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Antioxidant and Anti-Inflammatory Activities of Kecombrang (*Etlingera elatior*) extracts: a Systematic Literature Review

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ABSTRACT

Kecombrang (Etlingera elatior) is a plant commonly used in traditional medicine and as a food seasoning by the Indonesian community. It contains various secondary metabolites such as saponins, tannins, alkaloids, steroids, flavonoids, and phenolic compounds, which are distributed from its rhizomes to its flowers. Several studies have shown that kecombrang can reduce foot edema due to inflammation ranging from 67.4%, ulceration index and inflammatory cell infiltration, caspase-3, NO, PGE2, and PGE2. This literature review aims to provide a deeper understanding of the active compounds in kecombrang and their potential health benefits for humans. The study was conducted as a literature review using the PRISMA method, with data sources from four major databases: ScienceDirect, PubMed, Scopus, and Google Scholar. Findings from several studies involving rats as test subjects indicate that the active compounds in kecombrang exhibit antioxidant effects that protect cells from oxidative damage. Additionally, kecombrang extract demonstrates anti-inflammatory activity by directly inhibiting the enzymes COX and lipoxygenase, thereby reducing the biosynthesis of prostaglandins and leukotrienes.

1. INTRODUCTION

Kecombrang (*Etlingera elatior*) is a spice plant from Indonesia that belongs to the Zingiberaceae family. This plant grows widely in Southeast Asia and is traditionally used for both culinary and medicinal purposes (Resna et al. 2021). According to research conducted by Setiawan et al. (2024), kecombrang contains phytochemical compounds such as flavonoids, tannins, triterpenoids, steroids, and essential oils. Various parts of the plant, including leaves, stems, flowers, and rhizomes, contain essential oils that have bioactive properties. The highest essential oil content was found in leaves at 0.0735%, followed by flowers 0.0334%, stems 0.0029%, and rhizomes 0.0021% (Setiawan et al. 2024).

Kecombrang (*Etlingera elatior*) has a variety of benefits in everyday life, from its rhizomes to its flowers. Kecombrang leaves are used as deodorizers, wound medicines, antioxidants, antibacterials, and tyrosinase inhibitors. While the flowers also have active ingredients as antibacterial, antifungal, and antioxidants (Wahyuni et al. 2021). Kecombrang rhizome contains high antioxidant compounds, making it effective in fighting free radicals (Yuliana, 2023). In addition, kecombrang is often used to facilitate breast milk production, heal wounds, and add a distinctive flavor to dishes. Previous research has proven that there is antibacterial and antioxidant activity in kecombrang (Wardani, 2020).

One of the benefits of kecombrang is its ability as an anti-inflammatory and antioxidant. Phytochemical screening results show that E. elatior leaf extracts with ethanol, ethyl acetate, and n-hexane solvents contain phenolic compounds that have the ability to inhibit the inflammatory process. In other words, the kecombrang plant has potential as an alternative anti-inflammatory

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drug derived from natural ingredients. Natural medicines have been increasingly used in recent years as an alternative treatment for inflammation due to their relatively small side effects compared to chemical drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs) (Resna et al. 2021). Existing research gaps are that although several studies have shown anti-inflammatory, antioxidant, and nephroprotective effects, the molecular mechanisms behind these effects are still not fully understood.

Based on this background, the writing of this literature review aims to examine in depth the bioactive compounds in kecombrang plants that act as antioxidants and anti-inflammatory and the mechanism of their activity based on various available scientific literature. The urgency of this literature study is expected to be the basis for the development of kecombrang plants as an alternative in the field of plant-based medicine, safer and more effective natural anti-inflammatory drugs, disease therapy involving oxidative stress, developed into more practical pharmaceutical preparations such as herbal ointments or gels for acute and chronic wound care and adjuvant therapy for sepsis.

