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**Original Research Article**

# The High Sucrose Diet Effects on Expression of Bone Morphogenetic Protein-7 in the Alveolar Rats' Extraction Socket: Immunohistochemical Study

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## ABSTRACT

A crucial function of wound regeneration is the mineralization and presence of calcium compounds and minerals for the survival of bone following tooth extraction. Bone morphogenetic proteins, or BMPs, are crucial for new bone growth. BMP-7 is one BMP that is highly crucial. For the newly generated bones to be perfectly formed, they also really need high-quality minerals. Among the numerous factors that can influence post-extraction healing, nutrition plays a central role. Adequate dietary intake of macronutrients and micronutrients is essential for sustaining tissue repair, angiogenesis, and bone remodeling. A high-sucrose diet can accelerate the loss of mineral-rich bone, and osteoclast resorption of alveolar bone can also raise calcium levels in plasma and urine. This study aims to investigate BMP-7 expression in Wistar rats that have undergone tooth extraction following a high-sucrose diet. ANOVA test was used to statistically analyze the outcomes. On days 10, there was a significant difference in BMP-7 expression compared to the control group.

**KEYWORDS:** Extraction Socket, High Diet Sucrose, BMP-7, wound healing.

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## INTRODUCTION

Teeth extraction is necessary due to failing teeth that result from a variety of factors, including loose alveolar bone, advanced periodontitis disease, tooth fractures, failed endodontic therapy, and large caries that cannot be maintained. The alveolar sockets and mucous membranes would be harmed during the extraction. In order to restore normalcy to damaged soft and hard tissues, four processes must occur hemostasis in the wound socket, tissue remodeling, cell proliferation, and inflammation of the hard and soft tissues [1-2].

The presence of calcium and other minerals, as well as mineralization to make the bone survival following the extraction, is one of the key responsibilities of wound regeneration. Mesenchymal connective tissue plays a major part in the process of intramembranous ossification, which happens during tooth extraction. The mandibular cancellous layer, which can be found on the structure of the mandibular complex, and the portion of the outer surface responsible for skeletal resilience have a major influence on the structure of bone. The mandible and maxilla skeleton is a dynamic and intricate organ made of bone. High microvascularization in the tissue is advantageous for remodeling. The mechanism

of maintaining bone homeostasis plays a crucial part in controlling stability against injury and mineral loss. Additionally, the microvasculature of the bone creates progenitor cells and molecules that are crucial for the repair of bone structure. It also contains oxygen and nutrients [3-4].

The process of bone healing necessitates the osteogenesis process from bone cells. Mesenchymal cells found in bone marrow are the source of numerous cells, including muscle, bone, fibroblast, and cartilage cells. Mesenchymal cells have the unique capacity to develop into a wide variety of distinct cell types. Osteoprogenitor cells and other microvascular components of bone, such as endosteal and periosteal cells in the marrow cavity and the outer layers, can supply the bone's nutritional needs. Bone morphogenetic proteins, or BMPs, are essential for the development of new bone. BMP-7 is a BMP whose performance is essential. In order for the process of making new bones to be flawless, they also absolutely need high-quality minerals [4-6].

A diet rich in sucrose can accelerate the loss of mineral-rich bone. Osteoclast resorption of alveolar bone can also cause an increase in calcium in plasma and urine. A high-sucrose diet has been linked to poor bone health in numerous prior studies, but no research has examined the influence of high sucrose diet on BMP-7 protein expression after tooth removed [7].

This study aims to investigate BMP-7 expression in Wistar rats following tooth extraction following a high-sucrose diet.

## MATERIALS AND METHODS

The sample in this study, which used a Post-Test Control Group Design, was assigned at random to receive the intervention. 24 male Wistar rats, aged 100 days and weighing between 150 and 200 grams, were used in this investigation. Ad libitum food, drink, and healthy conditions must be provided for all samples. All phases of the experimental procedures for this study have already been authorized by Airlangga University's Animal Care Committee. In this investigation, Wistar rats were utilized for tooth extraction therapy due to their higher survival rate and ease of treatment. It is possible to extract the lower incisor with reduced complications, including bleeding or fractured alveolar bone.

Every sample was split into 3 groups, each with eight rats, using randomization. Group 1 (consisting of 20% energy from sucrose for 10 days), Group 2 (consisting of 40% energy from sucrose for 10 days), and Group 3 (control for 10 days). The lower incisive of Wistar rats were extracted after being fed a sucrose diet for ten days. The sample was fixed with 10% buffered formaldehyde after being severed head-on utilizing sagittal cutting. 96% ethanol was used to remove the water from the sample fragment. The following step involves utilizing a graduated sequence of alcohol for dehydration and xylene for clarifying. Paraffin was used for tissue embedding, and 5 µm sectioning was carried out. The sections were incubated overnight at 4°C with primary antibodies anti-BMP-7 (1:200, Abcam, UK) Following the completion of all histology specimens, each sample was inspected using a light microscope with a 400x magnification.

