CHAYOTE (SECHIUM EDULE) AS AN ANTIOXIDANT TO REDUCE OXIDATIVE STRESS DUE TO PARAQUAT EXPOSURE: SYSTEMATIC LITERATURE REVIEW

Maria Eka Patri Yulianti[1,2*], Endang Mahati[1,3], Ari Suwondo[1,4], Udadi Sadhana[1,5], Neni Susilaningsih[1,6], Meiny Suzery[1,7], Suhartono[1,4]

*Corresponding Author E-mail: mariaekapy18@gmail.com

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Abstract

Oxidative stress is a condition caused by an imbalance between the production of free radicals and the antioxidant defense system in the body. One of the free radicals that is harmful to the body is exposure to paraquat, which enters the body in several ways, namely through ingestion, broken skin, and inhalation. Paraquat poisoning causes various diseases, damage to cells, tissues, liver, kidneys, heart, and degenerative conditions such as aging, arthritis, cancer, and others. The large amount of free radicals in the body cannot be neutralized by endogenous antioxidants, so the body needs a supply of exogenous antioxidants. The chayote has secondary metabolites such as alkaloids, saponins, cardenolides/bufadienol, folifenol, flavonoids, vitamin C and minerals that are beneficial to the body. As a free radical neutralizer, the role of exogenous antioxidants such as chayote in health is very large. This study attempts to relate the content of chayote as an exogenous antioxidant to paraquat exposure by PE Search studies through the PubMed, Scopus, and ScienceDirect databases using keywords based on the PICO formulation (Population, Intervention, Comparison, Outcome). After going through the PRISMA flow selection stage, 15 of the most suitable literature was obtained. Studies were selected using multiple inclusion and exclusion criteria, full articles were screened, and evaluated studies were appraised using an evidence-based critical appraisal checklist.

Keywords: antioxidant, chayote, free radicals, paraquat.

[1]Doctoral Study Program in Medical and Health Sciences, Faculty of Medicine, Diponegoro University.
[2]Department of Biology, Faculty of Medicine and Health Sciences, University of Bengkulu
[3]Department of Pharmacology and Therapy, Faculty of Medicine, Diponegoro University
[4]Faculty of Public Health, Diponegoro University
[5]Department of Anatomical Pathology, Faculty of Medicine, Diponegoro University
[6]Department of Anatomy of Histology, Faculty of Medicine, Diponegoro University
[7]Department of Chemistry, Faculty of Science and Mathematics (FSM) Diponegoro University.

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1. Introduction

Herbicide poisoning is a public health problem in developing countries, with an estimated 300,000 deaths in the Asia-Pacific region. Inappropriate use of paraquat can cause a variety of health problems, including damage to the heart, kidneys, lungs, adrenal glands, central nervous system, and can cause damage to the liver (1). As a regulator of metabolism, the liver functions to metabolize chemical substances that enter the body. Liver damage can occur when the chemicals in paraquat are converted to active toxins in the liver, causing hepatocyte swelling, hepatic sinusoidal congestion, fibrosis, and necrosis (2). High antioxidant status is usually followed by a decrease in MDA (malondialdehyde) levels. High MDA levels are influenced by the level of lipid peroxidation, which indirectly indicates a high number of free radicals and an oxidation process in the cell membrane (3). Other markers of oxidative stress can be seen in increased levels of nitric oxide (NO) in the body; NO is produced enzymatically from L-arginine by NO synthase, and paraquat directly or indirectly induces NO synthase, which mediates nitric oxide. Reactive oxygen and nitrites that are formed will cause toxicity to the organs of the body. As a result, paraquat may cause oxidative damage to fats, proteins, and DNA (1). Another marker of oxidative stress is the formation of DNA adducts (8-OHdG). 1vReactive oxygen species can interact with biomoleculars such as DNA, causing DNA damage if not repaired, which can lead to carcinogenicity. Under conditions of oxidative stress, there is a decrease in the enzyme systems superoxide dismutase (SOD) and glutathione peroxidase. When the production of free radicals exceeds the ability of endogenous antioxidants to neutralize them, the excess free radicals have the potential to cause cell damage. Thebody has endogenous antioxidants or enzymatic antioxidants to fight free radicals that have the potential to disrupt the balance of body functions. The superoxide dismutase (SOD) enzyme is the first line of defense against the activity of reactive oxygen compounds (ROS) (4).

