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EFFECTIVENESS OF ROSELLA AS AN ANTI-INFLAMMATORY

Salsabila Putri Uno*
University of Prof. Dr. Moestopo (Beragama) Jakarta, Indonesia
Salsabila Sri Winaprilia
University of Prof. Dr. Moestopo (Beragama) Jakarta, Indonesia
Sekar Riandani Putri
University of Prof. Dr. Moestopo (Beragama) Jakarta, Indonesia
Evie Lamtiur Pakpahan
University of Prof. Dr. Moestopo (Beragama) Jakarta, Indonesia

*Correspondence: salsabilaputriuno2@gmail.com

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ABSTRACT

Rosella flower (Hibiscus sabdariffa L.) can be used in the health sector. Rosella petal extract contains flavonoids such as gossypetin, hibiscetin, sabdaretine, alkaloids, and saponins. Rosella has properties such as an antiseptic, diuretic, anti-inflammatory, antibacterial, antioxidant, and can increase endurance. This paper discusses the anti-inflammatory effect of the rosella plant. The purpose of this article is to describe the effectiveness of rosella plant as an anti-inflammatory. This article collects research results from journals, textbooks, and websites accessed through the National Library of Medicine and Google scholar databases as a method. The reference source inclusion criteria are published in 2012-2022 with topics that are in line with the effectiveness of rosella as an anti-inflammatory. The reference source exclusion criteria were literature published before 2012. A total of 25 references were found, 15 references were selected, and 10 references were excluded. The studies have shown that the content of rosella flower extract is able to inhibit the cyclooxygenase enzyme thereby inhibiting the synthesis of inflammatory mediators, namely leukotrienes and prostaglandins and reducing the number of neutrophils so that it can accelerate the wound healing process, however administration of high doses of rosella extract is less effective as an anti-inflammatory because the levels of flavonoids decreased activity at high extract concentrations.

INTRODUCTION

Inflammation is a broad and ancient medical term that has been used for centuries to describe a range of signs and symptoms associated with tissue damage or irritation. These signs include edema, which is the swelling of tissues due to fluid accumulation; erythema, or redness of the skin caused by increased blood flow; warmth, pain, and a loss of function, such as stiffness or immobility. Historically, inflammation was viewed as a relatively simple process, but modern medical science now recognizes it as a highly complex and dynamic response of the body to injury or infection. It is not only triggered by physical

trauma but can also be initiated by exposure to toxic chemicals, environmental irritants, overuse of muscles or joints, or infections caused by bacteria, viruses, or other pathogens. Some inflammatory responses are beneficial in wound healing and control of infections or pathologies such as in many chronic diseases. Various plants have been studied for their anti-inflammatory properties (Page & Stone WL, Basit H, 2022).

Humans have long relied on a variety of plants and fruits for the treatment and prevention of diseases, a practice that dates back to ancient times. This traditional use of plants has been well-documented across various cultures throughout history. According to Eni et al., as cited by Shallangwa et al. in 2017, the medicinal value of plants is recognized only when their biological activity has been substantiated either through ethnobotanical reports or scientific research. This means that for a plant to be considered a viable medicine, its efficacy and safety must be supported by evidence from traditional knowledge or validated through scientific studies. This rigorous approach ensures that the use of medicinal plants is based on both historical experience and modern scientific understanding, providing a solid foundation for their therapeutic applications (Shallangwa et al., 2017). Therapeutic plants have been studied as powerful phytochemical agents for managing various diseases, one of which is rosella. Rosella is a superlative plant for developing countries because it is relatively easy to cultivate. Rosella plants are underutilized but are a potential source of bioactive compounds (Mariod et al., 2021).

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 anti-inflammatory.

