapical radiographs taken on days 3, 21, and 40 in both groups. The results were interpreted with the help of Image J software®.

Results: The mean difference of 0.003, 0.091, and 0.139 in grey values of RBD was observed in the control and experimental group on days 3, 21, and 40 respectively. A statistically significant difference was observed (p-value <0.001) in the value of RBD at days 21 and 40 of the experimental and control groups.

Conclusion: The increased value of RBD in the experimental group suggest14s better bone healing as compared to the control group. Therefore, *Ziziphus* honey is a type of honey that can be used as an adjunct to expedite the healing of bone after the extraction of a tooth.

KEY WORDS: Bone density; Healing; Honey; Radiographic; Tooth sockets; *Ziziphus.*

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INTRODUCTION

Tooth extractions are very common in Pakistan nowadays due to various causes such as dental caries, periodontitis, orthodontic purposes, and trauma due to accidents.[1] A tooth extraction can lead to various complications like delayed wound healing and post-operative bleeding which can lead to improper bone healing.[2] In almost 89% of healthy individuals undergoing tooth extractions, uneventful healing of the extraction sockets has been observed whereas the rest of 11% had some kind of complications.[3] In normally healed extraction wounds, there is gradual migration of advanced tissues into the wound till the extraction socket is occupied two-thirds by the cancellous bone.[4]

If an alveolar socket does not follow the normal bone healing pattern, the newly formed connective tissue replaces the granulation tissue and results in fibrous healing instead of normal bone formation.[5] which is not a suitable site for Dental implants.[6] The quality and volume of bone have a significant effect on implant therapy after tooth extraction.[7] The pattern of the bone healing of an alveolar socket after tooth extractions determines the ridge volume and density which are crucial for an implant placement.[6] The lack of ideal bone thickness and density can lead to the poor stability of an implant. [8]

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Ziziphus Honey also known as Sidr honey comes from *Ziziphus* trees. [9] This type of honey is known to have the highest amount of minerals present in it as compared to the different types of honey.[10] In multiple studies, the positive effects of *Ziziphus* honey on tooth sockets have been noted.[11] In a study on children between the ages of 4 to 9 years, *Ziziphus* honey application after tooth extraction decreased the size of the extraction wound and accelerated the healing process.[12] *Ziziphus* honey has been used in the management of alveolar osteitis where a significant reduction in inflammation, hyperemia, and swelling was observed. In an animal study, *Ziziphus* honey was injected into the alveolar sockets after tooth extraction, and better bone quality was observed. Therefore, *Ziziphus* honey can improve the healing quality of the bone of the extracted tooth sockets.

An intervention is always required to achieve a better quality of bone after tooth extractions. The present study was designed to evaluate the effect of *Ziziphus* honey on bone healing of extracted tooth sockets. It can help expedite the bone healing of alveolar sockets after tooth extractions. This intervention can help to achieve a better quality of bone for future implant placement and fixed or removable prostheses.

MATERIAL AND METHODS:

It was a randomized controlled trial using a random sampling technique. The study has been registered with the universal website 'clinicaltrials.gov' with ID: NCT05025306. The study was conducted at the Dental section of Lahore General Hospital for a duration of one year, from January 2020 to December 2020. The total size of the sample was 30 was used calculated through Rao Soft calculator.

Ziziphus honey used in this study was attained from colonies of *Apis Mellifera* found at the Honey Bee Research Centre at the University of Punjab in Lahore. The procedure was started with the tooth extractions done in both control and experimental groups.

The study was started after taking approval by the Ethical Review Board of the Post Graduate Medical Institute (PGMI), Lahore. The informed consent was taken from all the participants. The participants were included who were otherwise healthy, male or female with an adult age of 18 years and above who needed extraction of the permanent mandibular or maxillary molars. Those participants with a history of chemotherapy, radiotherapy, or any debilitating disease like diabetes or hypertension and participants on steroids, oral contraceptives, antibiotics, or NSAIDs were omitted from the study.

A total number of 30 participants were divided randomly into two equal groups, the control and experimental groups. There were 15 participants in each group. After tooth extractions in the experimental group about 100 mg/kg/BW [13] of *Ziziphus* honey was injected into the extraction socket using a syringe and a cotton gauze was used to secure the tooth socket. In the control group, no intervention was done after tooth extraction.

The participants were asked to retain the cotton gauze in place for at least 30 minutes after tooth extractions and they were asked to prevent spitting or eating or drinking during this duration. An analgesic, Paracetamol (1000 mg) was prescribed for pain relief. Postoperative antibiotics were not prescribed as they could interfere with bone healing.

The periapical radiographs were taken successfully on days 3, 21, and 40 during follow-up visits in control and experimental groups after tooth extraction. Images of the periapical radiographs were entered into ImageJ® software.

The paralleling technique was used to record the digital periapical radiographs for which an extension cone paralleling film holder was used for the posterior teeth (first and second molars). A digital radiographic system was used by Digora ®.