Siamese pumpkin (Sechium edule) is a plant species belonging to the Cucurbitaceae family (5). The results of TLC and phytochemical screening showed that the ethanolic extract of chayote (Sechium edule) contains alkaloids, saponins, cardenolin/bufadienol, and flavonoids. In this case, the antioxidants produced by Sechium edule, such as polyphenols and flavonoids, can scavenge free radicals, thus expected to prevent oxidative stress (6). The results of the research conducted (7), proved that the chayote fruit contains several substances, such as sodium, iron, potassium, phosphorus, calcium, fat, protein, carbohydrates, fiber, and contains a lot of water. The study results showed that chayote extract at a dose of 0.75 g/kg BW was able to reduce glucose levels better than distilled water, but it was not more effective than metformin (8). A study (Soyadesita et al., 2013) reported that administration of chayote (Sechium edule) juice at a dose of 121 mg/kg BW had an effect, although not significant, on streptozotocin-induced malondialdehyde (MDA) levels in the pancreas and liver of mice (Mus musculus). In another study, administration of Siamese pumpkin extract (Sechium edule) at a dose of 200 mg/kg to rats with kidney damage resulted in a significant decrease in creatinine, urea, and uric acid, accompanied by an increase in the histologic status of tubules and glomeruli (10).

Based on some of the above descriptions and supported by several scientific studies, it proves that chayote has so many benefits and is safe, inexpensive and easy to obtain. Indonesians, from children to adults, on average like this fruit. Siamese pumpkin is effective as an antioxidant needed by the body. It has the effect of reducing free radicals so that the aging process can be prevented or delayed.

2. Reference Search Method

The preparation of this article is based on a systematic review or systematic flow. The search strategy uses an electronic database obtained from the site PubMed, Science Direct, and Scopus based The PICO (Population, Intervention, Comparison, Outcome) that was determined is P: All research subjects, I: Exposure to paraquat, C: Giving chayote extract, O: Impact of giving paraquat.

The collected and collected literature is then selected through systematic steps, including removing duplicate literature, both titles and abstracts. Inclusion criteria in filtering the data according to keywords, namely antioxidants, chayote, free radicals, paraquat, journal of the last 10 years. Then, the journal is read and manually reviewed again by selecting journals that discuss the compounds contained in chayote (flavonoids, tannins, vitamin C, and other compound contents) that have a relationship with oxidative stress. The exclusion criteria were journals that discussed oxidative stress not caused by paraquat exposure.

The literature search was carried out in stages, as shown in the PRISMA Flowchart 2020 diagram (figure 1). searches obtained using keywords obtained 110 literatures (PubMed 70 literatures, Google Scholar 29 literatures, and Scopus 11 literatures). The results of the search were checked for duplication using the Mendeley application and found 1 duplication of literature from the three databases. Then a filter was carried out in the form of literature for the last 10 years and can be accessedin its entirety or open access/full text, and 27 literatures were obtained. After that, researcharticles were filtered and 19 literatures were obtained. Then it was reviewed based on abstracts and titles based on inclusion criteria through the manual method to 16 journals.

