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Alpha-Mangostin As Potent Osteogenesis And Anti-Inflammation Bioactive Material - Literature Review

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ABSTRACT

Mangosteen or Garcinia mangostana is one of the most widely grown plants in Indonesia. Many studies say that this fruit has a high antioxidant content, especially alpha-mangostin, and is widely used as a therapeutic drug. The purpose of this paper is to speak about the capacity of α-mangostin as a bioactive ingredient for anti-inflammatory and osteogenesis triggers, which is greater specific to be used for growth, bone regeneration, and wound recuperation. Literature observation is a research technique conducted via examining 18 previous studies concerning the phytochemical analysis of mangosteen peel: purposeful and fitness advantages. The outcomes of the literature evaluation defined that α-mangostin from mangosteen peel has been proven to have numerous pharmacological effects along with antioxidant anti-inflammatory. The ability of α-mangostin as a bioactive component for anti-inflammatory and triggering osteogenesis can be visible especially from bone regeneration wherein α-mangostin can cause bone recovery through the present process of a regeneration system via osteoclast absorption pastime, to hold bone high-quality. Furthermore, in terms of wound recuperation, α- mangostin in xanthones can lessen irritation or accelerate wound restoration with the absorption of mangostin and an increase in oxygen absorbance, as a result affecting the digestive gadget and renewing problematic cells or antioxidant system.

Keywords: antioxidant, α-mangostin, osteogenesis, inflammation, medicine.

INTRODUCTION

Inflammation is a defense response in the body against foreign body invasion and tissue damage or both. The causes of inflammation include microorganisms, mechanical trauma, chemical substances, and physical influences, symptoms of the anti-inflammatory response

include rubor (redness), calor (heat), dolor (pain), and tumor (swelling). Inflammation is the body's response to harmful stimuli caused by various harmful agents such as infection, antibodies, or physical injury.[1] Treatment of patients with inflammation is generally to slow or limit the process of tissue damage that occurs in the area of inflammation.[2] Modern drugs are generally used for anti-inflammatory drugs, namely non-steroidal anti-inflammatory drugs (NSAIDs), however, they have side effects that are detrimental to the body such as stomach ulcers. Furthermore, various treatment developments look at alternative ways by minimizing the impact of damage to gastric ulcers, namely anti-inflammatory drugs that can be used orally or topically at the site of inflammation.[3]

Alpha-mangostin, a natural xanthonoid as secondary metabolite derived from the pericarp, dried sap, and bark of mangosteen (Garcinia mangostana), has been widely used in Asian conventional medicine.[4] Previously, numerous studies have demonstrated a variety of pharmacological activities of α-mangostin, including antimicrobial, anti-inflammatory, antioxidant, anti-aging, anticarcinogenic, anti-obesity, neuroprotective, and cardioprotective.[5] The content of α-mangostin in mangosteen peel is known to inhibit the cyclooxygenase activity pathway (COX-2) and can lower the level of Prostaglandin E (PGE).[6]

Phytochemical studies display that antioxidant compounds in mangosteen peel, mainly xanthones, anthocyanins, and other companies of phenolic compounds, have useful residences and fitness benefits such as anti-diabetic, anti-cancer, anti-inflammatory, immune-boosting, antibacterial, antifungal, antiplasmodial, and so on. Xanthones are reported to have pharmacological activity as anti-bacterial, anti-fungal, anti-inflammatory, anti-platelet aggregation, besides that xanthones can stimulate the central nervous system and have anti-tuberculosis in vitro against Mycobacterium tuberculosis bacteria.[2,4]

According to Chen et al. (2018), it is known that the peel of mangosteen fruit contains active compounds belonging to the xanthone group, namely substances formed from the isolation of the mangosteen peel, and the levels reached about 123.97 mg per ml. The chemical content of mangosteen peel is Xanthones, mangostin, garsinone, flavonoids, epicatechin, and tannins.[7] Research on xanthones has been started in 1970 and until now more than 40 types of xanthones have been found, including α-mangostin and γ-mangostin which are believed to have the ability to prevent various diseases including anti-inflammatory. That both types of xanthones can help prevent infection by inhibiting the production of the COX-2 enzyme that reasons inflammation.[8]

