

# Impact of Bromelain on wound healing and complications after periodontal surgery

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## Abstract

**Background:** we intend to examine the effect of Bromelain on the wound healing after periodontal surgery. **Methods:** In this split mouth study, we selected 20 patients with generalized moderate to severe chronic periodontitis requiring periodontal surgery and referred to the periodontology section of the Mashhad Dental Faculty. Then, we randomly considered one side of the mandible as the control group and the other side as the case group, Bromelain and placebo tablets was prescribed for case and control sides respectively; 3 tablets per day from day 1st to 3rd and 2 tablets per day from day 4th to 7th after surgery. Then REEDA index (Redness, edema, ecchymosis, discharge from the wound, approximation), VAS scale (Visual Analog Scale) in the day 3th and 7th after surgery and GI (Gingival Index) in day 7th and 14th were measured. The obtained data was analyzed using SPSS software and statistical tests of Kolmogorov-Smirnov, Friedman, Wilcoxon and Mann-Whitney. **Results:** Following data analysis, we found that none of REEDA indices such as edema, Redness, discharge, ecchymosis and GI had significant difference between two groups and only the VAS diagram has a significant difference between case and control group (P-value<0.05). **Conclusion:** According to the present study, we suggest that use of Bromelain after Periodontal surgery has a significant effect on pain reduction but wouldn't result in decreasing of inflammation and accelerating wound healing.

**Keywords:** Wound Healing, Bromelain, Periodontal Surgery

**Key Messages:** Use of Bromelain after Periodontal surgery has a significant effect on pain reduction but wouldn't result in decreasing of inflammation and accelerating wound healing.

## INTRODUCTION

Since reducing the pain of patients during and after dental treatment is one of the main concerns of researchers and clinicians. Many studies have been designed to introduce and examine various effective factors on this issue.

Bromelain is the extract obtained from stem and fruit of pineapple that contain a high level of Proteolytic enzymes and its combination depend to the method, resource and purification [1, 2]. Bromelain affects directly on pain mediators like bradykinin [3]. Also its anti-pain properties are significantly related to its anti-inflammatory features [4, 5]. It has been shown that this Fibrinolytic agent may reduces swelling, bruising, pain and duration of wound healing after trauma and surgery [5, 6]. Evidences have shown that Bromelain through digestion of fibrin helps to remove edema. Indirectly, Bromelain can increase the time needed to convert prothrombin to thrombin and plasminogen to plasmin. Thereby, it prevents fibrin formation [7]. Moreover, it inhibits the synthesis of inflammatory prostaglandin, in particularly PGE2 [8]. NSAIDs also inhibit both inflammatory and anti-inflammatory prostaglandins, but Bromelain inhibits only prostaglandins that induce inflammation, such as PGE2.

Periodontal disease is one of the most prevalent diseases involving human that if is diagnosed timely and treated properly has a good prognosis. Periodontal surgery is one of the certain methods to stop progression of periodontitis which can accompany by pain and illness. So, finding solutions that lead to reduction of side effects after surgery can help to the improvement of the disease conditions and accepting it by patient. Accordingly, in this study we examined the effect of

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Anahil tablet (Bromelain) on the clinical status of patients after periodontal surgery.

## MATERIALS AND METHODS

In this split mouth study, 20 patients with generalized moderate to severe chronic periodontitis (10 male and 10 female) in age of 30-40 years old were entered. All of them required periodontal surgery and referred to the periodontology section of Mashhad Dental Faculty. Informed consent forms were assigned by the volunteers. Initial therapy including scaling and root planning was performed for them. After that in surgical phase, resistant periodontal pockets in the posterior quadrant of the mandible were eliminated by Widman flap technique. Surgery in each quadrant was performed by a surgeon in 15 days interval. One side of the mandible in each patient, was randomly selected as control and the other side as case group. Simple randomization was performed using sealed envelopes with an equal number of envelopes for every group. Such a way that in the case side, we prescribed the Anahil tablet in the form of 3 tablets (each tablet with dose of 50 mg) per day up to the day 3rd and from day 4th to 7th after surgery 2 tablets per day. In the control side, placebo medicine (capsules containing starch with Anahil capsules with the same dose) was prescribed. Medicines was coded by the pharmacist and delivered to the surgeon. Also patients received common explanations after surgery. Evaluation of wound condition was made using REEDA scale (Redness €, Edema€, Ecchymosis €, Discharge from the Wound (D) and Approximation (A)) (Table 1)<sup>[9]</sup> and applying examination light by researcher in the days 3rd and 7th after surgery. In view of the wound healing after periodontal surgery, in our study the approximation factor wasn't used.