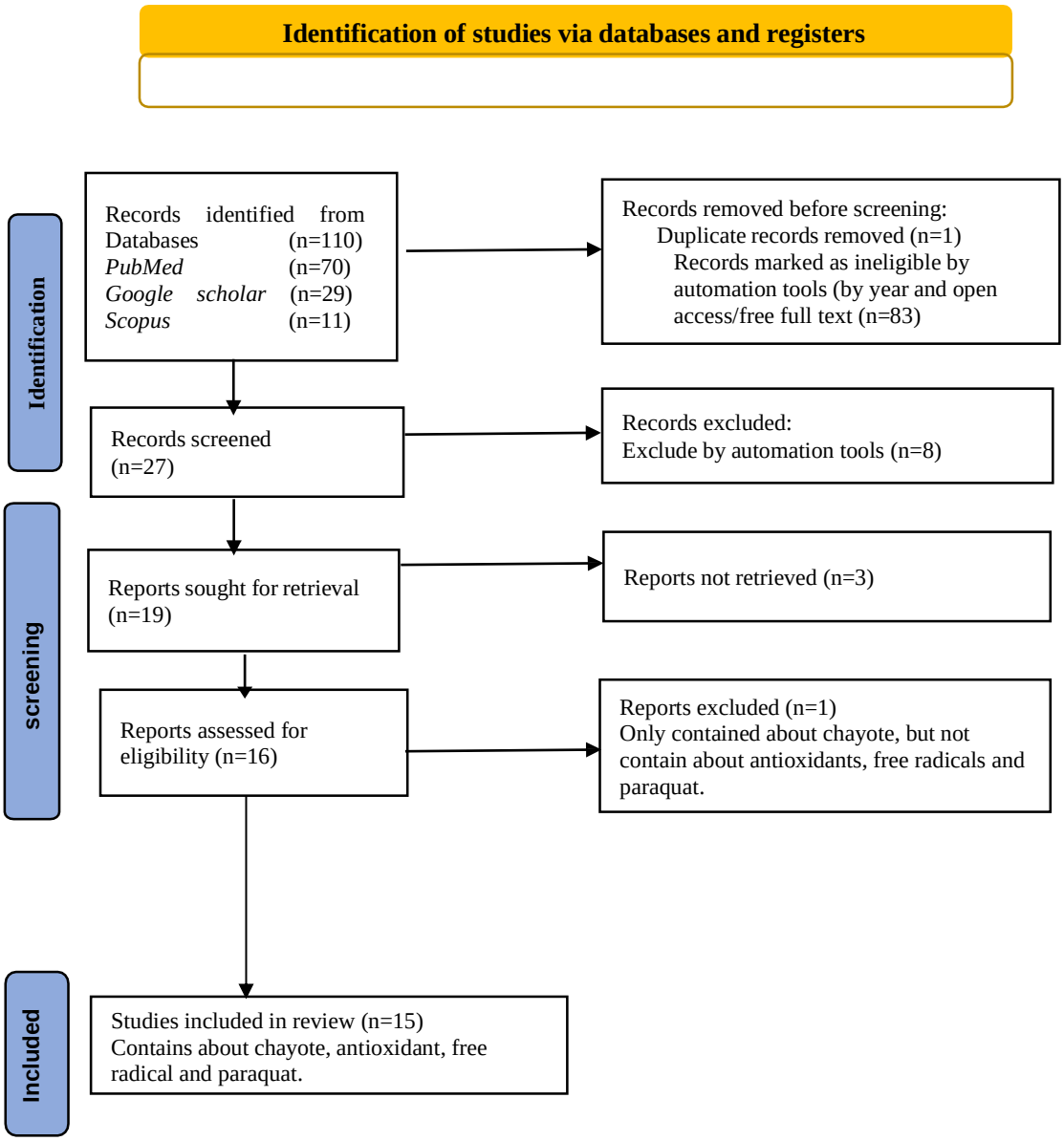

Figure 1. PRISMA Flow Chart, 2020

3. Results

Several previous studies have found that chayote extract (Sechium edule) as occurs in the body through various pathways and mechanisms. We conclude and select several main roles of chayote on paraquat, which are also listed in Table 1.

