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The Potential of Anthocyanin on Osteoporosis

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ABSTRACT
Osteoporosis is a chronic disease commonly associated with menopause, primarily triggered by estrogen deficiency, oxidative stress, and inflammatory processes. These factors contribute to bone density loss, increasing the risk of fractures and reduced quality of life. This study aims to investigate the potential of anthocyanins, natural compounds found in various plants, in preventing osteoporosis by mitigating oxidative stress and promoting bone health. A comprehensive literature review was conducted by searching multiple scientific databases for relevant studies on the effects of anthocyanins on bone health. The selection criteria included experimental and clinical studies focusing on the antioxidant and bone-regulating properties of anthocyanins. The findings reveal that anthocyanins possess significant antioxidant properties that help reduce oxidative stress by lowering malondialdehyde (MDA) activity and increasing superoxide dismutase (SOD) activity. Additionally, anthocyanins promote bone formation by increasing the number of osteoblasts while decreasing the number of osteoclasts in animal models of menopause-induced osteoporosis. Anthocyanins hold potential as a natural therapeutic agent for preventing osteoporosis, particularly in menopausal women. Their antioxidant and bone-regulatory effects could complement existing osteoporosis prevention strategies, offering a safer and more natural approach to maintaining bone health.

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INTRODUCTION

Biologically, every woman experiences the aging process, involving various physiological changes. The transition from a reproductive to a post-reproductive state is known as menopause (Santoro et al., 2021). One of the chronic diseases associated with menopause, with high morbidity, disability, and mortality rates, is osteoporosis. Osteoporosis is characterized by weakened bone tissue, compromised structure, and reduced bone strength, increasing the risk of fractures (Sarafrazi et al., 2021). In menopausal women, estrogen deficiency is a major factor contributing to osteoporosis. Estrogen plays a crucial role in maintaining bone growth and homeostasis. Its reduction triggers increased production of reactive oxygen species (ROS), causing oxidative stress (Mohamad et al., 2020). This process is accompanied by elevated levels of pro-inflammatory cytokines such as interleukin (IL)-1, IL-6, and tumor necrosis factor-α (TNF-α), promoting bone loss and raising the risk of osteoporosis (Zhou et al., 2019).

Hormone replacement therapy (HRT) is commonly used to manage menopause-related symptoms and prevent osteoporosis by addressing estrogen deficiency (Kartika et al., 2021). However, concerns about the long-term safety of HRT, including risks of breast cancer, endometrial cancer, and ischemic stroke, have led to its restricted use (Cagnacci & Venier, 2019).

Given these concerns, alternative approaches such as using antioxidants have gained attention. Antioxidants help protect body cells from damage caused by free radicals (Denova-Gutiérrez et al., 2018). Phytochemicals with antioxidant properties, such as anthocyanins, are abundant in plants and have shown promising health benefits (Munteanu & Apetrei, 2021). Anthocyanins are easily absorbed

in the gastrointestinal tract and detected in plasma, urine, and tissues, making them valuable nutraceuticals for managing and preventing chronic diseases, including osteoporosis (Mao et al., 2021).

The purpose of this review is to explore the potential role of anthocyanins in osteoporosis prevention and treatment by compiling relevant research on their antioxidant and anti-inflammatory effects. Understanding these mechanisms can contribute to developing safer antioxidant-based therapies for osteoporosis, offering a promising alternative to conventional treatments.

METHOD

The research focused on peer-reviewed articles published between 2014 and 2024, sourced from databases such as Google Scholar, PubMed, Elsevier, and other reputable platforms. The search employed specific keywords, including "Anthocyanin," "Osteoporosis," "Menopause," and "Antioxidant," in both Indonesian and English. Inclusion criteria encompassed articles with relevant titles, abstracts, and full texts that aligned with the research objectives. Exclusion criteria involved studies lacking sufficient methodological detail or data reliability. A standard quality assessment tool, such as PRISMA for systematic reviews, was applied to enhance transparency and reproducibility. Data from selected studies were synthesized using thematic analysis to identify patterns, relationships, and key findings.

RESULT AND DISCUSSION

Anthocyanins are flavonoid-derived compounds that are naturally hydrophilic in red, purplish, blue, and black colors that can be found in plants. Some types of anthocyanins that are easily found are delfinidin, malvidin, peonidin, petunidin, and pelargonidin (Mattioli et al., 2020).

Anthocyanins are stable when in acidic conditions, and the potential level of hydrogen (pH) will also affect the color of anthocyanins. A reddish color tends to be in acidic pH conditions, while a more neutral and alkaline pH will be bluish in color (Ayvaz et al., 2022). Anthocyanins have the ability to reach the highest concentration in plasma within 30 minutes to two hours after consumption of anthocyanin-rich foods (Bendokas et al., 2020). In the first five minutes of oral exposure, anthocyanins will be absorbed and enter the blood plasma. However, when exposed to enzymatic reactions and high temperatures, it can cause anthocyanin levels to disappear by up to 50% (Ayvaz et al., 2022).

