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EFFECTIVENESS OF ROSELLA ON BONE REPAIR

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ABSTRACT

Background: Bone destruction can occur as a result of pathological processes that destroy bone components. The healing process from bone destruction can take time due to several factors such as the size and shape of the damage, metabolic factors, hormones, nutrition, and other factors. One of the plants that can repair bones is Rosella. Rosella flower (Hibiscus sabdariffa L) is a medicinal plant that grows in tropical and subtropical countries such as Saudi Arabia, India, Thailand, Malaysia, and Indonesia. Hibiscus sabdariffa L contains saponins, tannins, phenols, flavonoids, triterpenoids, and glycosides that can inhibit alveolar bone destruction. **Purpose:** To explain the effectiveness of Rosella (Hibiscuss Sabdariffa L.) on bone repair **Methods:** Journals were analyzed and accessed via Google Scholar, NCBI, and EBSCO from 2017 to 2024. **Result:** From 20 reference that have been found, after being analyzed based on inclusion and exclusion criteria, there is 20 reference has been choosed and 5 reference excluded. **Conclusion:** Rosella contain flavonoids that can promote the bone healing process, flavonoids can protect against bone loss by regulating signaling pathways that improve osteoblast function, by reducing the effects of oxidative stress or chronic low-level inflammation.

INTRODUCTION

The alveolar bone, also called the alveolar process, is a part of the jawbone that supports the teeth and the mouth's function (Omi & Mishina, 2022). Alveolar bone is a dynamic and vital tissue. Normally, alveolar bone is subjected to mechanical stimulation and undergoes a continuous remodeling cycle due to the coordinated activity of two important cell types: osteoblasts, osteocytes, and bone-lining cells, and bone-resorption cells, such as osteoclasts (Huang et al., 2020).

Bone damage is a serious disease that can occur due to pathological processes, which can be caused by extensive trauma or infection. Healing of bone damage is the process of bone tissue reconstruction. Most bone damage can heal spontaneously under a suitable physiological environment because of the bone's regenerating ability.

The bone healing process takes a long time and the formation of new bone is slow due to the size of the wound, the wound environment, metabolic factors, hormones, nutrition, and stress (Majeed & Ghani, 2018).

Rosella flowers (Hibiscus sabdariffa L.) contain saponins, tannins, phenols, flavonoids, triterpenoids, and glycosides that can inhibit alveolar bone damage (Dharma Utama et al., 2019). Rosella has many functions (Ramadhan et al., 2021). Rosella flowers (Hibiscus sabdariffa L.) High calcium can activate bone loss, while certain substances in rosella flowers are able to rejuvenate the body cells and protect the body from infection of germs and viruses. The function of calcium helps the density of bone density. Calcium in bone has two functions as an integral part of bone structure and as a storage place of calcium.(Dharma Utama et al., 2019)

The rosella flower (Hibiscus sabdariffa L.) is an ornamental plant with thick flower petals that belongs to the Hibiscus or Malviceae family (Nasri & Imran, 2017). The herbal plant rosella or Hibiscus sabdariffa L. can be used in the health sector. The chemical content contained in rosella petals are polyphenols, saponins, tannins, and flavonoids consisting of flavonol and anthocyanins (Kusparmanto et al., 2024). This article aims to show and describe the antiinflammatory effects on Hibiscus sabdariffa L based on scientific literature. Therefore, rosella possesses a range of beneficial properties, including antiseptic, diuretic, anti-inflammatory, antibacterial, and antioxidant effects. These qualities make it a valuable natural remedy for various health conditions. Additionally, rosella has the potential to enhance the body's immune system, contributing to overall health and well-being by supporting the body's ability to fight off infections and maintain balance (Unita & Singarimbun, 2018). Based on the description above, researchers want to analyze further the study of the potential of chemical compounds of rosella flower extract (Hibiscus sabdariffa L.) as an antiinflammatory.are medicinal plants that grow in tropical and subtropical countries such as Saudi Arabia, India, Thailand, Malaysia, and Indonesia. The use of Rosella flowers in Indonesia is not yet very popular, however, in other countries it is used in the field of medicine. Rosella in Nigeria is often used for various treatments such as lowering blood pressure (antihypertensive), antiseptic, diuretic, lowering blood sugar (hypoglycemic), laxative, preventing the formation of kidney stones, antihelmintic, treating coughs and antibacterial, while in Thailand rosella tea is believed to lower cholesterol (Suniarti et al., 2022). Natural materials can be used as an alternative as the prevention method.(Kusparmanto et al., 2024)

From the explanation above, the authors assume that there is an effect of adduction of rosella extraction petal on bone repair. The purpose of this research is to see the composition and content of the bioactive compound of rosella petal extract which can be used as an alternative material to accelerate the growth of alveolar bone. The study aims to see the contents of the compound and bioactive substances, as well as the amount contained in the gel and injection of Rosella petals, extract that can accelerate the remodeling process of the alveolar bone.