Table 1 Systematic Review analysis results

No	Name of Researcher / Year	Research title	Design	Compare	Results
1.	(Firdous Mumtaz et al., 2013)	Effect of Sechium edule on chemically induced kidney damage in experimental animals.	Experimentall using a post test only randomized controlled group design	Reported potent antioxidant flavonoids suchas C-glycosyl and O-glycosyl flavones present in S. edule have nephroprotective activity against gentamicin-induced nephrotoxicity	S. edule extract (200 mg/kg) significantly ($p<0.001$) decreased blood urea, blood urea nitrogen and serum creatinine levels and also significantly ($p<0.001$) increased serum total protein levels. Serum uric acid levels were also significantly decreased ($p<0.001$) indiabetic rats treated with the extract (200 mg/kg). The extract also improves kidney histology. The results showed that aqueous extract of S.edule leaves had a protective effect against gentamicin- and potassium dichromate-induced nephrotoxicity and streptozotocin-induced diabetic nephropathy in experimental animals.
2.	(Siahaan et al., 2020)	The Effect ofEthanol and Ethyl Acetate Fraction of Chayote fruit (Sechium edule Jacq. Swartz) on the Oxidative Stress and Insulin Resistance of Male White Rat Model Type 2 Diabetes Mellitus	Experimentall using pre and post randomized controlled group design.	Ethanol extractand chayote fractionation can increase SOD levels anddecrease MDAlevels in Metformin-inducedDM rats.	Treatment of chayote extract of ethyl acetate fraction (45 mg/kg bw). The lowest blood sugar level in the group, with an average 2-hour glucose load of 112.5 ± 27.00 was found in group G which was treated with chayote ethanol extract (150 mg/kg body weight). The highest SOD in the squash extract treatment group was 1.27 ± 0.20, found in group H with 45 mg/kg ethyl acetate treatment, and the lowest MDA content was 0.86 ± 0.70 in group H with 45 mg/kg ethyl acetate treatment The lowest fasting blood glucose spectrophotometer level was 150.54 ± 17.24 mg/dl in group K treated with metformin, followed by 155.16 ± 31.92 mg/dl in group K treated with 45 mg/kg ethanol. The highest insulin level was 6.14 ± 0.71. Ethanol extract and chayote fractionation can increase SOD levels and decrease MDA levels

					in Metformin-induced DM rats.
3.	(Aguiñiga-Sánchez et al., 2020)	Phytochemical Analysis and Antioxidant and Anti-Inflammatory Capacity of the Extracts of Fruits of the Sechium Hybrid.	Define antioxidants and the anti-inflammatory capacity of Sechium hybrid fruit extract in vitro and in vivo.	Reduced levels of tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ),and interleukin-6 (IL-6) but increased levelsof interleukin-10 (IL-10) and glutathione peroxidase.	Phytochemical analysis using HPLC showed that the Sechium hybrid extract had at least 16 phenolic compounds; galanin, naringenin, phloretin and chlorogenic acid are the most abundant. In vitro tests, this extract inhibited the activity of 2,2-diphenyl-L-picrylhydrazyl (DPPH) and protected the cell membrane model phospholipid dimyristoylphosphatidylethanol amine (DMPE) from hypochlorous acid (HClO)-mediated oxidation. In vivo, it was identified that the most abundant metabolite in the extract entered the bloodstream of the treated mice. On the other hand, the extract reduced the levels of tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), and interleukin-6 (IL-6) but increased the levels of interleukin-10 (IL-10) and glutathione peroxidase. These findings suggest that intake of Sechium hybrid fruit leads to antioxidant and anti-inflammatory effects in a mouse model. Therefore, these results support the possibility of exploring the clinical effects of this hybrid in humans.
4.	(Fadliya et al., 2018)	Analysis of vitamin C and protein on Chayote (Sechium edule) fruit seeds.	Quantitative Analysis Methods.	The vitamin C concentration of old chayote seeds obtained was 56.542 mg/L, so that the vitamin C content of old chayote seeds was 0.56% in 0.025gram sample.	Testing using a spectrophotometer, UV-Vis, vitamin C levels were 0.56% and protein levels with the Kjeldahl method were 0.81% and 0.11%
5.	(Senoadji, 2019)	The effect of Sechium edule pumpkin on the reduction of wistarrated blood glucose levels induced	Experimentalus ing pre and post randomized controlled group design.	Calcium plays arole in the process of insulin secretion. Glucose metabolis m induced by glucokinas e causes	Chayote extract at a dose of 0.75 g/kg bw has the ability to reduce glucose levels, but its effectivenessis not better than metformin.

		with alloxan.		changesin the ratio of ATP/ADP andthis causes the closing of potassium ion channels and depolariza-tion of pancreatic βcells occurs. There is the activation of calcium ion channels and these ions will enter the β-celland then intracellula r calcium stimulates insulin secretion fromits granules.	
6.	(Lage et al., 2019)	Analysis of potassium, Magnesium and Sodium content in Chayote (Sechium edule Sw.) from sedoa, North Lore District, Poso.	Analysis Method Quantitative.	In addition to fiber content and its benefits, Chayote is rich in minerals that are beneficial to the body when consumed in sufficient quantities. Minerals are one of the nutrients needed by the body. Such as potassium, magnesium, sodium and others so on which are	Based on the research conducted, it can be concluded that the average potassium content in old chayote pulp is 80.059 mg/100g; young chayote flesh, namely 45.431 mg/100g; Old chayote seeds are 65.287 mg/100g and young chayote seeds are 73.014. The average content of magnesium levels in old chayote fruit flesh, namely 47.327 mg/100g; young chayote meat, namely 74.324 mg/100g; Old chayote seeds are 57.658 mg/100g and young chayote seeds are 58.529 mg/100g. While the average content of sodium content in the old chayote pumpkin flesh is 61.032 mg/100g; young chayote flesh, namely 49.936 mg/100g; Old chayote seeds are 61.101 mg/100g and