According table 1, for each variable a score from 0 to maximum 3 was considered. The scores derived from each variable were combined and the total scores were from 0 to 12 that suggested the degree of wound healing. The closer this figure to zero, the wound has been healed better. The pain level of patients in the days 3rd to 7th also was examined using scale VAS that was scored in terms of pain severity from 0 to 10. The inflammation condition of gingiva in the day 0, 7 and 14 was evaluated using GI index.

### Inclusion criteria:

1. The patient has Attachment Loss more than 3 mm.
2. The patient has no history of allergy to fruits and vegetables like pineapple, carrot, celery and olive.
3. They weren't undergone surgery during the last 6 months.
4. Patients were in good condition mentally.

### Exclusion criteria:

1. Patients with hemophilia, diabetes, kidney failure, liver, arrhythmia and tachycardia.

2. Smokers.
3. The consumer of blood diluents, anticoagulants and thrombolitics.

We analyzed data using Kolmogorov-smirnov, Friedman, Wilcoxon and Mann-Whitney test.

This study has a clinical trial code number: IRCT2016102918834N2.

## RESULTS

After gathering data and statistical analysis of them, the results indicated that GI and REEDA indices between two groups in all periods had more reduction in the Bromelain group than control group but statistically had no significant difference. The VAS index (Visual Analog Scale) in the Anahil group in both periods has significant reduction compared to control group (table 4).

## DISCUSSION

Use of herbal medicines has been applied from ancient time up to day in order to treat different diseases. Natural resources are considered one of the important research fields to prevent immunologic and chemical side effects of medicines<sup>[10]</sup>.

Many scholars yet use herbal medicines as adjunctive to treat Alzheimer<sup>[11]</sup>, diabetes, cancer and cardiovascular diseases in which free oxygen radicals play an essential role<sup>[12]</sup>.

More than 700 bacterial species are found within mouth that can contribute to periodontitis and caries<sup>[13]</sup>. As mouth health has a significant effect on the quality of life and general health, so timely diagnosis and treatment and attracting patients' cooperation for treatment can has a significant effect on the quality of life of community members.

Periodontitis is one of the most common diseases involving communities which in some cases surgery is inevitable. Accelerating the wound healing and reducing pain of patients has been one of the investigation objectives from past to the present.

Wide range of health benefits for Bromelain has been identified that includes reversible inhibition of platelet aggregation, sinusitis and bronchitis, and angina pectoris and increased absorption of drugs, particularly antibiotics<sup>[6, 14, 15]</sup>. It is applied for treatment of acute inflammation and sport damages as well<sup>[16]</sup>.

Given the Bromelain properties, we decided to examine its effect on the wound healing after periodontal surgery. In order to evaluate the process of wound healing, we used four indices of REEDA (Redness (R), Edema (E), Ecchymosis (E), Discharge from the Wound (D)). In the other hand, in order to examine the clinical process of inflammation, GI index was examined over two weeks. In the previous studies evidences of bromelain effectiveness to reduce the side effects of dental surgery have been observed. For example,

Hozt *et al.* in 1989<sup>[17]</sup> and Barrera<sup>[18]</sup> evaluated the anti-inflammatory effect of Anahil after extraction of third molars. In both studies in spite of different method of Bromelain prescription, results were similar with reduction of swelling and inflammation.