METHOD

This paper is arranged by collecting various relevant academic sources. The sources collected from this paper include books and various scientific journals, which are obtained from credible databases such as EBSCO and Google Scholars. There are several keyword searches used from various relevant sources in writing this paper, such as "rosella", "Hibiscus sabdariffa L.", "bone repair", "bone healing", and also "bone remodeling". Specific inclusion criteria were used to select literature in writing the paper; the literature used must be published in the period 2017 to 2022, with the results of sources used are valid and the literature used has the latest information. In addition, the language used in searching for sources for this paper must be in Indonesian or English. In writing this paper, research sources must be related to the topic effectiveness of rosella on bone repair, ensuring that the search for these sources must be more selective with the aim that the paper presented has strong literature sources with topics related to effectiveness of rosella on bone repair.

RESULT

The results are obtained from 25 reference libraries in writing this paper through a comprehensive search. Further analysis of the reference libraries are obtained according to the inclusion criteria and exclusion criteria to achieve relevant sources relevant to the topic. Additionally, from the results of analyzing the sources obtained and according to the established criteria, there are 20 references that met the criteria, while 5 others are eliminated from the bibliography. The reason is the year of publication is more than 5 years ago, making it not relevant to the current paper. Strict evaluation and careful analysis of the sources found were carried out to obtain credible sources for research in writing this paper. Explanations of several journals obtained are summarized in the following table 1.

Table 1. List of references and summary (Majeed & Ghani, 2018; Porth, 2011).

Reference	Aim	Method	Sample	Result
Idrus Erik *et al* (2020)	To conduct an in vivo study to determine the effect of two concentrations of rosella flower extract on alveolar bone destruction using a periodontitis model in mice with ligature wire application on the maxillary molar teeth and a calvaria bone destruction model with LPS injection into the calvaria.	Bone damage repair in both models was done by applying rosella extract with a concentration of 5% and 10% on the damaged bone area before bone damage induction with ligature (pre-ligature) as a preventive effect and histological analysis. Then, the level of bone damage was measured using micro CT and after three days of ligature placement in the periodontitis model as a	30 8-week-old mice weighing 20 - 25 grams and rosella flowers extracted with ethanol in 5% and 10% preparations.	10% rosella extract resulted in a decrease in bone damage in the calvaria bone in the post-ligation group, which showed the anti-inflammatory and anti-bacterial potential of the extract.

		therapeutic effect		
Masjeed ss et al (2018)	To evaluate the effects of topical application of flavonoid extracts on experimentally induced bone defects in rabbit tibia.	A hole was induced in the left tibia as a control and allowed to heal spontaneously, whereas, a second hole was induced in the right tibia where topical application of flavonoid extract was performed as an experimental site, and the flavonoid extract was applied with a pipette. The specimens were fixed in 10% formalin for 48 hours, decalcified with a formic acid solution, then the bone tissue was dehydrated with alcohol and embedded in paraffin. 5µm sections were prepared in the usual manner, and stained with hematoxylin and eosin. Histological examination was performed using a light microscope.	There were 24 animals divided into four groups according to the healing interval (3 days, 1, 2, and 4 weeks) of six animals each.	Histological findings revealed that the development of the bone healing process was accelerated after flavonoid application. The results obtained in this study indicate that flavonoid extract from Hibiscus sabdariffa L. has the potential activity in enhancing the bone healing process.

The results obtained in this study in table 1 showed that rosella or *Hibiscus sabdariffa L* extract has flavonoid content, which is potential activity in increasing the bone healing process, as much as 10% resulting in a decrease in bone damage. And shows the potential for anti-inflammatory and anti-bacterial extracts.