				macro minerals	young chayote seeds are 71.621 mg/100g
7.	(Hu et al., 2018)	Therapy with high-dose long-term antioxidant free radicals for severe paraquat poisoning: A pilot study	Experimental using a randomized controlled group post test design	Antioxidants directly combat ROS-induced cells damage. Numerous cell and animal experiments have demonstrated that antioxidants can reduce PQ-induced ROS formation, reduce cell death and protect the function of the lungs, liver, and kidneys of patients.	The main pathogenesis of PQ poisoning is the induction of ROS and the mass production of inflammatory cytokines. Acute lunginjury in patients and pulmonary fibrosis in later life are the main causes of death in patients. To the best of our knowledge, it was proposed in this study for the first time that high-dose long-term antioxidant therapy is a specific treatment for serious PQ poisoning. The results prove that this therapy significantly increases patient survival rates, prevents pulmonary fibrosis in advanced stages, and improves the lung and liver function ofpatients.
8.	(Arista-Ugalde et al., 2022)	Antioxidant and anti-inflammatoryEffect of the Consumptionof Powdered Concentrate ofSechium edule var. nigrum spinosum in Mexican Older Adults with Metabolic Syndrome	Experimental using pre and post randomized controlled group design	Compounds in Sechium edule have antioxidant, anti-inflammatory, hypotensive effects, protect against DNA damage, and have significant effects on Controlling metabolic syndrome in older adults.	The results showed that the composition of chayote powder given to elderly adults with metabolic syndrome has effects ashypoglycemic, hypotensive, anti-inflammatory antioxidants caused by OA.
9.	(Daulay et al., 2021)	Antioxidant Activity Test of Chayote (Sechium edule (Jacq.) Swartz) Ethanol Extract using	Define antioxidantsand prevent oxidation ofthe Ethanol Sechium extract by the DPPH measurement	The antioxidant activity found in chayote can prevent the oxidation of a molecule, thereby	The results of the phytochemical screening of chayote ethanol extract contained chemical compounds of alkaloids, flavonoids, saponins, tannins, and

		DPPH Method	method	stopping the chain reaction of free radicals and maintaining the work systemin the body	glycosides.
10	(Muhartono et al., 2015)	Effect of oral paraquat dichloride herbicide on the liver of white rats.	Experimental using a randomized controlled group post test design	There is the effect of giving herbicides paraquat dichloride per−oral against swelling hepatocytes in male white rats (Rattus norvegicus). Sprague Dawley strain	The results showed that the averagescore for hepatocyte swelling and sinusoid congestion increased. Oraldoses of Paraquat dichloride to rat liver at doses of 25,50,100 and 200mg/kg BW, for 2 days orally
11	(Muhartono et al., 2016)	Risk of Paraquat Dichloride Herbicide to the Kidney of Spraque Dawley White Rats	Experimental using a post test only randomized controlled group design	The kidneys experience damage to the glomeruli and tubules that are reversible and irreversible	The results showed that the averagescore of kidney damage was K1: 0,K2: 1.8, K3: 2.0, K4: 3.6, K5; 4,4. The data obtained was tested with the Kruskal Wallis test and found asignificant difference (p=0.001). In conclusion, the oral administration of the herbicide Paraquat dichloridegroup can damage the kidneys of male white rats (Rattus norvegicus) Spraque Dawley strain
12	(Yulianti, 2020)	Effect of SOD levels in Paraquat-induced mice.	Experimen-tal using pre and post randomized controlled group design.	Giving paraquat s will result in the formation ofROS, causing oxidative stress.	There was a decrease in SOD serumlevels in Paraquat-induced mice
13	(Parra et al.,2018)	Phytochemi -cal characteriza tion and	in vitrostudies	Apigenin 7-O-rutinoside and luteolin	Variants of Sechium edule grown inCosta Rica have high levels of antioxidants