Other studies have proven that γ-mangostin has a better anti-inflammatory impact than different anti-inflammatory capsules sold within the marketplace.[5,9] This type of xanthone can protect you from a variety of infections, including arthritis and Alzheimer's disease, which is a brain illness. Xanthones can also help prevent cancer cells and tumors from growing. Its antioxidant potential is considerably greater than that of the most powerful antioxidants, vitamins C and E. The content of α-mangostin and γ-mangostin in the mangosteen fruit is likewise antibacterial.[8] The α-mangostin is likewise recognized to have the same effect as antibiotics in the marketplace consisting of ampicillin and minocycline.[6]

Research by Widowati et al. (2016) revealed that mangosteen is abundant in an outstanding nutrient known as xanthones, which are found in abundance in the pericarp. The pericarp makes up 70-75% of the xanthones, whereas the pulp makes up just 10-15% and the

seeds make up 15-20%.[1] The highest content of xanthones is found in the mangosteen peel, which is 107.76 mg per 100 g of the peel.[8] The purpose of this paper is to discuss the potential of α-mangostin as a bioactive ingredient for anti-inflammatory and osteogenesis triggers, which is more specific for use for growth, bone regeneration and wound healing.

RESEARCH METHOD

The research approach used is a literature study. Literature look at is a research technique performed via examining 18 preceding research concerning the capability of α-mangostin as a bioactive element for anti-inflammatory and osteogenesis triggers.

DISCUSSION

Phytochemicals of Mangosteen Peel and Fruit

Mangosteen (Garciana mangostana) is a functional plant because most of these plants can be used as medicine. Apart from its delicious taste, mangosteen flesh can treat diarrhea, tonsillitis, vaginal discharge, dysentery, hemorrhoids, inflammation, and toothache.[10] In addition to the mangosteen, the community has also used the pericarp of the mangosteen as medicine for cancer sores, dysentery, diarrhea, gout, natural dyes, and materials for making anti-rust paint.[8] Mangosteen peel has anti-aging properties, lowers high blood pressure, loses weight, has antiviral and antibacterial properties. Mangosteen bark is also used to treat abdominal pain, while the roots are used to treat irregular menstruation.[5,7,11,12]

According to research by Bumrungpert et al. (2010) indicate that there are compounds contained in the mangosteen peel, namely xanthones which include mangostin, mangosterol, mangostinon α and β, trapezifolixanthone, tovophyllin B, and α and β mangostin, garcinon β, mangostanol, flavonoid epicatechin, and gartanin. The xanthone compounds in the mangosteen peel are high levels of antioxidants, therefore xanthones are needed in the body as a pro-oxidant balancer, such as oxidizing radicals, carbon centered, UV rays, metal, and so on. Xanthones can bind unstable free oxygen, namely free radicals that destroy cells in the body so that xanthones can inhibit the process of cell degeneration (damage).[3] Xanthones also stimulate the regeneration (recovery) of damaged body cells quickly so that they stay young. Xanthones compounds have the ability as an antioxidant, antibacterial, antifungal, anti-inflammatory, bacteria can inhibit the growth of Mycobacterium tuberculosis bacteria and can increase immunity and maintain heart health. Now there is a lot of mangosteen peel extract production, so we can easily find mangosteen peel and fruit extracts.[5]

Xanthones are compounds in the mangosteen peel that function as anti-functions consisting of mangostin and its derivatives. Xanthones can be isolated from the pericarp, fruit, and leaves of the mangosteen. Xanthones are widely distributed in tall plants, ferns, fungi, and mosses. Most of the xanthones found in higher plants can be isolated from four families, namely, Guttiferae, Moraceae, Polygalaceae, and Gentianaceae. Xanthones are one of the minor flavonoids that have a color reaction and chromatographic movement similar to those of other flavonoids. α-mangostin and γ-mangostin is a Xanthone derivative whose most abundant content is found in mangosteen and is reported to have anti-inflammatory effects.