2. METHOD

The method used in writing this article is a literature review. This research was conducted as a literature review with the PRISMA method approach, using literature sources from four main databases, namely ScienceDirect, PubMed, Scopus, and Google Scholar. In the initial stage of searching journal articles, 247 articles from 2020 to 2024 using the keywords "Etlingera elatior" OR "kecombrang", "antioxidant" OR "antioxidant", "anti-inflammatory" OR "antiinflammatory" or Combine: ("*Etlingera elatior*" OR "kecombrang") AND ("antioxidant" OR "antioxidant") were explored for relevance to the articles to be compiled. The purpose of sorting articles is to group articles that meet the inclusion criteria and are suitable for review as many as 49 articles which are then continued with the exclusion process. Of these there were only 10 articles that were considered relevant. Sorting articles based on the PICO method, namely P: population: in this literature review in the form of mice, I: intervention: in this literature review in the form of giving leaf / flower extracts (at most) kecombrang, C: comparison, namely the existence of standard drug treatment as a comparison, and O: outcome in the form of knowing the benefits of active substances in kecombrang for health. Therefore, the inclusion criteria obtained include: (1) experimental research, (2) research subjects in the form of rats or in vitro (3) discussing the active content of kecombrang as an antioxidant and anti-inflammatory, (4) Publication in English or Indonesian. Meanwhile, the exclusion criteria include: (1) not original research (2) data obtained cannot be extracted (3) types of articles in the form of case reports, reviews, conference abstracts, and editorials. The prism flow shows the selection flow. Here is the PRISMA flowchart.

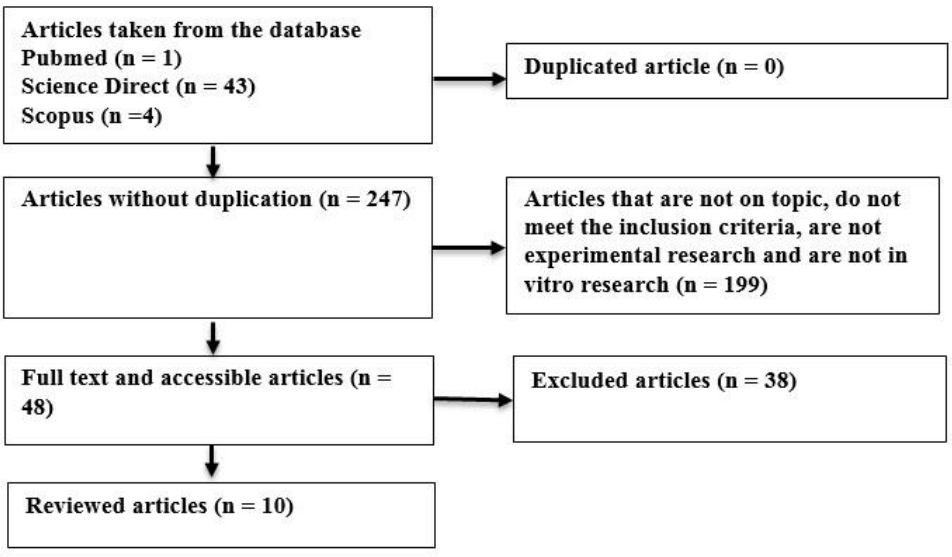

Figure 1. Flowchart of Literature Selection

3. RESULT AND DISCUSSION

Result

Tabel 1. Reviewed Aticles

Researcher, Year	Title	Variabels	Sampel	Intervention	Results
Alfanda et al., 2021	Anti-Inflammatory Activity Test of n-Hexan, Ethyl Acetate and Ethanol Leaves of Kecombrang (Etlingera Elatior) on Wistar Male White Rats (Rattus Norvegiucus)	Independent Variable: Anti-Inflammatory n-Hexan, Ethyl Acetate and Ethanol Leaves of Kecombrang (Etlingera Elatior) Bound Variable: Wistar Male White Rat (Rattus Norvegiucus)	Wistar male white rats were divided into 6 groups, each group consisting of 5 test animals.	Ethanol extract of kecombrang leaf was given orally: • I: positive control (Na.diclofenac) • II: negative control (PGA) • III: dose of 50 mg/kgBB • IV: 100 mg/kgBB • V: 150 mg/kgBB • VI: 200 mg/kgBB	Ethanol, ethyl acetate and n-hexane extracts of kecombrang leaves have anti-inflammatory effects on udem of the soles of male white rat wistar strains with the most optimal dose of 200 mg / kgBB able to reduce udem by 82.29%, 72.70%, 67.40%.
Fristiohady et al. 2020	Nephroprotective effect of extract Etlingera elatior (Jack) R.M. Smith on CCl4-induced nephrotoxicity in rats	Independent variable: Etlingera spp. extract. Dependent variable: CCl4-nephrotoxicity	45 rats (+/- 23 months old; weight 20-30 g) were acclimatized for 7 days.	Kecombrang flower extract: • I: negative control (Na-CMC) • II: normal control (Na-CMC) • III: extract dose of 200 mg/kg BW ● IV: extract dose of 300 mg/kg BW ● V: extract dose of 400 mg/kg BW	Kecombrang flower extract is able to normalize the levels of urea CCl4-induced rats at concentrations of 200; 300; and 400 mg / kg BB and reduce creatinine at a concentration of 400 mg / kg BB, as well as at concentrations of 200 and 300 mg / kg BB has the activity of protecting tubular cells, while at concentrations of 400 mg / kg BB shows the activity of protecting tubular cells. Activity of protecting tubule cells, while at a concentration of 400 mg / kg BB