DISCUSSION

Rosella Flower

a. Definition of Rosella Flower

Hibiscus sabdariffa L., also known as rosella flower, is a wild tropical plant belonging to the Malvaceae family. This flower has striking red petals, originating from Asia such as India and Malaysia. Rosella flowers can be used as food and medicine in various countries such as Egypt, China, Thailand, Indonesia, and South America (Wang et al., 2022).

Rosella flower has several synonyms, including Abelmoschus cruentus (Bertol.) Walp., Furcaria sabdariffa Ulbr., Hibiscus acetosus Noronha, Hibiscus cruentus Bertol., Hibiscus fraternus L., Hibiscus gossypifolius Mill., Hibiscus palmatilobus Baill., Hibiscus sanguineus Griff., Hibiscus sabdariffa Rottb, and Sabdariffa rubra Kostel (Nurnasari & Khuluq, 2017).

This plant has many branches, dense leaves, and a height of up to 1 - 2 m. The stem is green or red, depending on the seeds of the plant. Rosella flowers have strong taproots, and the flowers have pale yellow petals (can be pink or red). Flowers usually grow singly in the leaf axils. The petals are at the base of the flower and the fruit is large with colors varying from dark purple to bright red (maybe white) when ripe. The flowers are red to yellow, with a dark center containing a short stalk, and have male and female organs (Nurnasari & Khuluq, 2017). The type of rosella flower leaf is a single leaf that is round and oval, has finger-like leaf veins, a blunt leaf tip, serrated leaf edges, and a notched leaf base (Suwadi et al., 2021). The length of the rosella flower leaf can reach 6-15 cm and a width of 5-8 cm. The roots that support the stem are taproots. The flower crown is funnel-shaped and consists of 5 petals.[10] The fruit of the rosella flower is oval or round, tapering at the end like a capsule, and is formed 1-2 days after pollination. The rosella plant has kidney-shaped seeds with pointed and hairy corners.(Suwadi et al., 2021)

The length of the seeds is about 5 mm and the width is 4 mm. Each fruit contains 30 - 40 seeds, and the size of the seeds is 3- 5 mm x 2 - 4 mm and is reddish brown(Suwadi et al., 2021).

Rosella flowers or Hibiscus sabdariffa L. have the following taxonomy:(Nurnasari & Khuluq, 2017)

- Kingdom: Plantae
- Subkingdom: Viridiplantae
- Infrakingdom: Streptophyta
- Super Division: Embryophyta
- Division: Tracheophyta
- Subdivision: Spermatophytina
- Class: Magnoliopsida
- Superorder: Rosanae
- Order: Malvales
- Family: Mavaceae
- Genus: Hibiscus
- Species: Hibiscus sabdariffa Linn

b. Rosella Flower Content

According to the Indonesian Ministry of Health, every 100 g of rosella flowers contains 260–280 mg of Vitamin C, Vitamin D, B1, and B2. In addition, rosella contains high calcium (486 mg/100 g), magnesium, and omega 3. Rosella flower petals also have active ingredients, namely grossypeptin, anthocyanin, glucose hibiscin, niacin, riboflavin, beta carotene, iron, polysaccharides, and flavonoids. Flavonoids is a polyphenol compound that has functions as an anti-inflammatory, anti-oxidant, and anti-carcinogenic, and it can help stimulate bone formation (Ramesh et al., 2021).

Figure 1. Rosella flower leaves (Nurnasari & Khuluq, 2017).

Figure 2. Rosella fruit and flower petals (Nurnasari & Khuluq, 2017).

Flavonoid content is found in various plant foods ranging from fruits and vegetables, herbs and spices, essential oils, and drinks, and has the most potential food components to improve bone health besides calcium and vitamin D. Flavonoids as one class of phytochemicals have the potential to protect against bone loss, most likely related to their anti-inflammatory properties. The flavonoids that have been most widely studied about bone health are isoflavones, especially those from soybeans. Isoflavones, along with flavonoids from other plant foods promise bone health (Weaver et al., 2012).

The most widely studied mechanism of flavonoid benefits for bones is the estrogenic action of phytoestrogens, including soy isoflavones, lignans, and coumesterol. The ability of phytoestrogens to bind to ER or estrogen receptors has a positive effect on bone (Weaver et al., 2012).

The benefits to bone are due to several potential factors, including acid-base balance, potassium or other micronutrients (such as boron or vitamin K), and certain bioactive compounds (Li et al., 2021).