		antioxidant profile of Sechium edule (Jacq) Swartz Cucurbitac ea) varieties grown in CostaRica.		7-O-rutinoside was identified in thesamples and their antioxidant activity was confirmed	that can reduce free radicals which can lead to the formation of lipid peroxidation. In addition, the oxidation-reduction potential determined by the electrochemical method indicated the presence of flavonoids, which was confirmed by isolation apigenin 7-O-rutinoside and luteolin 7-O-rutinoside.
14	(Elenga et al., 2018)	Clinical features and prognosis of paraquat poisoning in French Guiana	Cross-Sectional Design	No treatment has proven its effectivenes s indeath. Preventive administrat ion of activated charcoal withinthe first hour after taking paraquat is Important	French Guiana has the highestparaquat poisoning rate in theEuropean Union, with a high fatality rate of 52%. The mainfactor affecting the patient's prognosis is the consumption number of paraquats. No treatmenthas proven its effectiveness in death. Preventive administration of activated charcoal within the first hour after taking paraquat is important.
15	(Vieira et al., 2019)	Chayote (Sechium edule): A review of nutritional composition, bioactivities and potential applications.	Systematic Literature Review	Reducing levelsof urea, nitrogen, uric acid and creatinine, Increasing total protein levels inthe kidneys	Chayote has a high nutritional content including thiamine, riboflavin, niacin, ascorbic acid, calcium, and many more. Chayote has a low molecular weight trypsin inhibitor, which can be used in a synthesis program for the development of new protease inhibitors for biological purposes by modifying the amino acid sequence.

Flavonoids in S. edule have nephroprotective activity

The results of a study conducted by Firdous Mumtaz et al., 2013 showed that the extract S. edule water has nephroprotective activity against gentamicin-induced nephrotoxicity which may be due to the antioxidant potential of reported flavonoids such as C-glycosyl and O-glycosyl flavone present in S. edule leaves (10).

Ethanol extract and chayote fractionation reduce MDA levels

Ethyl acetate fraction in chayote fruit can inhibit the performance of the pancreatic lipase enzyme as an enzyme that plays an important role in fat metabolism and fat absorption. In addition, Ethyl acetate fraction also plays a role in inhibiting α-glucosidase thereby reducing carbohydrate absorption. Ethyl acetate fraction of 45 mg/kg bw can increase SOD endogenous antioxidant activity whilereducing MDA levels in Metformin-induced

DM rats so as to reduce oxidative stress (13).

Vitamin C in chayote fruit
Analysis of vitamin C levels in old chayote seeds (Sechium edule) was determined using UV-Vis spectrophotometry. The absorbance value obtained is entered into the standard curve equation (linear regression) of vitamin C to determine the concentration of vitamin C in the sample using the formula.

The vitamin C concentration of old chayote seeds obtained was 56.542 mg/L, so that the vitamin C content of old chayote seeds was 0.56% in 0.025 gram sample. Vitamin C is easily oxidized because the compound contains a hydroxy functional group (OH), which is very reactive in the presence of a hydroxy group oxidizing agent which will be oxidized to a carbonyl group (7).

Siamese pumpkin fruit extract (Sechium edule) as a lowering of blood glucose levels
Flavonoids present in chayote work as inhibitors of important enzymes that play a role in breaking down carbohydrates into monosaccharides that can be absorbed by the intestine, namely alpha amylase and alpha glucosidase enzymes (8).

Long-term anti-oxidant therapy for paraquat poisoning affects
Research conducted by Hu et al., 2018 states that the main pathogenesis of paraquat poisoning is the induction of ROS and the mass production of inflammatory cytokines. Acute lung injury in patients and pulmonary fibrosis are the main causes of death in patients. High-dose long-term antioxidant therapy is the specific treatment for serious PQ poisoning. The results prove that this therapy significantly increases the patient's survival rate, prevents pulmonary fibrosis at an advanced stage, and improves the patient's lung
and liver function (12).