METHOD

This paper was meticulously prepared using a wide range of relevant and similar references that were gathered from various academic sources. These sources include textbooks, peer-reviewed scientific journals, scholarly articles, and credible websites, all of which were accessed through well-established and reputable databases such as PubMed, EBSCO, and Google Scholar. The primary keywords utilized in the search process were "Hibiscus sabdariffa L.," "rosella," "anti-inflammatory," "extract," and "effectiveness," ensuring that the search focused on highly relevant content. The inclusion criteria for selecting the literature were quite specific: only publications from 2012 to 2022 were considered, and these had to be either in English or Indonesian. Additionally, the selected studies needed to be directly related to the central theme of the discussion, which is the effectiveness of rosella as an anti-inflammatory agent. This approach ensured that the literature used was both current and aligned with the topic, providing a strong foundation for the analysis and conclusions drawn in this writing.

RESULT

The results obtained from the comprehensive literature search included a total of 25 references. Subsequently, a detailed analysis was conducted using specific inclusion and exclusion criteria to ensure the relevance and quality of the sources. As a result of this thorough evaluation, 15 references were deemed suitable and selected for further review, while 10 references did not meet the criteria and were therefore excluded from consideration. Additionally, another 10 references were removed from the list due to their publication dates; these references were either published more than 5 years ago in the case of journals or more than 10 years ago in the case of textbooks. This rigorous selection process was essential to ensure that only the most current and relevant literature was included in the study, thereby enhancing the credibility and accuracy of the research findings.

Table 1. List of references and summary.

Reference	Aim	Method	Sample	Result
Shallangwa GA., 2017	Knowing the total phenolic and flavonoid content, evaluating and comparing the anti-inflammatory effect of the ethanol extract of both extracts and a 1:1 mixture of extracts on protein denaturation in vitro.	The test extract and drug control (Ibuprofen) with various concentrations were incubated with egg albumin under controlled experimental conditions and absorbance was determined to assess anti-inflammatory properties.	Malus domestica fruit and Hibiscus sabdariffa petals.	Concentration-dependent inhibition of protein denaturation by both extracts, a 1:1 mixture and the control drug.
Nasri & Imran H., 2017	To determine the effect of gargling with Rosella tea on the speed of healing after scaling	Comparative analysis of pre-test and post-test using paired t-test and comparative analysis of treatment group and control group using independent t-test.	60 people gargled with rosella tea and 60 people in the control group gargled with salt water.	Gargling with rosella tea is more effective in curing post-scaling gingivitis.
Lubis M., et al., 2020	To determine the effect of rosella flower petals (Hibiscus sabdariffa) on dextran sodium sulfate (DSS)-induced colitis model, anti-inflammatory cytokine (IL-10) expression and histological colitis	In the first phase, 5 DSS-induced colitis mice were sacrificed and compared with 6 healthy mice after induction (70 days). For the second phase, DSS-induced colitis	Fifty-five healthy male mice (Mus musculus) (Charles River, Inc., Kanagawa, Japan), 6-8 weeks old, weighing 30 grams.	Rosella flower petals can relieve inflammation in DSS-induced colitis in mice. Roselle extract can be given as additional therapy in first-line therapy to increase anti-inflam

	inflammation score (HCIS).	mice treated with roselle were sacrificed on days 7, 14, 21, and 28 after induction and compared with DSS-induced colitis mice treated with mesalazine.		matory effects by increasing the expression of anti-inflammatory cytokines and reducing pro-inflammatory cytokines.
Mumpuni CN., et al., 2021	To determine the effect of systemic administration of rosella extract on healing time and ulcer diameter and to determine the dose of rosella extract that is effective in healing ulcers in Wistar rats.	20 rats had an ulcer made on the left buccal by heating an amalgam stopper over a Bunsen flame for 30 seconds and touching it for one second then waiting 48 hours.	The samples used were 20 mice that had ulcers made on the left buccal area.	Healing time and reduction in ulcer diameter were faster in the treatment group than in the control group. Ulcer healing was fastest at a dose of 0.17 mg/gBB of rosella extract. In conclusion, rosella extract at a dose of 0.17 mg/gBW had the most effective effect on healing ulcers.
Patil SB, Munoli S., 2017	Evaluating the anti-inflammatory effect of aqueous extract of HibiscussabdariffaL leaves. in albino mice.	The anti-inflammatory activity of H.sabdariffa (200mg/kg or 400mg/kg) was studied and compared with the standard drug, indomethacin (25mg/kg).	Albino mice weighing 150-250 g.	H.sabdariffa did not show anti-inflammatory activity in acute and chronic inflammatory edema caused by carrageenan and formalin.
Bayani GF., et al., 2018	To understand the underlying mechanism of impaired spatial memory consolidation due to overtraining and to observe the potential of H. sabdariffa in preventing systemic inflammat	H. sabdariffa extract was administered orally by oral gavage, 3 hours before physical exercise, 5 times a week until the end of the study	20 adults male Wistar rats (Rattus norvegicus) aged 8-11 weeks were randomly divided into 4 groups.	Administration of H. sabdariffa at 500 mg/kg body weight can prevent impaired spatial memory consolidation.