2. Bone Destruction Process

The alveolar bone is an important part of the maxillofacial skeleton, a connective tissue that supports the teeth, experiences mechanical stress, and undergoes continuous bone remodeling characterized by resorption of damaged bone by osteoclasts, followed by replacement with newly formed bone by osteoblasts (Li et al., 2021; Ramesh et al., 2021).

The fine-tuning of the osteoclast-osteoblast balance can produce a tight synchronization of bone resorption and formation, which maintains the structural integrity and homeostasis of bone tissue. Conversely, irregular bone remodeling can lead to pathological osteolysis, in which inflammation plays an important role in driving bone destruction (Li et al., 2021).

Factors involved in bone destruction are mediated by bacteria and the host. Bacterial biofilms induce the differentiation of bone progenitor cells into osteoclasts and stimulate gingival cells to release mediators that have the same effect. Bacterial biofilms and inflammatory mediators can also act directly on osteoblasts or their progenitors, inhibiting their action and reducing their numbers (Takei & Carranza, 2019).

Bone resorption is a complex morphological process associated with the presence of erosion on the bone surface and osteoclasts. Osteoclasts originate from hematopoietic tissue and are formed from the fusion of mononuclear cells. When osteoclasts are active, there is a large increase in hydrolytic enzymes that will be secreted in the ruffled border area where these enzymes damage the organic part of the bone (Takei & Carranza, 2019).

Another mechanism of bone resorption consists of a collection of acidic environments on the bone surface that will result in the loss of bone mineral components. This can be caused by different conditions including protons flowing through the osteoclast cell membrane, bone tumors, or local pressure out through the secretory activity of osteoclasts (Takei & Carranza, 2019).

Ten Cate (1994) describes the sequence of bone resorption processes as follows:(Takei & Carranza, 2019)

1) Osteoclast attachment to the mineralized bone surface.
2) Formation of an acidic environmental cover through the action of proton pumps, where the bone is demineralized and the organic matrix is exposed.
3) Degradation of the organic matrix that has been exposed with the main elements of amino acids by the action of enzymes released, such as phosphoric acid and cathepsin.
4) Destruction of mineral ions and amino acids in osteoclasts.

3. Bone Repair Process

Bone healing depends on the location of the fracture, hematoma formation, and other factors. In children, the bone repair process occurs within 6 - 8 weeks, while in adults it occurs within 10 - 18 weeks(Porth, 2011).

There are 4 stages in bone repair: hematoma formation, fibrocartilaginous callus growth, ossification, and remodeling (Porth, 2011). Hematoma formation occurs on the first to second day after the fracture. Hematoma formation develops from torn blood vessels in the periosteum and adjacent muscles and soft tissues. Damaged blood vessels also cause bone cells to be deposited at the fracture site. In 2 - 5 days, the hemorrhage forms a large blood clot. By the end of the first week, most of the blood clot is organized by blood vessel invasion and early fibrosis. As a result of hematoma formation, clotting factors remain in the injured area to initiate the formation of a fibrin network, which serves as a scaffold for the growth of new fibroblasts and capillary buds. At the same time, degranulating platelets and migrating inflammatory cells release growth factors that stimulate the proliferation of osteoclasts and osteoblasts (Porth, 2011).

The second stage is the formation of granulation tissue or soft tissue callus. In this stage, fibroblasts and osteoblasts migrate to the fracture site from the adjacent periosteal and endosteal membranes, initiating the reconstruction of the bone. Fibroblasts form collagen that spans the fracture and connects the broken bone ends, some of which differentiate into chondrocytes that secrete a collagen matrix. At the same time, osteoblasts begin to incorporate bone into this matrix. After a few days, a fibrocartilage “collar” becomes evident around the fracture site. The edges of the collar on either side of the fracture eventually fuse to form a bridge, connecting the bone fragments. In less severe fractures, the repair tissue reaches its maximum thickness by the end of the second to third week (Porth, 2011).

Ossification is the deposition of mineral salts into the callus. This stage begins in the third to fourth week of healing. Mature bone gradually replaces the fibrocartilaginous callus and excess callus is resorbed by osteoclasts (Porth, 2011).

Remodeling involves the axial bone of the callus that develops in the marrow space and surrounds the external aspect of the fracture site. When the mature callus provides a load-bearing force, the parts that are not under pressure will be reabsorbed, in this way the callus is reduced in size until the shape and lines of the bone are formed (Porth, 2011).