Anti-oxidant and anti-inflammatory in metabolic syndrome
The bioactive compounds present in S. edule are able to modulate the oxidant/antioxidant balance towards a less oxidized state in patients with metabolic syndromes, which supports the recommendation to consume S. edule concentrate supplements as an adjunct to treatment. control of oxidative stress in older adults with the metabolic syndrome (14).

Ethanol extract in chayote as an antioxidant
Research conducted by Daulay et al., 2021 states that the ethanol extract of chayote contains secondary metabolites, namely alkaloids, flavonoids,tannins, saponins, and glycosides. The FTIR results of the ethanol extract of chayote have the functionalgroups OH, CH, C=C, C≡C, CN and CO. Theresults of examining antioxidant activity with DPPH for chayote ethanol extract had IC50 values: 1281.098 and 847.5 µg/ml and vitamin C of 18.623 µg/ml. Its antioxidant activity is relatively weak because the inhibitory concentration (50%) is greater than 150 µg/ml (15).

Effect of oral paraquat dichloride herbicide on the liver of white rats.
Sinusoidal congestion, which worsened with increasing doses of paraquat dichloride in each rat in each group, was caused by the use of the herbicide paraquat dichloride, which is a toxic substance that can interfere with circulation, depriving cells of oxygen and nutrients. Congestion is a state of increased blood volume due to dilated blood vessels (2).

Effect of SOD levels in Paraquat-induced mice.
Research conducted by Yulianti, 2020 states that adose of 20 mg/kg BW of mice can increase the levels of the superoxide dismutase (SOD) enzyme in Swiss Webster mice induced by paraquat. Giving paraquat will result in the formation of ROS, causing oxidative stress. Disturbing the balance of endogenous anti-oxidants, especially SOD, so that SOD levels decrease. Administration of B. makassar extract which is rich in vitamin C, phenol, flavonoids, and tannins can increase serum SOD levels of paraquat-induced mice. The content of this active compound has the potential to neutralize free radicals and prevent oxidative stress (16).

4. Discussion

The herbicide paraquat is a toxic substance. While it may be beneficial in agriculture, it can also have a negative impact on public health. Pesticide residues are certain substances present in agricultural products or animal feed as a direct or indirect result of the use of pesticides. Paraquat is used as a herbicide to control the growth of weeds in agricultural or plantation areas under the brand name Gramoxone. Its herbicidal properties were discovered in 1955 and patented in England in 1962. Paraquat was first used on rubber plantations in Malaysia in 1961. Paraquat has been used in more than 120 countries and is currently the third best-selling pesticide in the world (17). In developing countries, paraquat is often used freely without regard to hazards and warning labels, resulting in high exposure rates. Exposure to herbicides either by inhalation or ingestion can cause poisoning and is potentially harmful to humans, causing cancer, birth defects, genetic mutations, and nerve damage (17). Paraquat is a type of herbicide most commonly used in developing countries, including Indonesia. Paraquats are widely used in plantations and agriculture. Improper use of paraquat without heeding the warning label can lead to poisoning (18). Paraquat that enter the body is absorbed and

distributed through the blood vessels to all organs. Paraquat disrupts the body's biochemical metabolic processes, causing cell death and multi-organ failure. Paraquat can also alter the levels and activity of several enzymes found in the blood, liver, and kidneys (19).

Paraquats induce toxicity through their ability to affect redox cycles and generate reactive oxygen species that cause tissue damage. In the human body, paraquat is reduced by NADPH to a reduced radical form. Reduced paraquat reacts with oxygen to produce superoxide anion, a class of reactive oxygen species in the human body. An increase in the number of reactive oxygen species that is not matched by an increase in antioxidants from the body causes oxidative stress (20). Other previous research was conducted on experimental animals in Lampung City, entitled Oral paraquat dichloride herbicide against rat liver at doses of 25, 50, 100 and 200 mg/kg bw, for 2 days orally. The research results show that the mean scores of hepatocyte swelling and sinusoidal congestion increased. In previous research on the risk of the herbicide paraquat dichloride on the kidneys of White Sprague-Dawley rats, the results of the study proved that the mean score was an increase in kidney damage in White Sprague-Dawley rats (2). Antioxidants are substances that the body needs to neutralize free radicals and prevent the damage they cause. Antioxidants stabilize free radicals by making up for the lack of electrons they possess and inhibiting the chain reaction of free radical formation that can cause oxidative stress. Oxidative stress is an imbalance between free radicals (pro-oxidants) and antioxidants caused by two general conditions: a lack of antioxidants and an excess production of free radicals. The human body naturally produces endogenous antioxidants that act as electron donors for ROS to inhibit the negative effects generated by ROS. Due to the large accumulation of free radicals that exist in the body under certain conditions (22).