α-mangostin is the main component (78% content) and has been used worldwide as a traditional medicine for its anti-inflammatory, antibacterial, and anticancer effects.[3]

Flavonoids are a set of phenolic compounds that will be predisposed to bind to proteins, thereby disrupting metabolic processes. Flavonoids are herbal phenolic compounds that have the ability as antioxidants and have bioactivity as pills. Pigments/dyes found in plants such as red, purple, blue, yellow, and green dyes are classified as flavonoid compounds. Flavonoids in the human body function as antioxidants so they are very good for cancer prevention.[9] Alpha-mangostin is a compound that is very efficacious in suppressing the formation of carcinogenic compounds in the colon. In addition to α-mangostin, xanthone compounds also contain γ-mangostin which also has many benefits in providing protection or making efforts to prevent disease.[13]

Anthocyanins have the ability as good antioxidants and have an important role in preventing several diseases such as cancer, diabetes, cardiovascular, and neuronal.[8] Anthocyanins are a group of pigments found in plants and are usually found in flowers, vegetables, and fruits such as mangosteen, strawberry, raspberry, apple, and others. Saponins are active substances that can increase membrane permeability so that cell hemolysis occurs. If saponins interact with bacterial cells or fungal cells, the bacteria will be damaged or lysed.[11]

Alpha-mangostin

Alpha-mangostin (α-mangostin) is a xanthone derivative compound with a chemical name (1,3,6 – trihydroxy – 7 – methoxy – 2, 8 – bis (3 methyl – 2 – butenyl) – 9H-xanten-9-0n), and a secondary metabolite compound isolated from mangosteen peel extract.[4] Alpha- mangostin has been shown to have various pharmacological effects including antioxidant, anti-inflammatory, anti-pain, anti-allergic, antifungal, antibacterial, anti-obesity, antiparasitic, anti-tuberculosis, Alzheimer's, can improve the immune system, and as anti-cancer.[9] Alpha-Mangostin is one of the most successful compounds found as a candidate for new anticancer and anti-inflammatory drugs.[4]

Potential of α-mangostin as Bioactive Ingredients for Anti-Inflammation and Trigger Osteogenesis

Alpha-mangostin on Bone Regeneration

Mangosteen (Garcinia mangostana) is a plant that has potential as a medicine. Potential especially in the skin of the mangosteen fruit. The use of mangosteen peel is traditionally used for the treatment of canker sores, dysentery, cystitis, diarrhea, gonorrhea, and eczema.[14] Furthermore, Widowati, et al. (2016) stated that the mangosteen peel can provide pharmacological effects such as antioxidant, antifungal, antibacterial, and anticancer. These pharmacological effects are related to the content of chemical compounds. The main bioactive compounds and the major compounds of xanthone derivatives contained in the mangosteen peel are α-mangostin. The compound α-mangostin in the form of a yellow substance, insoluble in water, soluble in methanol, ethanol, ether, acetone, ethyl acetate, and chloroform.[1]

The pericarp (hull) of Garcinia mangostana is a rich source of mangostin, which exhibits various pharmacological effects and biological activities.[5] Mangosteen peel and fruit are used as dyes, including for textiles, and boiled water is used as a traditional medicine to treat dysentery. Meanwhile, in Thailand, mangosteen peel has become a traditional herb for generations to treat skin infections, wounds, and diarrhea. Even in developed countries such as the United States, extracts from mangosteen peel have become a dietary supplement recommended by the Food and Drug Administration (FDA) United States Government because of its potential as an antioxidant, it has even been widely used as an anti-cancer, anti-inflammatory, and anti-microbial.[11]

Mangosteen has been used for loads of years around the sector, often in Southeast Asia[15] as a treatment for important ailments of numerous ailments. Some of the researches have shown that distinctive components of the extract contain sorts of secondary metabolites together with prenylated and oxygenated xanthones. Xanthones as the main bioactive secondary metabolites are stated to have many pharmacological sports inclusive of antioxidant, antifungal, antibacterial, cytotoxic, anti-inflammatory, antihistamine, anti-HIV, antimalarial, and different sports.[1]