4. Effect of Rosella Flowers on Bone Repair

Flavonoids can stimulate the proliferation of osteoblast cells into osteocytes by increasing the activity of estrogen receptors and increasing the growth of TGF-1 so that it can stimulate the proliferation of osteoblast cells (Sherman Salim & Mefina Kuntjoro, 2015). Apart from 203 flavonoids, rosella extract also contains tannin and quercetin compounds which also have an effect on bone repair. Sukmana et al., (2017) stated that tannin compounds can reduce IL-1β expression and increase BMP-2 during the bone remodeling process. Both of these things greatly influence the bone density process, IL-1β plays a role in inflammatory cells at the bone resorption stage, while BMP-2 induces the formation of osteoblast cells (Sukmana, Budhy, & Ardani, 2017).

Research by Sok Wong et al., (2020) shows that the quercetin compound can increase new bone formation and reports that this compound is osteogenic or has great potential in increasing bone formation. The alveolar bone remodeling process has an important role in preventing relapse after orthodontic treatment, as in research by Franzen et al., in their research with animals. Bone remodeling is controlled by osteoclast cells that absorb bone and osteoblast cells that produce new bone. Thus, relapse after orthodontic treatment can be prevented with activities that can inhibit bone resorption and stimulate bone formation (Auliadini & Pakpahan, 2024).

Rosella (Hibiscus sabdariffa L.) is an herbal plant that has the potential to treat bone damage because of its anti-inflammatory and antibacterial effects. Specific elements in rosella make it very beneficial for human health, including anthocyanins, polyphenols, niacin, riboflavin, ascorbic acid, calcium, iron, potassium, and magnesium. Rosella also contains delphinidin-3-sambubioside, which can reduce the production of inflammatory mediators, and inhibit osteoclastogenesis. The antibacterial properties of Rosella imply that it can prevent plaque formation, which is the main etiology of bone damage (Idrus et al., 2020).

4.1. Characteristics and Analysis of Flavonoids

Flavonoids, tannins, and quercetin are bioactive compounds with significant roles in supporting bone remodeling processes, including preventing relapse after orthodontic treatment. These components work through complex mechanisms involving the regulation of bone cells, such as osteoblasts and osteoclasts, as well as growth mediators like transforming growth factor-beta (TGF-β) and bone morphogenetic protein-2 (BMP-2). Below is a detailed explanation of the characteristics of each compound based on research studies:

Regulation of Estrogen Receptors: According to Sherman Salim & Mefina Kuntjoro (2015), flavonoids enhance estrogen receptor activity, which is essential in supporting osteoblast differentiation into osteocytes. Estrogen receptors play a protective role in bone by reducing bone resorption and promoting new bone formation.

Induction of TGF-β: Flavonoids stimulate the release of TGF-β, which functions to promote osteoblast proliferation, accelerate mineralization, and strengthen the bone matrix. Antioxidant Activity: The antioxidant properties of flavonoids help reduce oxidative stress, a common contributor to bone resorption. Transforming Growth Factor Beta (TGF-β) is a family of multifunctional cytokines that play a critical role in regulating various biological processes, including bone formation, tissue remodeling, immunomodulation, and cellular regeneration. This protein is found in nearly all human tissues and acts as a signaling molecule that ensures balance between tissue damage and new tissue formation. In the context of bone, TGF-β is highly significant for bone homeostasis, new bone formation, and healing after injury. TGF-β is produced by various cell types, such as osteoblasts (bone-forming cells), fibroblasts, and immune cells. Initially, TGF-β is synthesized in an inactive form (latent) and is later activated by protease enzymes or interactions with extracellular matrix (ECM) components. Once activated, TGF-β binds to specific receptors on the cell surface to initiate signal transduction. TGF-β is a multifunctional cytokine that plays a vital role in various biological processes, particularly in bone formation and remodeling. It promotes osteoblast proliferation and differentiation, regulates osteoclast activity, and accelerates mineralization. Its anti-inflammatory and immunomodulatory activities also contribute to systemic balance during tissue regeneration. An imbalance in TGF-β activity can lead to conditions such as osteoporosis, fibrosis, or chronic inflammation, highlighting the importance of proper regulation in the body. As a therapeutic target, TGF-β offers significant potential in applications related to bone healing and immunotherapy. Its use in biomaterials and growth factor combinations is particularly promising for enhancing bone regeneration and preventing bone-related diseases (Halloran et al., 2020).