	ory processes and preventing malfunctions in spatial memory consolidation in overtraining syndrome.	(11 weeks).

Ingredients and Benefits of Rosella

The rosella plant (Hibiscus sabdariffa Linn) has a single ovoid leaf with rays, a blunt tip, edges, and a notched base. The leaf measures 6-15 cm in length and 5-8 cm in width. The rounded petiole is green and measures 4.7 cm in length. Rosella flowers (Hibiscus sabdariffa Linn) have brightly colored flowers, with dark red, bell-shaped, and not deciduous petals (Kusparmanto et al., 2024).

The Rosella plant is a kind of shrub belonging to the family—Malvaceae and genus Hibiscus. Rosella stems are reddish or green, with no or no branches at the base. The stems can be hairy or bald and have small tubercles. The leaves are serrated, and the lower leaves are round like eggs. The upper leaves have 3 to 5 lobes. Rosella flowers are yellow with a dark red core. The epicalis is fused at the base with dark red petals (Onyeukwu et al., 2023).

The Rosella plant, scientifically known as *Hibiscus sabdariffa L.*, is a bushy plant that can grow up to 2 meters in height. Native to North Africa and Southeast Asia, Rosella thrives in tropical climates around the world. Its cultivation has spread widely, with significant farming occurring in regions such as Africa, Thailand, China, and Mexico. The plant is valued for its various parts, including the petals (which are the outer portion of the flower base), the flowers themselves, and the leaves. These components contain a range of beneficial bioactive compounds, notably flavonoids such as anthocyanins, which are known for their health-promoting properties. The rich array of flavonoids in the petals and flowers contributes to the plant's antioxidant, anti-inflammatory, and antimicrobial effects, making it a valuable resource for both traditional and modern medicinal applications (Andrew, 2016)

Roselle leaf or calyx infusion is conventionally used for its diuretic, choleretic, antipyretic, and antihypertensive properties, as well as to thin the blood and induce intestinal peristalsis. Roselle calyx extract formulations are used in Egypt to treat heart and nervous system disorders, facilitate urination, and act as a cooling agent. In Sudan, roselle calyx extract is used to treat high blood pressure, cold and flu symptoms. People in Zimbabwe use the calyx, which is edible, to treat cancer. According to surveys, roselle flowers have been used to treat all types of cancer. Roselle is used to treat type 2 diabetes mellitus in the East African islands, a population with a high prevalence of diabetes. Roselle is processed into juice by people in Africa using the fruit part. The seeds of the fruit must be removed and cooked for 10 minutes in 1 liter of water to make the juice. The juice that has been made is then strained and drunk twice a day (Kusparmanto et al., 2024).