Studies at macrophage cells proved that α-mangostin can reduce nitric oxide production and inhibit inflammation. Treatment with Garcinia mangostana extract resulted in a sizable reduction of bone erosion and osteoclast floor region. Further, LPS-infected calvarial bone turned into administered with α-mangostin in two concentrations (250 and 125μg/ml) also confirmed a large reduction of bone breakdown in comparison to controls. Moreover, a probable mechanism of osteoclast by utilizing Garcinia mangostana extract and α-mangostin may also act through several pathways.[16]

Osteogenesis is bone cells that live and contribute to the process of bone remodeling (bone cell maturation). Osteogenesis occurs when active osteoblasts derived from bone graft material contribute to the growth of new bone along with the resulting bone growth through two other mechanisms (osteoconductive and osteoinduction). The bone healing process after a fracture has many similarities to the skin healing process, except for the classification process of the connective tissue matrix. Bone is a tissue that has special features in its healing process, where bone heals by undergoing a regeneration process rather than a repair process.[16]

Osteoclast bone resorption is activated via inflammatory stimuli, proven in numerous inflammatory illnesses accompanied by way of arise in the quantity and activity of osteoclasts. In a preceding study, the compound α-mangostin showed its effectiveness as an inflammatory disease drug through inhibiting nitric oxide manufacturing, TNF-α, and IL-8 secretion in numerous cellular lines.[13] According to this theory, α-mangostin may also have bone repair properties that fit the rational pharmacy standard for acquiring bone recovery features triggered by an increase in TGF-β1 and followed by a significant increase in bone quantity.[16]

Idrus & Kiswanjaya (2016) additionally described the therapeutic effect of extracts of Garcinia mangostana which function as traditional medicines against the exceptional resorption of the old osteoclasts which therefore can preserve bone best.[13] Lestari et al. (2021) determined that mangostin can result in a growth in TGF-β1 titer, that's in line with a boom inside the mandibular bone quantity of Rattus norvegicus. The boom in bone extent corresponds to the formation of the latest bone which starts to evolve with depletion of the

osteoid role. Horiba et al (2014) explained that α-mangostin can stimulate muscle cell development by way of blockading the myostatin signaling pathway and regenerating new bone tissue.[16]

Alpha-mangostin additionally attenuates LPS-mediated irritation in M and insulin resistance in adipocytes, probable utilizing stopping the activation of MAPK, NF-κβ, and AP-1, which can be imperative to inflammatory cytokine manufacturing. aggregate induction from mangosteen peel extracts and demineralized freeze-dried bovine bone xenograft is powerful in reducing inflammation, reducing osteoclasts, reducing alveolar bone resorption, and also increasing the activity of bone morphogenetic protein-2 and alveolar bone regeneration.[10]

Alpha-mangostin on Wound Healing

Overall, this review describes the many benefits of mangosteen extract compounds in the fields of medicine and health that are utilized and are currently trending, even used in various studies.[8] Mangosteen peel extract is also known as a high source of antioxidants that can scavenge free radicals, induce antioxidant enzymes (increase antioxidant capacity) for reperfusion so that it can be anti-inflammatory and prevent injury.[15]

Widowati, et al. (2016) and Zhang et al. (2021) discovered that Garcinia mangostana peel extract has anti-inflammatory capacity via inhibiting COX-2, IL-6, IL-1β, and NO. This extract may have a healing capacity for the modulation and regulation of macrophage activation and may provide a safe and effective remedy choice for various anti-inflammatory diseases.[1,9]

Infection is a normal protective reaction to tissue damage that involves enzyme activation, the release of mediators, extracellular fluid, cellular migration, tissue damage, and repair.[9] Irritation is a complex procedure this is frequently associated with pain and involves activities that include accelerated vascular permeability, expanded protein, and membrane denaturation. The inflammatory process if left untreated can lead to diseases such as vasomotor rhinorrhoea, rheumatoid arthritis, and atherosclerosis.[4] Furthermore, it is important to understand the role of chemical mediators or reactions that tend to direct the inflammatory response. Various studies have reported that protein denaturation is one of the causes of inflammation. Auto-antigens produced in inflammatory disease may be responsible for protein denaturation. Auto-antigen production in several rheumatoid arthritis may be due to protein denaturation in vivo.[5] The mechanism of protein denaturation occurs through changes in electrostatic, hydrogen, hydrophobic, and disulfide bonds.