The remaining anthocyanins then enter the stomach to stabilize due to the low pH in the stomach (1.5-5.0), and a longer incubation time can increase the absorption rate of anthocyanins. The structure and molecular weight, as well as the presence of glucose transporter (GLUT)1 and GLUT3, are thought to aid the absorption of anthocyanins in the stomach. Anthocyanins will enter the small intestine, and absorption occurs in large quantities by active and passive diffusion to epithelial cells in the intestinal lumen. Absorption here requires the role of transporters, including sodium-glucose cotransporter-1 (SGLP-1). Afterward, anthocyanins enter the colon and undergo phase 1 and 2 metabolism by enzymes in the digestive tract, liver, and kidneys (Hornedo-Ortega et al., 2021).

There are several studies related to the effects of anthocyanins on the condition of osteoporosis in menopausal model rats. Previous studies have shown that the ethanol extract of red dragon fruit skin (Hylocereus polyrhizhus) at a dose of 60 mg/200 grBB/day can reduce kidney Malondialdehyde (MDA) levels in menopausal rats (Suta et al., 2022).

The results indicated that anthocyanin-rich extract from black rice (AEBR) dose-dependently decreased the blood glucose, increased the bone mineral density and decreased the serum bone turnover markers. The bone microstructure and osteoclast numbers in bone tissues returned to normal in the high AEBR dosage group; at the same time, the AEBR dose-dependently suppressed bone marrow adipogenesis (Qi et al., 2019).

The effects of Superjami rice bran extract on bone metabolism and antioxidant enzyme activity in ovariectomized rats, a model for postmenopausal osteoporosis. Findings indicate that supplementation with this rice bran extract significantly reduces bone turnover markers and oxidative stress indicators while enhancing antioxidant enzyme activities. The results suggest that Superjami rice bran extract may serve as a potential alternative for estrogen replacement therapy, helping to prevent bone loss and oxidative damage in postmenopausal women (Chung et al., 2021).

Black rice extract (BRE) stimulated the alkaline phosphatase activity, a marker for osteoblast differentiation. Black rice extract also promoted Alkaline phosphatase (ALP) activities in freshly isolated rat primary bone marrow cells. The reduced bone mineral density induced by ovariectomy was significantly protected by a daily dose of 200 mg kg−1 of BRE administration and increases in bone density. In addition, bone strength, measured by forces to induce fractures, was also decreased by ovariectomy (OVX), and BRE treatment at both doses recovered the OVX-induced weakness in bone strength (Jang et al., 2015).

The effects of petunidin, a B-ring 5′-O-methylated derivative of delphinidin, on bone health, particularly its role in osteoclast and osteoblast differentiation. Through in vitro and in vivo experiments, petunidin was shown to enhance osteoblast differentiation and mineralized matrix formation while inhibiting osteoclastogenesis, suggesting its potential as a natural alternative for preventing bone loss associated with osteoporosis. The research highlights the mechanisms by which petunidin promotes bone health, including the regulation of gene expression and the reduction of bone resorption markers (Nagaoka et al., 2019).

Oral administration of delphinidin can suppress the activity of NF-kB, c-fos, and Nfatc1, the main transcription factors for osteoclastogenesis. delphinidin is able to inhibit osteoclast differentiation most potently and will be effective in preventing bone loss in postmenopausal osteoporosis (Moriwaki et al., 2014).

Deoxypyridinoline (DPD) in 57 menopausal women, as a corrected urinary marker of bone resorption based on urine creatinine levels, showed significant changes ($p < 0.05$) in the raspberry treatment group. There was a significant reduction in the Raspberry intervention group from baseline to midpoint and baseline to final (Igwe, 2018).

Healthy female postmenopausal subjects (n=112) were recruited. The subjects were instructed to consume the DP in divided doses three times per day. DP were given at a dose equivalent to approximately 50g/day (six DP) or 100g/day (twelve DP) until 52 weeks. The impact of dried plum (DP) consumption on inflammatory mediators is of interest because it is possible that the immune system mediates the connection between DP consumption and improvements in BMD. In the context of bone health in postmenopausal women, modulation of monocyte cytokine secretion after one year of DP consumption could theoretically contribute to less osteoclastogenesis and higher BMD compared to postmenopausal women who did not consume DP (Van Every, 2021).

The effects of black current (BC) on bone mineral density (BMD), gut microbiota, and blood inflammatory and immune biomarkers were evaluated using DXA, stool, and fasting blood collected from a pilot three-arm, randomized, double-blind, placebo-controlled clinical trial. Fifty-one peri- and early postmenopausal women aged 45–60 years were randomly assigned into one of three treatment groups for 6 months. Daily BC consumption for 6 months mitigated bone loss in this population potentially through modulating the gut microbiota composition and suppressing osteoclastogenic cytokines (Nosal et al., 2024).

Anthocyanins, which act as antioxidants, can counteract free radicals and prevent oxidative stress (Tena et al., 2020), reduce MDA levels, increase Superoxide dismutase (SOD) levels and affect the increase in osteoblast cell activity and suppress the formation of osteoclast cells, thus preventing bone damage (Mao et al., 2021).

CONCLUSION

In conclusion, this study underscores the potential of anthocyanins in preventing osteoporosis. Key findings indicate that anthocyanins from various plants can act as powerful antioxidants, reducing free radical activity by lowering MDA levels and boosting SOD levels. Additionally, their role is supported by evidence of increased osteoblast activity and reduced osteoclast production in menopausal animal models. However, current research is limited by a lack of human clinical trials. Future research should focus on conducting well-designed clinical studies to determine optimal doses of anthocyanins for osteoporosis prevention, enhancing their applicability in managing osteoporosis in menopausal women.

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