Rosella (Hibiscus sabdariffa Linn) is known to have a variety of properties that have been utilized in the health sector (Kusparmanto et al., 2024). Rosella flowers contain polyphenols, several vitamins, minerals, and 18 types of amino acids. Several studies showed that polyphenols have antiviral, antioxidant, and antibacterial activity (Nasri & Imran, 2017). The polyphenol content of roselle petals is in the form of phenolic acids and flavonoids. Rosella petals are dark red in an acidic medium because of the presence of betacyanin compounds and contain gel. Rosella petals contain glycosides, calcium oxalate salts and vitamin C. Rosella sepals contain organic acids such as malic, tartaric, citric, glycosides, and hepiscin chloride, oils that are stable in the seeds, glycosides, salts

(calcium oxalate, potassium salt (K), magnesium salt, iron salt), and vitamin C. Rosella flowers have a sour taste because they contain lots of natural acids, are rich in iron, vitamin (B) complex, calcium, phosphorus, and the leaves contain a small amount of cellulose. The flavonoids, anthocyanidins, triterpenoids, steroids, and alkaloids contained can be extracted and separated from rosella(Mariod et al., 2021)

Numerous scientific research has revealed that Roselle calyces are rich in flavonoids and polyphenols, which have enhanced the nutritional value of Roselle, as their antioxidant properties distinguish these compounds. Polyphenols of the flavonol type and flavanol found in Roselle are in the form of a simple or polymer form. The most flavonoids isolated from the Roselle extracts were, hibiscetin3-glucoside (hibiscitrin), gossypitrin, gossytrin, sabdaritrin and other gossypetin glucosides, quercetin and luteolin; also, chlorogenic acid, protocatechuic acid, pelargonidic acid, eugenol, quercetin, luteolin, and the sterols b-sitosterol and ergosterol (Wu et al., 2018).

Rosella is highly valued for its rich nutritional content, as it is abundant in a variety of essential compounds, including carotene, riboflavin, anthocyanin, ascorbic acid, niacin, and vitamin C. These nutrients contribute to its health-promoting properties. In addition to its flowers, the young leaves and stems of the Rosella plant are commonly consumed raw as green vegetables, providing a source of vitamins and minerals in many traditional diets. One of the standout features of Rosella flowers is their high ascorbic acid content, which is around 260-280 mg per 100 grams, making them a potent source of vitamin C. Beyond its raw consumption, Rosella is often processed into a variety of products, including syrups. When preparing Rosella syrup, the concentrate can either be heated or left unheated depending on the desired preparation method. The characteristic sour taste of Rosella is directly linked to its high ascorbic acid content. Interestingly, research indicates that boiling Rosella for a short duration, around 10 minutes, can increase the amount of vitamin C in the extract. However, prolonged boiling leads to a gradual reduction in vitamin C content, as heat tends to degrade the nutrient over time. This balance between cooking time and nutrient preservation is crucial when processing Rosella for consumption (Mariod et al., 2021).

Rosella, a versatile plant, can be processed into a refreshing tea, which is known for its ability to provide a soothing effect on hot and feverish conditions. The petals of the rosella plant can serve as a gentle herbal remedy, offering relief from common ailments such as colds, coughs, and chest problems. Additionally, rosella is beneficial for digestion and can stimulate appetite, making it a valuable addition to one's diet for overall well-being. The petals and flowers of the rosella plant have been recognized for their ability to reduce cholesterol levels, contributing to cardiovascular health. Moreover, all parts of the rosella are utilized in traditional medicine to alleviate mild pain and address inflamed mucous membranes in both the digestive and respiratory tracts. Various clinical studies have demonstrated that rosella has a beneficial impact on lowering high blood pressure, further highlighting its potential as a therapeutic agent. This comprehensive range of uses underscores the significant health benefits associated with incorporating rosella into both preventive and remedial health practices (Andrew, 2016).

Some scientists have achieved extreme efficacy of the rosella plant as an antioxidant that lowers high blood pressure, increases blood circulation speed, and strengthens the heartbeat. Rosella can be used as a refresher and medicine for the body to prevent thirst, useful on hot days and when fasting. Due to its high vitamin C content, it can help in treating colds, coughs, and high fever. Due to its antioxidant properties, it is recommended in cancer patients undergoing chemotherapy and is used to fight cancer as a disease. HS contains

disinfectants and kills microbes, which makes it useful in treating fever and microbial infections and for getting rid of tapeworms and roundworms (Ascaris) in the intestines. HS appears to be useful for contractions of the uterus, stomach, and intestines and relieves pain during the menstrual cycle (Mariod et al., 2021).