The anti-inflammatory bioactivity of xanthone derivatives itself has been proven from several research results that have a healing effect on inflammation. Activity test of prenylated xanthone derivatives from mangosteen peel against Mycobacterium tuberculosis. Among the xanthone-derived compounds, α-mangostin, β-mangostin and garsinon B have high inhibitory power with a MIC (Minimum Inhibitory Concentration) value of 6.25 g/ml, while demethy lcalabasanthone and trapezifolisanthone have a MIC value of 12.5 g/ml, meanwhile γ-mangostin, garsinon D, mangostanin, mangostenon A and topovilin B MIC value 25 g/ml.[16]

Furthermore, α-mangostin and β- mangostin had been found to attenuate LPS-precipitated irritation of the TNF-, IL-1β, IL-6, IL-eight, MCP-1, and Toll-like receptor-2 genes. Impact of G. mangostana and its compounds in opposition to irritation caused by

Propionibacterium acnes thru suppression of seasoned-anti-inflammatory cytokines. G. mangostana and its compounds have extraordinary potential inside the remedy and prevention of rheumatoid arthritis, an anti-inflammatory persistent disease, verified via inhibition of TNF-α and IL-6 manufacturing in LPS-inspired mice, reduce of leg edema in carrageenan-triggered rats, and reduction of arthritis ratings in the mouse. This research reveals that α-mangostin and β-mangostin have anti-inflammatory capacity by inhibiting COX-2, IL-6, IL-1β, and NO. These compounds may have the therapeutic capability for the modulation and regulation of macrophage activation and may offer a secure and effective treatment option for numerous irritation-mediated diseases.[1]

Mangostin has been said to have anti-inflammatory action. The principal bioactive components found within the mangosteen peel are xanthones and α-mangostin. On the synthesis of anti-inflammatory mediators in the LPS-brought 264.7 cell line as a model. In the presence of GMPE concentrations, cytotoxic testing was performed to determine the safe and non-poisonous line, which was supplemented by assessing the metallic content material included inside the GMPE. The existence of greater than 90% mobile viability was used to validate the nontoxicity of the substrate using the MTS test. Mangosteen and propolis extracts are both safe herbal items with no cytotoxicity when used against hTERT-hNOF cells. In vitro, a mixture of 1 lg/ml mangosteen extract and 34 lg/ml propolis extract could be very effective as an anti-inflammatory and as a bone formation and irritation healing agent. These findings suggest that a mixture of mangosteen extracts and propolis may be effective in the prevention and treatment of periodontal disease.[2]

Furthermore, Bumrungpert et al. (2010) found that rat glioma cells, human adipocytes, and mice can be treated with human MF and α-mangostin to reduce inflammation. When the experiment was carried out, the experimental subjects were given a blend of mangosteen juice containing α-mangostin, which lowered the levels of C-reactive protein, influencing biomarkers of inflammation and obesity issues that the patients had. In healthy individuals, ingesting a xanthone-rich mangostin drink containing 100 mg/L of α-mangostin elevates the plasma concentration of α-mangostin to 0.1 mmol/L after 1 hour. The absorption of α-mangostin increased with dose and was linked to an increase in oxygen radical absorbance capacity, which was further studied using a digestive system simulation.[3]

Xanthones are digested and incorporated into micelles within the intestinal lumen, according to the findings Bumrungpert et al. (2010). They are then absorbed by enterocytes, incorporated into chylomicrons, transported across the basolateral membrane, and distributed to peripheral organs. Alpha-mangostin, on the other hand, can be converted to a conjugated form and then delivered peripherally through section I-II enzymes. In basic terms, the absorption of mangostin and growth oxygen absorption by α-mangostin in xanthones can reduce inflammation or damage, impacting the digestive system and regenerating difficult cells or tissues (antioxidant technique).[3]