					showed necrosis.
Wardani, I. G. A. A. K., 2020	Effectiveness of Kecombrang Flower Extract Gel (Etlingera elatior) as Anti-inflammatory for Carrageenan-Induced Mice	Independent variable: kecombrang flower extract gel (Etlingera elatior) Dependent variable: anti-inflammatory effect on mice	Female white mice swiss webster strain weighing 20-30 grams and aged 2-4 months that have been induced suspension. carrageenan as much as 0.1 ml	Kecombrang flower extract: • Negative control group: gel base • Positive control group: voltaren gel • I: 1% extract gel • II: 2% extract gel • III: 3% extract gel	Kecombrang flower extract gel is effective as an anti-inflammatory with the optimal dose at 3% concentration.
Juwita et al., 2020	Anti-inflammatory Activity of Etlingera elatior (Jack) R.M. Smith Flower on Gastric Ulceration-induced Wistar Rats	Independent variable: Anti-inflammatory Activity of Etlingera elatior (Jack) R.M. Smith Flower Dependent variable: Gastric Ulceration-induced Wistar Rats	Healthy wistar male rats aged 3 months weighing 200-260 grams.	Kecombrang flower extract: • I: water (normal control) • II: Arabic gum suspension 2% (negative control) • III: mixed solution of quercetin 20 mg/kg+Arabic gum (positive control) • IV: 500 mg/kgBB extract • V: 1000 mg/kgBB extract • VI: 2000 mg/kgBB extract	Kecombrang flower extract is useful as an anti-inflammatory with the most optimal extract dose of 1000 mg/kgBB being able to reduce the index of ulceration and inflammatory cell infiltration.
Noordin et al., 2022	Etlingera elatior Flower Aqueous Extract Protects against Oxidative Stress-Induced Nephropathy in a Rat Model of Type 2 Diabetes	Independent variable: Etlingera elatior flower water extract Dependent variable: Oxidative stress-induced nephropathy	32 male Sprague Dawley rats aged 8-10 weeks, weighing 200-220 grams.	Water extract of kecombrang flower: • I : Control group fed standard diet • II : T2DR group induced into diabetes • III : given metformin 250 mg/kg orally every day for 6 weeks	Etlingera elatior flower water extract showed significantly reduced GDP, microalbuminuria, serum creatinine, and BUN in type 2 DM model rats, increased antioxidant activities (SOD, CAT, GSH, T-