Figure 1. Rosella plant (Hibiscus sabdriffa L.) (Unita & Singarimbun, 2018).

Figure 2. Rosella plant leaves (Nurnasari & Khuluq, 2018).

Figure 3. Rosella fruit and flower petals(Nurnasari & Khuluq, 2018).

Anti-Inflammatory Activity of Rosella

This writing focuses on the effectiveness of rosella as an anti-inflammatory. Inflammation is a physiological reaction that occurs in the response to different injuries or disease-causing agents (physical trauma or bacterial infection), thus limiting the damage caused by pathogens and promote tissue repair. In general, there are two types of inflammation, acute and chronic. Acute inflammation is characterized by a rapid onset over a very short period and is characterized by loss of plasma proteins and fluid from the blood vessels. Chronic inflammation begins within 2-4 days of the initial response and can last for months or years. This is indicated by the presence of macrophages and lymphocytes, which cause tissue necrosis and fibrosis (Mariod et al., 2021). The anti-inflammatory effect of rosella extract is thought to be the effect of flavonoids as one of the active ingredients which can inhibit prostaglandins and inhibit the activity of the lipoxygenase enzyme which is the first pathway to eicosanoid hormones (Engineering et al., 2024).

Anthocyanins that can be extracted from dried rosella flower petals have been known to play an important role in anti-inflammatory activity. Different compounds such as aglycone, cyaniding, and delphinidin can suppress the expression of inflammatory mediators, which are prostaglandins and cyclooxygenase. During chronic inflammation, primary cells released in the form of macrophages produce large amounts of nitric oxide mediators along with proinflammatory cytokines. Recent studies have shown that anthocyanins obtained from rosella, especially delphinidin-3-sambubioside and delphinidin, are effective in suppressing the expression of nitric oxide mediators, namely inducible nitric oxide synthase (iNOS), nitric oxide (NO), interleukin 6 (IL-6), monocyte chemoattractant protein-1 (MCP-1), along with cytokines such as TNF-α and MCP-1. The in vitro anti-inflammatory activity of rosella leaf extract has also been evaluated on murine RAW 264.7 macrophage cells by measuring the inhibition of nitrous oxide synthesis. The findings explain the dose-dependent inhibition of nitric oxide synthase with wider variations among different accessions of the plant. The anti-

inflammatory response of rosella extract is attributed to quercetin, kaempferol, and chlorogenic acid. During inflammation, lysosomal enzymes are released which cause many diseases. The activity of these extracellular enzymes is controlled by the magnitude of acute and chronic inflammation. Sometimes, nonsteroidal drugs used during inflammation work by stabilizing the cell membranes of these enzymes, thereby inhibiting their activity. It is important to mention that human erythrocyte membranes are similar to these lysosomal enzymes. The stabilization properties of cell membranes have been proven through in vitro experiments using methanol extract from rosella flowers. Rosella extract has also proven effective in inhibiting protein (albumin) denaturation. Inflammation results in protein denaturation leading to loss of its tertiary structure (Mariod et al., 2021).

Rosella Extract

Researchers have recently focused on the leaves of the Rosella plant which are shown to be a good source of several nutrients such as protein, carbohydrates, iron, calcium, ascorbic acid, riboflavin, and β-carotene. Rosella also contains high levels of phenolic compounds such as various phenolic acids and flavonoids which have various pharmacological effects, namely exerting beneficial anti-inflammatory and immunomodulatory activities by interfering with immune cell regulation, pro-inflammatory cytokine synthesis, and gene expression (Hussein ME et al., 2019). Rosella extraction is carried out by the maceration method using 60% ethanol and water. The extract is evaporated to obtain a concentrated extract and followed by freezing until dry. The preparation of nanoparticles uses the ionic gelation method. Nanoparticles were tested in vitro with thiobarbituric acid reactive substances (TBARS) testing (Jabeur et al., 2019).