Also Inchingolo *et al.* (2010) in their study examined the Bromelain effect on pain relief, edema and soft tissue healing after third molar extraction. They reported that reduction of edema was same in both groups<sup>[19]</sup>.

Considering that above studies, findings of our research is similar to the previous studies and confirms them regarding the insignificant reduction of swelling and edema after prescription of the therapeutic substance of Anahil.

Barrera<sup>[18]</sup> also examined inflammation in his study and concluded that although inflammation of Anahil treatment group was less than control group but inflammation between two groups hadn't significant difference. Considering the Barrera's study<sup>[18]</sup>, the findings of our research confirm the findings of Barrera's study.

But in our study VAS significantly differ in case and control group. This issue can be attributed to the less traumatic process of periodontal surgery compared to third molar extraction.

In a study in which local Bromelain in the incision area was used, it was observed that it results in regeneration of blood perfusion and increase of PO<sub>2</sub> in the wounded areas, control of TNF- $\alpha$  expression and increase of  $\beta$ -TGF expression. Enzymatic debridement by help of Bromelain is associated with fewer side effects during surgery than debridement. Surgical incision is associated with more pain and is more specific and can increase the probability of numbness and bleeding during working.

To our best knowledge, bromelain showed accelerating impact on healing of diabetic and burning ulcers in some studies<sup>[20]</sup>, but in oral cavity did not seen such impacts. Maybe it related to high ability of repairing and renewing of oral tissues and periodontium which can reconstruct itself by higher turnover rate.

According to modality of our study, it's not possible to daily observe periodontium status during drug consumption which is one of the limitations of the present research.

## CONCLUSION

According to the present study, we suggest that use of Bromelain after Periodontal surgery has a significant effect on pain reduction but wouldn't result in decreasing of inflammation and accelerating wound healing.

## Conflict of interest statement:

The authors declare no conflict of interest.

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**Table 1: REEDA Index**

Points	Score			Total
	Redness	Edema	Ecchymosis	Discharge
0	None	None	None	None
1	Within 0.25 cm of the incision bilaterally	less than 1 cm from incision	Within 0.25 cm bilaterally or 0.5 cm unilaterally	Serum
2	Within 0.5 cm of the incision bilaterally	between 1 and 2 cm from the incision	Between 0.25 cm and 1 cm bilaterally or between 0.5 and 2 cm unilaterally	Serosan-guinous
3	Beyond 0.5 cm of the incision bilaterally	greater than 2 cm from incision	Greater than 1 cm bilaterally or 2 cm unilaterally	Bloody, purulent

**Table 1: Examination of difference of GI index between the two groups in both periods**

	Mean	Standard deviation	Result of Mann-Whitney test
GI index of Bromelain group before surgery	2.54	.031	P = 0.58
GI index of control group before surgery	2.58	.0277	
GI index of Bromelain group 7 days after surgery	1.89	.044	P = .41
GI index of control group 7 days after surgery	2.02	.041	
GI index of Bromelain group 14 days after surgery	1.31	.029	P = .46
GI index of Bromelain group 14 days after surgery	1.44	.024	

GI: Gingival Index

**Table 2: Examination of difference of REEDA index between the two groups in both periods**

	Mean	Standard deviation	Result of Mann-Whitney test
REEDA index of Bromelain group 3 days after surgery	4.2	1.57	P = .64
REEDA index of control group 3 days after surgery	4.35	1.46	
REEDA index of Bromelain group 7 days after surgery	2.15	.098	P = .38
REEDA index of control group 7 days after surgery	2.4	1.09	

REEDA: Redness (R), Edema (E), Ecchymosis (E), Discharge from the Wound (D) and Approximation (A)

**Table 3: Examination of difference of VAS between the two groups in both periods**

	Mean	Standard deviation	Result of Mann-Whitney test
VAS of Bromelain group 3 days after surgery	3.4	1.52	P = .005
VAS of control group 3 days after surgery	2.2	2.24	
VAS of Bromelain group 7 days after surgery	5.2	.071	P = .008
VAS of control group 7 days after surgery	3.6	1.36	

VAS: Visual Analog Scale