				• IV : given EEAE 1000 mg/kg orally every day for 6 weeks	AOC) and decreased malondialdehyde (MDA), inflammatory markers (IL-6), fibrosis (TGF-β and CTGF) in the treated group.
Wardani et al., 2022	Activity Test of Kecombrang Flower Extract (Etlingera elatior Jack) as Hypolipidemia in Obese Wistar Rats	Independent variable: Administration of kecombrang flower methanol extract Dependent variable: Rat blood lipid parameters, namely total cholesterol, triglyceride (TG), LDL and HDL levels.	18 female white rats aged 2 months weighing ± 150 grams divided into 3 groups	Kecombrang flower extract: • I: normal group (fed standard diet only) • II: high-fat control (obese rats/with high-fat feed diet) • III: flower treatment group (obese rats/with high-fat feed diet + 100 mg/kgBB flower methanol extract)	Kecombrang flower extract has the potential to act as hypolipidemia by reducing total cholesterol levels by 55.5%, triglycerides (TG) by 57.4%, LDL by 76.73%, and increasing HDL by 42.96%.
Sagala et al., 2016	The Effect of Ethanol Extract of Kecombrang Flowers (Etlingera elatior) on Wound Healing in White Rats (Rattus norvegicus)	Independent variables: Combrang flower extract Dependent variable: wound healing	18 mice weighing 200-300 grams and divided into 6 groups.	Kecombrang flower ethanol extract: • I: 5% concentration. • II: 10% concentration. • III: 15% concentration. • IV: 20% concentration. • Positive control: povidone iodine • Negative control	The ethanol extract of kecombrang flowers is useful for accelerating wound healing The most effective concentration is 5% concentration.
Ginting et al., 2022	Incision Healing Test of Ethanol Extract of Kecombrang Fruit (Etlingera elatior Jack.) Against White Rats	Independent variable: Ethanol Extract of Combrang Fruit Dependent variable: Incision wound healing	25 white male rats, weighs 250-300 grams and is around 2-3 months old.	Kecombrang fruit ethanol extract ointment: • I : ointment base (negative control). • II: Betadine ointment 10% (positive control).	Kecombrang fruit ethanol extract ointment can accelerate wound healing with the most optimal dose of 12% concentration which is as effective as the

				• III: 8% extract. • IV: 10% extract. • V: 12% extract.	positive control (10% betadine ointment).
Nurhayatun et al., 2023	The beneficial effect of the ethanolic extract Etlingera elatior fruit on IL-1ß and caspase-3 levels in sepsis mice model	Independent variable: Administration of ethanol extract of kecombrang fruit (Etlingera elatior) Dependent variables: Levels of interleukin-1β (IL-1β) and caspase-3	32 male Balb/C strain mice aged 3-4 months with a body weight of 20-30 grams.	Kecombrang fruit ethanol extract (4.2 mg/20 g BW): • EE1: orally for 5 days before LPS induction. • EE2: orally for 5 days after LPS induction. • EE3: orally along with LPS induction. • Control: Mice only received LPS induction without extract administration.	The ethanol extract of kecombrang fruit at a dose of 4.2 mg/20 g significantly reduced caspase-3 levels with the best results in the EE-1 group. and reduced IL-1ß levels in all groups, with the best results in the EE-1 group.
Pipatrattanaseree et al., 2023	Potential in vitro Anti-inflammatory and Antioxidant Activities of Various Extracts of Etlingera elatior Inflorescences	Independent variable: E. elatior ethanol extract Dependent variables: anti-inflammatory (inhibition of NO, PGE2, and TNF-α production) and antioxidant (DPPH free radical scavenging test	In vitro, murine macrophage cells RAW 264.7 (ATCC TIB-71) were stimulated by LPS to trigger an inflammatory response.	Extracts were made from the bracts of E. elatior using ethanol solvent with concentrations of 95%, 70% and 50%, then anti-inflammatory and antioxidant tests were carried out.	Anti-Inflammatory Effects: ● 70% and 95% ethanolic extracts effectively inhibit NO production. ● 95% extract inhibits PGE2 ● No extract effectively inhibited TNF-α Antioxidant Effect: 50% ethanol extract showed the best DPPH activity.

Discussion

Table 1.1 shows that the types of samples used are mice, white mice, and macrophage cells with a total sample obtained from 10 journals reviewed as many as 186 white mice and 57 mice. The details of the sample consisted of 30 male wistar rats induced udem with 1% carrageenan, 45 male wistar rats, 18 male wistar rats in gastric ulcer conditions, 32 male Sprague Dawley rats induced diabetes, 18 obese female wistar rats fed a high-fat diet, 18 white rats whose backs were cut with a length of 2 cm and a width of 2 mm, 25 white male rats whose backs were cut with a length of 2 cm, 25 female Swiss Webster mice induced with 0.1 ml carrageenan, 32 male Balb/C mice induced with lipopolysaccharide sepsis, and 1 journal using RAW264 macrophage cells. 7. The 10 journals reviewed used various types of rats and mice, including Wistar rats, Sprague Dawley rats, Swiss Webster mice, and Balb/C mice. Wistar strain mice are most often used in research because they are easily available and relevant to human physiology and genetic makeup

(Maheshwari et al. 2018). Meanwhile, macrophage cells used in this study were used to test the anti-inflammatory effect of kecombrang extract by reviewing its ability to inhibit nitric oxide (NO), prostaglandin E2 (PGE2), and tumor necrosis factor α (TNF-α).