In research conducted by Hussein, et al, the defatted dried powdered leaves, weighing a total of 1.5 kilograms, were meticulously extracted using a solvent of 70% ethanol in a series of multiple extractions, each involving 2 liters of the ethanol solution for a total of 15 rounds. This process resulted in the production of 150 grams of defatted ethanolic extract (DEE) derived from the leaves of the Rosella plant. From this DEE, a portion of 100 grams was further suspended in water, after which it was subjected to partitioning using methylene chloride, ethyl acetate, and n-butanol, all of which were pre-saturated with water. Each solvent partition was repeated five times, using 350 milliliters of solvent per round, yielding specific fractions of 20 grams, 12 grams, and 5 grams for the methylene chloride, ethyl acetate, and n-butanol fractions, respectively. This systematic approach allowed the researchers to isolate different compounds present in the Rosella leaves, facilitating a more detailed investigation into their potential properties and uses (Hussein ME et al., 2019).

Research by Jabeur I, et al. (2019) used hydroethanol rosella extract, namely an extract using ethanol and water as a solvent. The extract was made by macerating with agitation (150 rpm) 1 g of dry sample (dried Rosella petals) and ethanol/water (80:20 v/v, for identification of anthocyanins, 0.5% TFA was added to the extract solvent), at a temperature of 25°C for 1 hour. After filtration (Whatman paper No. 4), the residue was extracted with an additional 30 mL of the same solution (25 °C at 150 rpm) for 1 h. The combined extracts were evaporated (rotary evaporator Büchi R-210, Germany) at 40 °C, frozen, and then lyophilized (Jabeur et al., 2019).

Rosella extract using a methanol solvent has also been the focus of several studies. In one such experiment, Rosella petals, which had been carefully air-dried for a period of 21 days at room temperature, were ground into a fine powder, achieving a particle size of approximately 1 millimeter. This ensured a consistent texture for optimal extraction. A sample of 350 grams of the powdered Rosella petals was then immersed

in a solvent mixture composed of methanol and water in a 4:1 ratio. The soaking process lasted for a period of 96 hours, allowing sufficient time for the solvent to thoroughly penetrate the plant material and extract key phytochemicals present in the petals. The use of methanol, combined with water, is known to be highly effective in extracting both polar and non-polar compounds, making it an ideal solvent for capturing a wide range of bioactive compounds from the Rosella petals. After 96 hours, the solution was filtered, and the resulting extract was ready for further analysis to determine its chemical composition and potential bioactive properties (Mariod et al., 2021).

The number of doses of Rosella plant extract used varies in each study. A study conducted by Anokwuru, et al stated that Rosella flower petals contain several phenolic compounds, with methanol extract providing the highest phenolic content and antioxidant activity against free radicals (Lubis et al., 2020). The anti-inflammatory properties of methanol extract of Rosella plant seeds have been studied in a mouse model which was injected with 1% carrageenan suspension (0.1 mL) in the back of the rat's right paw until edema appeared. Treatment was carried out with Rosella plant extract at doses of 200 and 400 mg/kg. The claw thickness of each mouse was calculated using a Zeitlin tool before carrageenan injection and every hour until 6 hours after carrageenan injection. The results showed a significant reduction in the healing of edema in the proximal paws of mice, dose-dependent, indicating anti-inflammatory activity (Mariod et al., 2021).

Research conducted by Dewi, et al regarding the anti-inflammatory effectiveness of rosella extract on carrageenan-induced Wistar rats reported that the dose that had the best anti-inflammatory effect was a dose of 326.16 mg/KgBW by inhibiting the formation of inflammation by 74.524% which was equivalent to the comparison drug diclofenac sodium tablets (4.5 mg/KgBW). Another study conducted by Ramadhani, et al stated that rosella extract at a dose of 410 mg/200gBW for testing in male white rats of the Wistar strain had anti-inflammatory activity with an inflammation inhibition percentage of 31.93%. Research to determine the effect of giving rosella extract on healing ulcers in Wistar rats was carried out by Mumpuni, et al 2021 with a sample of 20 rats divided into several groups. The results showed that the one that has the best effectiveness in healing ulcers is rosella extract at a dose of 0.17 mg/gBW with observation for up to 11 days (Mumpuni et al., 2021).