The Mean grey values were determined for each tooth socket and the surrounding bone with the help of ImageJ® software. Relative bone density (RBD) was calculated by using the following formula:[14]it is not clear whether the development of femoral cortical bone can be quantitatively evaluated according to a diet with inadequate magnesium supplementation. Therefore, we used a micro computed tomography (CT

RBD = (Mean grey scale value of bone defect)/ (Mean grey scale value of surrounding bone)

The RBD value of 1 specifies that the region of bone defect and surrounding alveolar bone have the same value of density of bone. [15]

For data analysis, Graph Pad Prism 8 was used. RBD was presented in the form of numerical data as descriptive statistics in the form of graphs and tables. An unpaired T-test was applied to find the significance of the results in both study groups. The value of $p < 0.05$ was considered statistically significant.

RESULTS

The study involved 30 participants, comprising 16 females and 14 males. Mean grey values of RBD in the control and experimental groups were 0.63 ± 0.035, 0.72 ± 0.019, and 0.82 ± 0.022 in the control group and 0.63 ± 0.026, 0.81 ± 0.018, and 0.96 ± 0.051 in the experimental group at day 3, 21 and 40 respectively as shown in Table 1. The mean difference of 0.003, 0.091, and 0.139 in grey values of RBD was observed in control and experimental groups on days 3, 21, and 40 respectively.

An unpaired t-test was applied to test the significance of the data and the *p*-value of < 0.05 was considered statistically significant. There was a statistically significant difference (p-value < 0.0001) in the RBD of an alveolar socket when compared between days 3, 21 and 40 after tooth extraction. As shown in Graph 1.

Table: 1 Comparison of RBD on different days in the experimental and control groups.

Groups	Relative bone density (RBD) %		
	Day 3	Day 21	Day 40
	Mean ± SD	Mean ± SD	Mean ± SD
Control Group	0.63±0.035	0.72±0.019	0.82±0.022
Experimental Group	0.63±0.026	0.81±0.018	0.96±0.051
Mean difference	0.003	0.091	0.139
p-value	0.7740	< 0.0001	< 0.0001

**p*-value ≤ 0.05 is considered statistically significant.

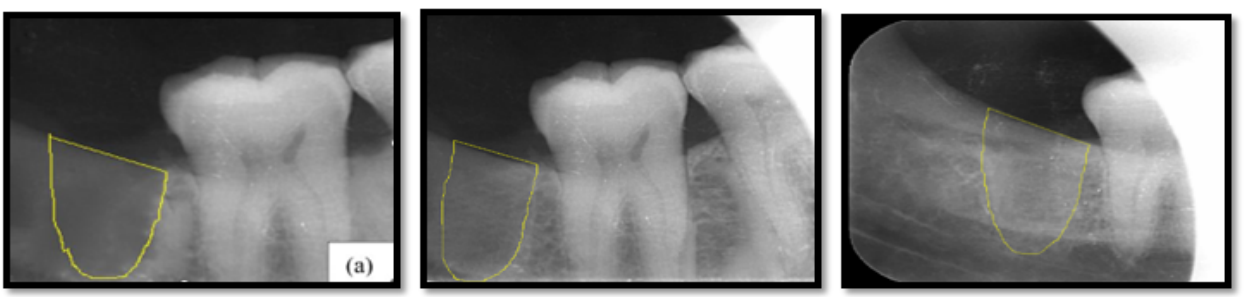


Figure 1: (a) At day 3, (b) at day 21, and (c) at day 40 after tooth extraction in control group (The yellow marked area showing the extracted tooth socket healing