This literature review shows that kecombrang extract has various properties according to the active compounds it contains. Some of the active substances contained in kecombrang extract include ethanol, ethyl acetate, and n-hexane which contain phenol compounds that function as anti-inflammatory. In addition, ethanol in kecombrang extract also has a neuroprotective effect by keeping urea and creatinine levels at their normal values and protecting renal tubular cells. Ethanol extract in kecombrang contains quercetin compounds as anti-inflammatory which can inhibit NF-6B-p65 expression in gastric ulcers. Ethanol extract can reduce IL-1ß and caspase-3 levels that cause increased oxidative stress and hyperinflammation. Antioxidants in kecombrang extract can prevent the increase of free radicals, so it can act as an antidiabetic. Flavonoid content in kecombrang extract acts as an anti-inflammatory by inhibiting the formation and release of pro-inflammatory substances from allergic reactions. The flavonoid content can also be utilized in wound healing. Methanol extract in kecombrang acts as hypolipidemia by reducing total cholesterol levels, LDL, TG, and increasing HDL. Various benefits of giving kecombrang (Etlingera elatior) are as follows :

Anti-Inflammatory Effects

Inflammation is a complex biological response that protects the body from harmful stimuli such as infection, tissue damage, exposure to chemicals and bacterial components. During inflammation, the body activates several types of cells such as neutrophils, mast cells, and macrophages that produce cytokines and proinflammatory mediators such as nitric oxide (NO), tumor necrosis factor alpha (TNF-α), and prostaglandin E2 (PGE2) that serve as signals to activate the immune response and repair damaged tissues. Over-activation of these cells and the resulting proinflammatory mediators can cause damage to healthy cells and tissues, leading to symptoms such as pain, swelling, redness, heat and loss of cell function. The common management of pain and inflammation is the administration of steroids and non-steroidal anti-inflammatory drugs (NSAIDs). However, long-term use of these drugs can cause side effects. To prevent these side effects, alternative treatments using natural or herbal ingredients are an option. One of the herbal plants known to have anti-inflammatory effects is kecombrang (Etlingera elatior) (Juwita et al. 2020; Wardani 2020; Alfanda et al. 2021; Pipatrattanaseree et al. 2023).

Research conducted by Alfanda et al. in 2021 showed that ethanol, ethyl acetate, and n-hexane extracts contained in kecombrang leaves have an effective anti-inflammatory effect in reducing swelling of the soles of the feet of male Wistar white rats. The extract contains phenolic compounds that work to inhibit inflammation through the mechanism of capturing free radicals, which usually cause tissue damage and trigger inflammation (Alfanda et al. 2021). Meanwhile, research conducted by Wardani in 2020 showed that kecombrang flower extract gel has an inflammatory effect in reducing the volume of edema on the soles of rats due to carrageenan induction because it contains flavonoids, terpenoid compounds, and tannin compounds. Flavonoids can inhibit the formation of substances that cause inflammation, terpenoid compounds can inhibit COX-2 expression thereby reducing prostaglandin production, and tannin compounds have antioxidant activity that can inhibit oxidant production thereby reducing H2O2 formation (Wardani 2020).

The gastric mucosa has an important function in the human digestive system. Acid production imbalance, the use of NSAIDs, antibiotics, and antidepressants can trigger inflammation in the stomach which, if left untreated, can lead to gastric ulcers and increase the risk of bleeding and perforation in the stomach. Acetic acid induction can cause local inflammatory reactions resulting in an increase in inflammatory cytokines and an increase in NF-kappaB-p65 expression in the stomach. In a study involving male Wistar rats induced with acetic acid, ethanol extract of Etlingera elatior flowers showed anti-inflammatory activity by reducing NF-kappaB-p65 expression in the gastric fundus, thus inhibiting gastric ulceration. The flower part of the E. elatior plant contains mainly phenolics and flavonoids, especially quercetin, which has a high anti-

inflammatory content. Quercetin is known to inhibit oxidative stress induced by gastric damage. (Juwita et al. 2020; Wardani 2020; Alfanda et al. 2021; Pipatrattanaseree et al. 2023).