4.2. Characteristics and Analysis of Tannins

Bone health plays a fundamental role in maintaining the structural integrity and functionality of the human body. The continuous process of bone remodeling, involving the resorption of old bone and the formation of new bone, is a dynamic equilibrium essential for preserving bone strength and repairing damage caused by injury or disease. However, disruptions in this balance, often due to aging, inflammation, or other systemic factors, can lead to conditions such as osteoporosis or delayed bone healing. As a result, understanding the molecular and biochemical pathways involved in bone remodeling has become a critical area of research. Tannins, as phenolic compounds, contribute to bone repair through the following mechanisms:

Reduction of IL-1β Expression: Sukmana et al. (2017) reported that tannins exhibit anti-inflammatory effects by suppressing IL-1β, a pro-inflammatory cytokine released by immune cells during the bone resorption phase. Reducing IL-1β levels helps decrease osteoclast activity, thereby inhibiting bone degradation.

Enhancement of BMP-2: Tannins increase BMP-2 expression, which is critical for osteogenesis. BMP-2 promotes the differentiation of osteoblast precursor cells into mature osteoblasts, essential for forming new bone tissue (Liu et al., 2024).

4.2.1. Reduction of IL-1β Expression

Interleukin-1 beta (IL-1β) is a pro-inflammatory cytokine produced primarily by activated macrophages and other immune cells. It is a potent mediator of inflammation and plays a critical role in the bone resorption phase of bone remodeling. IL-1β acts by stimulating osteoclastogenesis—the differentiation and activation of osteoclasts, the cells responsible for bone resorption. Osteoclasts degrade the mineralized matrix of bone tissue by secreting acidic substances and enzymes such as cathepsin K and matrix metalloproteinases (MMPs). In chronic conditions such as osteoporosis or inflammatory diseases, elevated IL-1β levels result in excessive osteoclast activity, leading to bone loss and weakening. Tannins, as phenolic compounds, have been shown to suppress IL-1β production, thus reducing the inflammatory response. By inhibiting IL-1β expression, tannins reduce osteoclast activity and therefore inhibit excessive bone resorption. This suppression of IL-1β not only diminishes bone degradation but also helps to limit the inflammatory milieu that contributes to bone diseases like osteoarthritis and rheumatoid arthritis, where chronic inflammation disrupts bone homeostasis. Studies by Sukmana et al. (2017) demonstrate that tannins reduce the expression of IL-1β in experimental models, thereby contributing to a more balanced bone remodeling process (Liu et al., 2024).

4.2.2. Enhancement of BMP-2 Expression

Bone morphogenetic proteins (BMPs) are a family of growth factors within the Transforming Growth Factor Beta (TGF-β) superfamily, known for their critical role in bone formation. BMP-2, in particular, is a key osteogenic factor that promotes the differentiation of mesenchymal stem cells (MSCs) into osteoblasts, the cells responsible for new bone formation. BMP-2 activates several intracellular signaling pathways, particularly the Smad and non-Smad pathways, leading to the transcriptional activation of genes like RUNX2 (Runt-related transcription factor 2), which is essential for osteoblast differentiation. Tannins enhance the expression of BMP-2, promoting osteoblast differentiation and proliferation. By upregulating BMP-2 levels, tannins facilitate the transition of progenitor cells into fully differentiated osteoblasts, thereby stimulating the formation of new bone tissue. This mechanism is particularly important in the repair of bone fractures or during periods of increased bone turnover, such as in osteoporosis. Moreover, BMP-2's involvement in osteoblastogenesis ensures that bone tissue is properly regenerated and mineralized. Therefore, tannins can contribute significantly to accelerating bone healing and improving bone density by promoting osteogenesis. tannins contribute to bone repair and remodeling through their ability to suppress inflammatory cytokines like IL-1β and enhance the osteogenic factor BMP-2. By modulating these key biological pathways, tannins help regulate the balance between bone resorption and formation, promoting bone health and accelerating healing processes. These findings suggest that tannins may hold therapeutic potential for conditions involving bone loss and impaired bone regeneration, such as osteoporosis, arthritis, and fracture healing (de Oliveira et al., 2024).