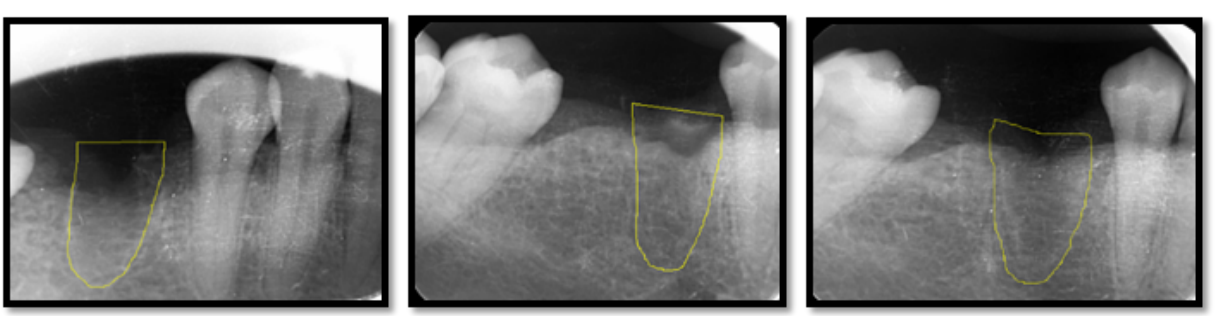
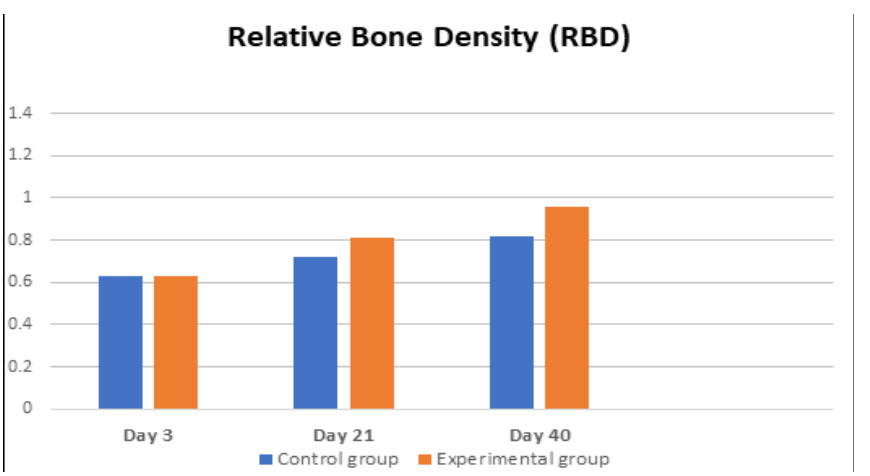


Figure 2: (a) At day 3, (b) at day 21, and (c) at day 40 after tooth extraction in the Experimental group (The yellow marked area showing the extracted tooth socket healing)



Graph 1: Mean difference (mean ± SE) in values of RBD in Experimental and Control groups (n=30)

The difference in quality of bone formation can be easily observed at extraction sites on periapical radiographs in Figure 1 and Figure 2 showing that the bone formed in the experimental group was denser and more radiopaque at days 21 and 40 of tooth extraction.

DISCUSSION

Due to a lack of oral hygiene measures and increasing health problems, the number of patients undergoing tooth extractions have been increased. [16] A good quality of bone along with sufficient ridge volume is needed after tooth extraction for implant placement as well as for conventional tooth prosthesis.[17] To get a better quality and volume of the alveolar bone after extraction socket healing, an intervention is always required.[18]

In this study, the difference in the quality of bone formation at extraction sites was observed. In the experimental group, the bone formed was more radiopaque in comparison to the control group. In an animal study, the rate of bone trabeculae formation was increased at the extraction sockets after one month of tooth extractions by the use of *Ziziphus* honey.[13] Our results also corroborate with this study where better density of bone was observed radiographically in the experimental group with the use of *Ziziphus* honey.

In the present study, most of the bone formation was also observed after one month of tooth extractions. In a similar study on radiographic evaluation, bone formation in an alveolar socket was observed during the first month of tooth extraction.[6] Also, in another study, a large number of hyperdense areas with thick bone trabeculae were observed after one month of tooth extraction [19]

There are many possible mechanisms through which the *Ziziphus* honey could accelerate the rate of bone formation. *Ziziphus* honey has hydrogen peroxide (H_2O_2) present in it which can regulate the expression of many growth factors so it could directly induce the bone markers and increase the bone formation activity.[20] The local nutrition of the wound site can be improved by *Ziziphus* honey as it contains a high quantity of sugars.[21] *Ziziphus* honey has a low pH which can provide an ideal environment for bone function.[22] The thick viscosity of *Ziziphus* honey can form a barrier over the wounds preventing infection which can contribute to better bone healing.[23]

RBD measurement by using ImageJ® software is a technique used to gauge the healing process of bone by measuring the mean grey values on radiographs in the advancement of bone healing[24] This software has been used extensively in medical image analysis and quantitative measurements of results. Moreover, the software is free of charge, easy to use, and a practical way to assess bone healing in a branch of maxillofacial surgery.[25]

CONCLUSION

Ziziphus honey can help achieve better quality of bone of an alveolar socket after tooth extraction. The Relative bone density (RBD) was increased which showed better quality of newly formed bone in extracted tooth sockets.

Limitations of study: The current study comprises of very small sample size. A large sample size should be used to calculate the outcomes of *Ziziphus* honey after tooth extractions. Moreover, the effect of *Ziziphus* honey in patients with bone diseases like osteoporosis and osteopetrosis should also be observed. Other variables of bone healing like bone markers should also be assessed for validation of the use of *Ziziphus* honey for bone healing of the extracted sockets.

Future Prospects of the Study: This study can be useful in the future to improve the quality of bone formation at tooth extraction sites which is crucial for a successful implant placement.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	MK, AM
Acquisition, Analysis or Interpretation of Data:	MK, AM, FI, OA, MMR, UMW
Manuscript Writing & Approval:	MK, AM, FI, OA, MMR, UMW

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.