Ethanol extract of kecombrang fruit (EEBK) ointment was proven effective in accelerating wound healing in white rats with stage II or partial thickness wounds. The study showed that the group of rats receiving EEBK with a concentration of 12% experienced the fastest wound healing, with wound diameter closure within 10 days. The effectiveness of EEBK is due to the tannin content that functions as an astringent and antimicrobial, which increases the rate of epithelialization, shrinks pores, and stimulates the formation of capillaries and fibroblasts. In addition, saponins in EEBK act as antioxidants, antimicrobials, and promoters of collagen formation, which support the wound healing process. Flavonoids in EEBK also help prevent oxidation processes that damage tissues. The results showed that 12% EEBK ointment had an effectiveness equivalent to the positive control of 10% Betadine ointment, while 8% and 10% EEBK concentrations showed a slower healing process (Ginting et al. 2022). In addition, another study found that ethanol extract of kecombrang flower was effective in accelerating wound healing with a concentration of 15%, namely wound healing occurred in 8 days compared to the positive control of povidone iodine which took 10 days for wound healing. The difference is in the part of the extract taken, in the previously mentioned study using extract from kecombrang fruit while this study used ethanol extract from kecombrang flowers. However, the compound content is not much different. Kecombrang flowers also contain flavonoids as antioxidants that prevent cell oxidation, so cell damage is inhibited. In addition, flavonoids also act as anti-inflammatory which will accelerate epithelialization. In addition to flavonoids, there are also tannin compounds that act as antibacterial and astringent to accelerate the shrinking of pores in wounds (Sagala et al. 2016)

Caspase-3 Neutralizers and IL-1ß Targets in Sepsis Conditions

In sepsis, endothelial cell dysfunction may occur, leading to the development of multiorgan disorders. The release of proinflammatory cytokines such as TNF-a, IL-1, and IL-6 from macrophages can exacerbate systemic infection and endothelial dysfunction in sepsis (Dolmatova et al. 2021). Endothelial apoptosis is also involved in the process of endothelial dysfunction characterized by increased caspase-3. IL-1ß is known to cause vasodilation and hypotension and increase integrin synthesis, leading to leukocyte attachment and also stimulates the expression of intercellular adhesion molecules to increase neutrophil adhesion to endothelial cells. This can trigger endothelial leakage and lead to septic shock. Thus, caspase-3 and IL-1ß can be markers of endothelial dysfunction in sepsis. Kecombrang fruit extract contains bioactive compounds such as vanillic acid which plays a role in fighting inflammation. In addition, flavonoids from kecombrang fruit extract have anti-inflammatory effects and inhibit endothelial cell apoptosis (Wardani 2020; Nurhayatun et al. 2023). Intervention of ethanol extract of kecombrang fruit is effective in reducing caspase-3, with the best results in the group of rats treated with extract 5 days before lipopolysaccharide (LPS) induction. Ethanol extract of kecombrang fruit can also reduce IL-1ß levels and is more effective when given before LPS induction. Thus, kecombrang extract can be used as an adjuvant therapy in the treatment of sepsis but further research is needed to determine the effective dose (Nurhayatun et al. 2023).

Antioxidant Effects

Antioxidants are compounds that neutralize free radicals. Free radicals can cause oxidative stress which contributes to various diseases including diabetes. Oxidative stress occurs when the production between free radicals and the antioxidant system is not balanced. Kecombrang flower extract (Etlingera elatior) has antioxidant compounds such as flavonoids, phenolics, and anthocyanins that have the potential to reduce oxidative stress and have antidiabetic effects. In the research of Noordin et al. (2022), kecombrang flower extract was able to reduce malondialdehyde (MDA) levels as a marker of lipid peroxidation, increase antioxidant enzyme activity (SOD, CAT, and glutathione, and total antioxidant capacity (T-AOC). As an antidiabetic, kecombrang flower extract can significantly reduce fasting blood glucose levels in type 2 DM model rats. Active compounds such as cyanidin-3-O-glycosides belonging to the

flavonoid family and anthocyanin subgroup can inhibit α-glucosidase and α-amylase enzymes, which reduces postprandial glucose utilization (Noordin et al. 2022).