## RESULTS

There were no problems or bleeding incidents during the removed of Wistar rats' incisive in this study, and neither anesthetic nor infection caused any animal fatalities. The mean and standard deviation of BMP-7 expression in Wistar rats following extraction are shown in Table 1. Kolmogorof-Smirnov test on the data to see if the distribution was normal. Every data set had a normal distribution since the results for every group under analysis were all $p>0.05$. Figure 1 displays data on BMP-7 counts per 400 times in patients treated for 10 days.

**Table 1:** The BMP-7 expression in the treatment and control groups.

| Group | X±SD Day 10 |
|---|---|
| Sucrose 20% | $15.14^{a}$±1.77 |
| Sucrose 40% | $11.71^{b}$±3.45 |
| K | $17.25^{a}$±1.70 |

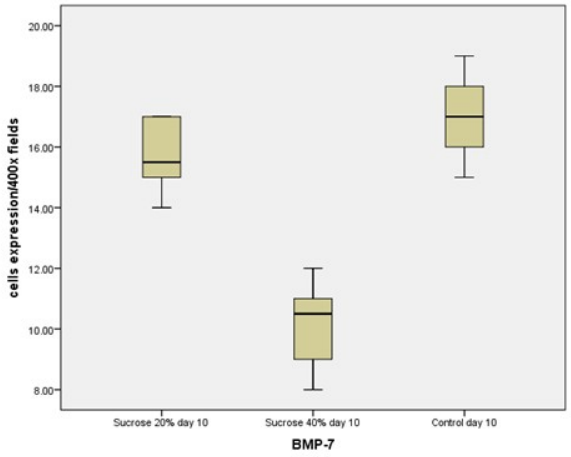


**Fig. 1:** The amount of of BMP-7 in the tooth extraction wound socket after ten days of treatment.

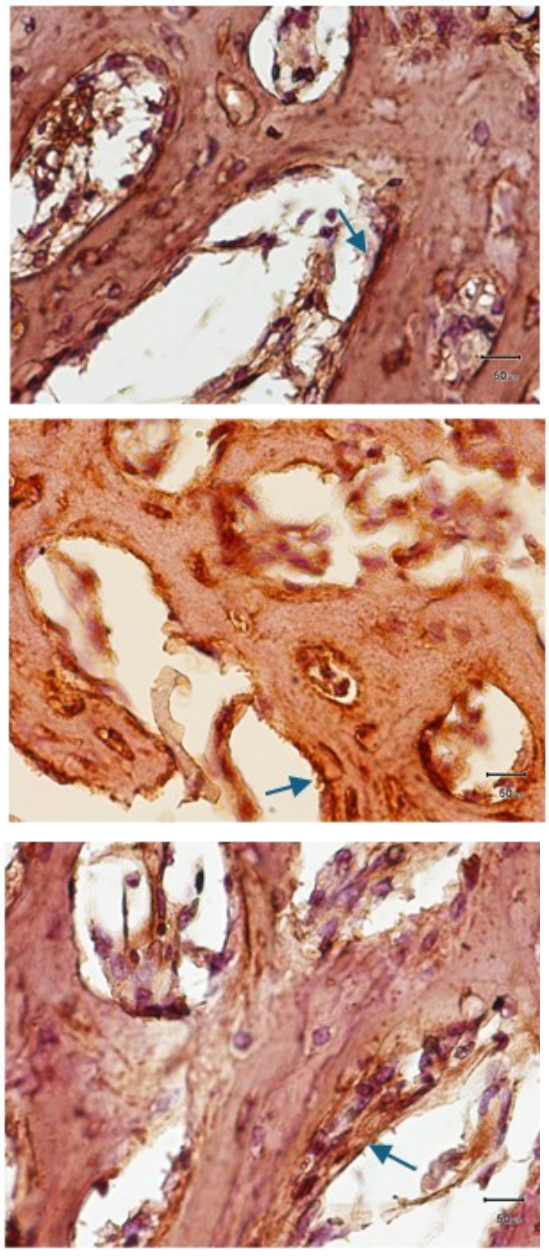

**Fig. 2:** Expression of BMP-7 in the socket on day 10 following tooth extraction under a light microscope with a 400x magnification. (A) Sucrose 20%, (B) 40%, and (C) as the Control group.