DISCUSSION

The in vivo test on Rosella extract conducted by Mumpuni, et al., in 2021 involved the use of 20 mice. In this study, Rosella extract was applied to ulcers on the buccal mucosa of the mice to evaluate its potential effects on wound healing. The extract was carefully administered to assess its ability to promote healing in the oral tissue of the mice. This study builds on prior research exploring the medicinal properties of Rosella extract. Similarly, in research by Patil & Munoli (2017), albino mice weighing between 150-250 grams of both sexes were used to investigate the effects of an orally administered drug. This research received ethical approval from the Institutional Animal Ethical Committee, ensuring compliance with animal welfare standards. Additionally, Bayani et al. (2018) utilized adult male Wistar rats (Rattus norvegicus) aged 8-11 weeks in their research. These rat models have been widely employed in scientific studies due to their suitability for exploring various therapeutic interventions. These studies collectively emphasize the value of using different rodent models to explore the effects of natural extracts like Rosella in promoting wound healing and health. (GULSHAN FAHMI EL BAYANI et al., 2018).

Roselle leaves are a good source of various nutrients such as protein, fat, carbohydrates, phosphorus, iron, β-carotene, riboflavin, and ascorbic acid. It

contains high levels of polyphenolic compounds, especially chlorogenic acid, and its isomers quercetin and kaempferol glycosides which contribute to its antioxidant capacity and anti-inflammatory activity (Riaz & Chopra, 2018).

The anti-inflammatory effect of roselle drink is caused by inhibiting cytokine production. Beltran-Debon et al. investigated the active components in Hibiscus sabdariffa extract in vitro and showed that it can effectively protect peripheral blood mononuclear cells (PBMC) from cell death caused by H2O2 by modulating the production of inflammatory cytokines. In clinical trials on healthy human volunteers, they have shown a reduction in plasma concentrations of monocyte chemoattractant protein 1 (MCP-1) which is a biomarker in the evaluation of inflammatory diseases (Riaz & Chopra, 2018).

According to in vivo research conducted by Mumpuni, et al., in 2021, the systemic administration of ethanolic Rosella extract has shown significant therapeutic potential. This research revealed that the extract can effectively inhibit the expression of COX-2 (cyclooxygenase-2), an enzyme that plays a crucial role in the inflammatory response. By suppressing COX-2, the ethanolic Rosella extract reduces the infiltration of neutrophils during the inflammatory phase of wound healing, which in turn accelerates the overall healing process. This suggests that Rosella extract could be a beneficial agent in managing inflammation and promoting tissue regeneration. Additionally, in vitro studies further supported these findings by examining the antioxidant potential and inhibitory power of Rosella flower extract against the cyclooxygenase enzyme. The research demonstrated that the bioactive compounds within the Rosella flower extract are capable of inhibiting the activity of cyclooxygenase, thereby reducing the synthesis of inflammatory mediators such as leukotrienes and prostaglandins. These mediators are directly involved in the development and maintenance of inflammation, and their inhibition underscores the potential of Rosella extract as a natural anti-inflammatory agent (Mumpuni et al., 2021).

Mumpuni et al also wrote that giving high doses of rosella extract was less effective as an anti-inflammatory. This is caused by flavonoid levels which experience a decrease in activity at high concentrations. Excessive addition of anthocyanin content as an antioxidant will damage tissue due to an increase in the concentration of the extract solution which reduces its antioxidant activity. Extract concentration levels that are too high can also inhibit saponin as an antibacterial (Mumpuni et al., 2021).

Research on the immunomodulatory activity of roselle flower petals using the hemagglutination test method was carried out in vivo by Fakeye et al. Their study also measured the concentration of interleukin-10 (IL-10) as an anti-inflammatory cytokine. Research results showed that roselle flower petals can improve the body's immune system. This is due to increased production of IL-10 so it can suppress the synthesis of other pro-inflammatory cytokines and influence B lymphocyte cells to produce antibodies. This study aims to determine the effect of rosella flower petals (Hibiscus Sabdariffa L.) on the dextran sodium sulfate (DSS) induced colitis model by measuring the expression of pro-inflammatory cytokines (IL-6, and TNF-α) and anti-inflammatory cytokine expression (IL-10). This can be attributed to the immunomodulating properties of phenolic compounds and also the antioxidant properties of anthocyanins contained in roselle flower petals (Lubis et al., 2020).