In the research of Wardani et al. (2022), kecombrang flower extract was shown to have potential as a hypolipidemic agent in obese Wistar rats. The administration of this extract is able to suppress the weight gain of rats thanks to the content of secondary metabolites, such as phenols, alkaloids, saponins, tannins, flavonoids, and steroids. Compounds that play a role in antiobesity activity include flavonoids, saponins, and steroids. Flavonoids in cockscomb flower extract act as pancreatic lipase inhibitors, which decrease appetite and reduce fat intake. As a result, the formation of free fatty acids from the catalysis reaction of triglycerides by pancreatic lipase is inhibited. Flavonoids can also reduce fat accumulation in the liver, inhibit glucose absorption, and prevent the breakdown of polysaccharides into monosaccharides. The steroids in this extract work to reduce cholesterol absorption in the intestines, resulting in reduced cholesterol levels in the blood. Decreased cholesterol in the bloodstream helps prevent the accumulation of fat in organs, thereby reducing the risk of obesity. Research shows that the administration of methanol extract of kecombrang flowers at a dose of 100 mg/kg body weight significantly reduces total cholesterol, triglyceride (TG), LDL, and increases HDL levels in obese rats. This effect is caused by antioxidant compounds such as polyphenols, flavonoids, alkaloids, tannins, saponins, and steroids contained in the extract (Wardani et al. 2022).

Reduced Nephrotoxic Effects

The kidneys have vital functions in the human body such as filtering blood and toxic substances, excreting waste substances through urine, regulating acid-base balance, and controlling body fluid volume. Drugs such as aminoglycoside antibiotics, immunosuppressant drugs, chemotherapy drugs, and NSAIDs can aggravate the work of the kidneys, making them vulnerable to injury to renal tubular epithelial cells. Renal cell damage can also be induced by CCl4 (carbon tetrachloride). CCl4 will be metabolized in the liver by P450 enzymes (CYP2E1) and will be converted to CCl3- (trichloromethyl radical) which is highly reactive and can cause cellular damage. When the body lacks antioxidants, the body's ability to fight free radicals will be reduced, making renal tubular epithelial cells susceptible to oxidative damage and leading to cellular destruction. Some natural resources contain high amounts of antioxidants, one of which is the Etlingera elatior plant. This plant contains flavonoids, especially quercetin and kaempferol, which act as antioxidants by binding free radicals to inhibit kidney damage. In a study using male Wistar rats induced by CCl4 (carbon tetrachloride), ethanol extract from E. elatior fruit was found to have activity to neutralize toxic effects on the kidneys by reducing urea and creatinine levels to normal limits and protecting renal tubular cells (Fristiohady et al. 2020).

The limitation of this study is that most of the existing research articles focus on the flowers and leaves of kecombrang, while research on the fruit, rhizome, or other parts of this plant is still limited. In addition, most studies only evaluate the pharmacological effects in the short term, without considering the potential toxicity or long-term side effects of using kecombrang extracts and there have not been many studies using animal models other than Wistar rats or mice or in vivo studies in humans.

4. CONCLUSION

Kecombrang has various benefits according to the active substance content in it, especially those discussed in this literature review, namely as anti-inflammatory and antioxidant. Kecombrang acts as an anti-inflammatory by reducing gastric ulcers and healing wounds with tannin and flavonoid content, reducing nephrotoxicity with flavonoid content, especially quercetin and kaempferol which can reduce urea and creatinine levels to normal limits and protect kidney tubules, neutralize caspase-3 and IL-1ß in septic white mice. Kecombrang as an antioxidant works by reducing free radicals in the body, so it can also be used as an antidiabetic and hypolipidemic. To prove the clinical benefits of kecombrang, further comprehensive studies are needed to analyze the composition of other active substances in kecombrang.

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