## DISCUSSION

Numerous factors can promote or impede bone repair. Factors to take into account include tissue resilience, wound kinds and conditions, type of pathogen and systemic variables. The initial stage of the healing process following tooth extraction is indicated by angiogenesis in the area of the soft tissue. This is followed by the expression of BMP-7 in osteoblast cells, which are in charge of alveolar bone growth. BMP-7 stimulates mesenchymal cells to proliferate and trigger active osteoblast cells, hence enhancing the quality of alveolar bone. This process aids in osteoblast differentiation and proliferation. Osteoblasts can produce both collagen and non-collagen matrix, mesenchymal cells called osteoblasts create the spherical, oval, or polyhedral osteoid, or bone matrix, which is distinct from the mineralized matrix. By manufacturing and secreting substances that regulate electrolyte changes in extracellular fluid and the organic matrix of bones, osteoblasts contribute to the process of mineralization. Osteoblasts contain mitochondria, the Golgi membrane, and the endoplasmic reticulum [8-12].

Alveolar bone is a mineralized tissue containing proteoglycans, osteocalcin, osteonectin, osteopontin, and sialoprotein collagen type I. Additionally, the alveolar bone have growth factors and serum proteins in it. The two types of alveolar bones that are most widely known are cortical and trabecular bones. The trabecular bone, that shaped like a sponge, is located inside the bone cortex, which is a solid bone on the outside [5,13-15].

Pleiotropic growth factor BMP-7 is essential for the growth of many tissues and organs. It preserves several physiological functions, including the growth of bones and the repair of fractures. When BMP-7 attaches itself to the surface of cells, it stimulates two main signaling pathways: the canonical/Smad dependent pathway and the non-canonical/Smad independent pathway. BMP-7 triggers regulatory Smads (Smad-1, 5, and 8) in the canonical or Smad-dependent pathway, so that they can be phosphorylated in the

cytoplasm. Following this, co-stimulatory molecule Smad-4 and phosphorylated regulatory Smad proteins combine to form a complex. After that, this complex is transduced to the nuclei, where it recruits cofactors and Run-related transcription factor 2 (Runx2), which controls the production of osteogenic genes and, in turn, affects the development of osteoblasts. Bone fracture healing, homeostatic skeletal remodeling, and embryonic skeleton creation all depend on mesenchymal stem cell differentiation into osteoblasts. The transcription factor osterix (Osx), also known as SP7, is upregulated by BMP-7 and has the capacity to promote osteoblast development in vivo as well as in vitro [16-19].

Bone metabolism and bone health are primarily regulated by nutrients, including carbohydrates such as sugars, proteins, and lipids. According to research, a diet high in fat and carbohydrates is linked to low bone mineral density (BMD). When bone density declines, the cancellous bone compartment experiences negative microstructure changes that are linked to lipid metabolism modulation disorder, altered bone marrow environment, and elevated inflammatory response.

In this investigation, BMP-7 expression decreased in response to a high-sugar diet (Table 1 & Figure 1). This research is in line with research conducted by Tjaderhane et al. After feeding a high sucrose diet to Wistar male and female rats for five weeks, it was found that their bone strengths were significantly lower than those of the control diet group. The sucrose-fed group of female rats exhibited significantly reduced femur and tibia weights, tibia widths, and Ca and P concentrations in bone compared to the control diet group. These findings imply that the variations in bone metabolism may be explained by the sugar diet, which caused a metabolic disruption [20,21].

Rats were given different dosages of a sugar diet to assess changes in their plasma calcium levels. The results show that when rats consume a high amount of sucrose, their plasma calcium levels rise. One mechanism suggested to explain how a high-sugar diet affects blood calcium is the loss of calcium in the urine [22,23]. The caloric impact of sucrose is thought to be caused by decreased tubular reabsorption. BMP-7 expression is disturbed by low calcium levels in the body, which permits the maturation of barriers to bone formation. High glucose levels result from a high sucrose diet, and osteoblast cells that exposed to high glucose have been shown to directly inhibit osteoblasts. Putrescine is assumed to decrease with glucose due to the action of ornitine decarboxylase (ODC). An essential enzyme for cell growth is ODC [24,25].

## CONCLUSION

In this study, BMP-7 expression in the extraction socket of alveolar Wistar rats was decreased by a 40% sucrose diet.

**Study limitations:** This research focused on a single distinct time point, specifically 10 days, while omitting subsequent stages, particularly the bone regeneration phases that occur up to 30 days. Additionally, the assessment was confined to histological and molecular markers; the inclusion of functional angiogenesis assays, such as micro-CT perfusion or CD31 staining, would yield a more thorough comprehension.

**Future directions:** Future studies should evaluate bone volume fraction, trabecular thickness, and mineral apposition rate and biomechanical testing.

**Ethical approval:** The Institutional Ethics of the Faculty of Dentistry at Airlangga University approved all of the procedures, which followed both institutional and national ethical guidelines for animal research.

## Author Contributions

**ck:** idea, write and conceptualized the manuscript
**irk:** compiled the statistics and research methods

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## Conflicts of Interests: None

**Declaration of Interest:**

The author has disclosed no conflicts of interest, and no research grant was used to fund or support the publication.

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