Another study showed that the anti-inflammatory activity of methanol extract from rosella petals was investigated in mice with excessive leg edema and physical exercise. Onuka et al. demonstrated that the extract (100 to 400 mg/kg bw) reduced leg size edema in a shorter time than aspirin (200 mg/kg bw). However, the effect in response is dose dependent. These results

were attributed to the downregulation of the expression of pro-inflammatory mediators promoted by polyphenolic compounds. Bayani et al. who reported that HS extract (at 500 mg/kg bw) exhibited potent anti-inflammatory properties in overtrained mice and prevented spatial memory impairment, associated with the ability of the bioactive compound to maintain the IL-1β/IL-1ra ratio in plasma and hippocampus (Montalvo-González et al., 2022). Rambe *et al* 2022 found a greater wound healing process in the 15% roselle leaf extract gel based on clinical and histological assessment. Although there were no statistically significant differences among the groups, roselle leaf extract brought forward the opportunity to be investigated further as a potential modality for wound healing (Rambe et al., 2022).

CONCLUSION

The Rosella plant, scientifically known as *Hibiscus sabdariffa L.*, is renowned for its potential health benefits due to its rich composition of bioactive compounds. Among these compounds are flavonoids, phenolic acids, and anthocyanins, which are known for their significant therapeutic properties. These bioactive compounds exhibit powerful anti-inflammatory, antioxidant, and antimicrobial effects. Specifically, flavonoids and phenolic acids have been shown to modulate inflammatory responses by inhibiting crucial enzymes such as cyclooxygenase (COX). This inhibition helps in reducing the production of inflammatory mediators, including prostaglandins and leukotrienes, which are involved in the inflammatory process. By decreasing the levels of these mediators, Rosella helps alleviate inflammation and oxidative stress. Furthermore, the antioxidant properties of these compounds contribute to protecting cells from damage caused by free radicals, thereby supporting overall health. The antimicrobial effects add another layer of benefit, potentially aiding in the defense against various pathogens. Consequently, Rosella offers a natural and multifaceted approach to managing inflammation and promoting health.

The study employed a thorough literature review method, analyzing a variety of research papers from 2012-2022 that focused on Rosella's anti-inflammatory potential. The analysis involved a selection of 15 references out of 25, focusing on the most recent studies. Results from various in vitro and in vivo experiments demonstrated that Rosella extract could effectively reduce inflammation by decreasing the number of neutrophils and accelerating the wound healing process. The research also highlights that high doses of Rosella extract might lead to decreased efficacy, as excessive flavonoid levels reduce the activity of the bioactive compounds. In terms of practical applications, Rosella extract has been shown to reduce inflammation in conditions such as dextran sodium sulfate (DSS)-induced colitis in mice and has been used to treat ulcers in rats, demonstrating a faster healing time compared to control groups. Additionally, clinical studies indicate that Rosella tea is effective in reducing post-scaling gingivitis and has potential benefits in improving systemic inflammation when consumed regularly. The potential for Rosella extract to be integrated into therapies for inflammation-related conditions is substantial, especially as an alternative or complementary treatment to conventional pharmaceuticals. However, the variation in efficacy at different dosages, particularly at higher concentrations, suggests that precise formulation is critical for maximizing its therapeutic benefits. In conclusion, Rosella (Hibiscus sabdariffa L.) shows significant potential as a natural anti-inflammatory agent. Its ability to modulate inflammatory pathways, coupled with its antioxidant properties, makes it a promising candidate for further research and development in medical and dental applications. Nonetheless, future studies must focus on refining dosage and administration methods to ensure the consistent efficacy of Rosella extracts in therapeutic contexts.

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