Another study shows that α-mangostin protects mice from DMBA/TPA-caused skin tumorigenesis by suppressing infection.[4] The compound α-mangostin has anti-inflammatory activity via inhibiting the manufacturing of nitric oxide, TNF-α, and IL-8 secretion recognized to motivate bone resorption and inhibit bone formation.[2] Among the several types of xanthones, alpha-mangostin was identified to be the major xanthone found in Garcinia mangostana. A

large study of the role of α-mangostin in cellular metabolism revealed that this xanthone is anti-inflammatory, anticancer, inducer of apoptosis, and anti-proliferative in the majority of cancer cells.[16]

Mangosteen peel also can be used to produce elevated antimicrobial pastime, which can be used for advanced remedy in orthopedics to deal with wound infections and operations resulting from microorganisms where mangosteen extract is used as a hydroxyapatite layer (HAp). MG-coated HAp granules inhibited bacterial growth, ensuing inside the highest region of inhibition for all examined microorganisms, particularly gram-tremendous microorganisms.[12]

Ioyah et al. (2019) additionally introduced the use of mangosteen peel extract at a dose of 40 mg/kg multiplied fracture healing. After a fracture, the genuine bone starts to self-healing in 5 fundamental levels. during the hematoma phase, phagocytic cells, along with neutrophils, enter the fracture area and convey free radicals consisting of nitric oxide, which modulate fracture recovery. However, if the amount isn't always supplied as desired, these free radicals have been demonstrated to hinder or even impair the wound healing process in cartilage.[17]

A recent study found that the xanthone in mangosteen peel extract can protect from free radical damage, which is comparable to the role nutrition vitamin C can play in the right quantities. As a result, this study looked at the antioxidant effect of mangosteen peel extract on rat femur fracture defects. The effects confirmed that management of mangosteen peel extract in small doses of 20 mg/kg and 40 mg/kg still inhibited bone recovery, although no longer considered, due to the fact the diameter of the defect inside the thigh bone had to be handled with twice the dose better than the femur treated with salt. The characteristic of compounds that may cause unfastened radicals, such as nitric oxide, is sincerely wanted within the bone recuperation technique. thus, the entire recovery calls for suitable antioxidants. Mangosteen peel is understood to have robust antioxidant homes and has been predicted to boost up the wound healing manner.[18] However with the management of excessive doses with a purpose to boost up the preferred healing.[17]

According to the literature review above, it can be explained that the various compounds contained in the mangosteen fruit broadly have various benefits that can be useful for human health, including as a trigger for bone regeneration and healing wound inflammation. It is recommended that further research be able to reveal the benefits in detail regarding tissues or compounds that inhibit bone regeneration and wound healing even though using mangosteen extract so that it is known how to overcome these obstacles more clearly.

CONCLUSSION

The potential of α-mangostin as a bioactive ingredient for anti-inflammatory and triggering osteogenesis can be seen in particular from bone regeneration where α-mangostin can trigger bone healing by undergoing a regeneration process through osteoclast absorption activity, to maintain bone quality. Alpha-mangostin is also able to stimulate the development of muscle cells so that they can regenerate new bone tissue. Additionally, it also has a potential

therapeutic value in the treatment of osteoarthritis in cases of osteogenesis by attenuating degeneration.

Furthermore, in terms of wound healing, α-mangostin can reduce inflammation or accelerate wound healing with the absorption of mangostin and an increase in oxygen absorption, thereby affecting the digestive system and renewing problematic cells or tissues (antioxidant process). Antioxidants in α-mangostin have been predicted to accelerate the wound healing process, but with the administration of high doses to accelerate the desired healing.

ETHICAL CLEARENCE : nil

SOURCE OF FUNDING : self

CONFLICT OF INTEREST : nil

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