4.3. Characteristics and Analysis of Quercetin

Quercetin is a flavonoid compound found in various plants, including roselle, and has been extensively studied for its potential in bone health. Recent research indicates that quercetin can significantly influence bone remodeling through several mechanisms. These include promoting osteoblast activity, inhibiting osteoclastogenesis, and providing antioxidant and anti-inflammatory benefits, making it a promising candidate for therapies aimed at improving bone density and preventing bone loss (Liu et al., 2024).

4.3.1. Promotion of New Bone Formation

Quercetin’s osteogenic potential has been highlighted in multiple studies. Research by Sok Wong et al. (2020) demonstrates that quercetin promotes new bone formation by increasing the activity of osteoblasts, the cells responsible for bone formation. Osteoblasts secrete the extracellular matrix, which is then mineralized to form new bone tissue. Quercetin has been shown to enhance the differentiation and proliferation of osteoblast precursor cells, thus accelerating the formation of bone tissue. By stimulating osteoblast function, quercetin can support bone regeneration, particularly in conditions where bone repair is compromised, such as fractures or osteoporosis. The osteogenic effects of quercetin are partly attributed to its ability to modulate several signaling pathways involved in bone formation. For instance, quercetin can increase the expression of bone-related genes such as osteocalcin and collagen type I, which are essential for bone matrix synthesis and mineralization. Additionally, quercetin can activate the Wnt/β-catenin signaling pathway, a critical regulator of osteoblast differentiation and bone formation (de Oliveira et al., 2024).

4.3.2. Anti-Osteoclastogenesis Effects

Osteoclasts are the cells responsible for bone resorption, and their excessive activity can lead to bone loss. Quercetin has been shown to inhibit osteoclast formation and activity, providing an anti-resorptive effect on bone tissue. One of the primary mechanisms through which quercetin achieves this is by modulating the receptor activator of nuclear factor kappa-B ligand (RANKL)/osteoprotegerin (OPG) pathway. RANKL is a cytokine that binds to the RANK receptor on osteoclast precursors, promoting their differentiation into mature osteoclasts, which then resorb bone. On the other hand, OPG acts as a decoy receptor for RANKL, preventing it from binding to RANK and thus inhibiting osteoclastogenesis. Quercetin has been shown to reduce the expression of RANKL and increase the production of OPG, resulting in a reduction of osteoclast activity and bone resorption. This dual effect—promoting osteoblast activity while suppressing osteoclastogenesis—helps to maintain a healthy balance between bone formation and resorption. By inhibiting osteoclast activity and promoting osteoblast function, quercetin contributes to bone density maintenance and reduces the risk of bone loss in conditions like osteoporosis, where osteoclast activity is typically elevated (Jing Li, Xuxia Wang, Yingzi Wang, Chengyan Lu, Dehua Zheng, 2019).

4.3.3. Antioxidant and Anti-inflammatory Effects

Quercetin is a potent antioxidant that helps protect bone tissue from oxidative damage caused by free radicals. Oxidative stress plays a significant role in bone degradation by impairing the function of osteoblasts and promoting the activity of osteoclasts. In addition to its antioxidant properties, quercetin also exerts strong anti-inflammatory effects. Chronic inflammation is a key factor in various bone diseases, as pro-inflammatory cytokines like IL-1β and TNF-α can stimulate osteoclastogenesis and suppress osteoblast activity. Quercetin reduces the expression of these pro-inflammatory cytokines, thereby mitigating the inflammatory response in bone tissue. The anti-inflammatory effects of quercetin are especially relevant in conditions such as rheumatoid arthritis or osteoarthritis, where excessive inflammation leads to joint and bone degradation. By reducing inflammation and oxidative stress, quercetin helps to protect bone tissue from damage and supports the regenerative process. Quercetin’s multifaceted role in bone health makes it a promising candidate for therapeutic applications aimed at bone regeneration and maintenance. Through its ability to promote osteoblast activity, inhibit osteoclastogenesis, and protect against oxidative stress and inflammation, quercetin can support the balance between bone formation and resorption, which is essential for maintaining bone integrity and treating conditions like osteoporosis, fractures, and bone-related inflammation. Its potential to improve outcomes in orthodontic treatments further underscores its utility in clinical bone health management (Jing Li, Xuxia Wang, Yingzi Wang, Chengyan Lu, Dehua Zheng, 2019).

CONCLUSION

The results obtained in this study indicate that flavonoid extracts from Hibiscus sabdariffa L. flowers have the potential activity in improving the healing process of bone damage.

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