An explanation of the benefits of the antioxidant content found in chayote:

Flavonoids

Flavonoids act as antioxidants by donating hydrogen atoms or by means of their ability to attach to metalsin the form of glucosides or in a free form called aglycones (23). Flavonoids inhibit enzymes responsible for the production of superoxide anion radicals, such as xanthine oxidase and protein kinase. Flavonoids also show inhibition of cyclooxygenase, lipoxygenase, microsomal monooxygenase, glutathione S-transferase, mitochondrial succinate oxidase, and NADH oxidase, which are all involvedin the formation of ROS (23). Flavonoids are rich antioxidants because they work by scavenging free radicals and ROS, such as superoxide anion radicalsand hydroxyl free radicals. Flavonoids can prevent damage caused by free radicals in several ways. Oneway is to destroy free radicals directly. Flavonoids are oxidized by radicals, producing more stable and less reactive radicals. Flavonoids stabilize reactive oxygen compounds by reacting with the reactive array of these radicals (24).

Polyphenols

Polyphenolic compounds are powerful antioxidants and safer than synthetic antioxidants. Phenol compounds act as antioxidants through reactions with various free radicals. The mechanism of antioxidant activity of a phenolic compound can be achieved through 3 mechanisms, namely: 1) single electron transfer by means of proton transfer (25); 2) transferof electrons by sequential loss of protons (26); 3) metal chelation transitions (27).

Saponins

The mechanism of saponin antioxidant activity is by restoring homeostasis gluthation (GSH). Saponins can also enhance cell survival rates by activating the mitogen-activated protein kinase (MAPK). Therefore, saponins may function as inhibitors of oxidative cellular damage by inhibiting cell apoptosis induced by oxidative stress in monogastric animals (28).

Tannins

Tannin is a polyphenol compound that has a large molecular weight consisting of hydroxyl and carboxyl groups. Tannin compounds consist of two types, namely condensed tannins and hydrolyzed tannins (29). Tannins are active compounds of secondary metabolites that are known to have several roles, namely as anti-diarrheal, antibacterial , and antioxidant.

The role of tannins as antioxidants is that tannins work by directly binding to these free radicals and also play an important role as chelating metals, especially iron and copper. Metal ions can increase reactive oxygen free radicals from the Fenton reaction or the Haber-Weiss reaction (29).

Vitamin C

Vitamin C is able to remove reactive oxygen compounds from neutrophil cells, monocytes, lens proteins, and retina. Also can react with Fe-ferritin. Outside the cells, Vitamin C is able to remove reactive oxygen compounds, prevent LDL from being oxidized, transfer electrons into oxidized tocopherols and absorb metals in the digestive tract. As an antioxidant, Vitamin C can directly react with superoxide anions, hydroxyl radicals, singlet oxygen, and lipid peroxide. As a reducing agent, vitamin C will donate an electron to form semidehydroascorbate, which is not reactive, and then undergo a disproportionation reaction to form dehydroascorbate, which is unstable. Dehydroascorbate will be degraded to form oxalic acid and threonic acid.

No.1 2O-2 + 2H+ + Ascorbate → 2H2O2 + Dehydroascorbic acid
No.2 H2O2 + 2H+ + Ascorbate → 2H2O2 + Dehydroascorbic acid

note:
No. 1 shows the reaction of ascorbic acid with superoxide
No. 2 shows the reaction with hydrogen peroxidecatalyzed by the enzyme ascorbate peroxidase.

Ascorbate can directly scavenge oxygen-free radicals, either with or without an enzyme catalyst. Indirectly, ascorbic acid can dampen activity by changing reduced tocopherol (31).

Alkaloids
Alkaloids can inhibit the activation of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase so that the production of superoxide and other ROS is inhibited, as well as help activate nuclear factor erythroid-2 related factor 2 (Nrf2), which acts as a protective gene that can neutralize ROS (32). According to a study conducted by Yulianti, et al. (20-22), chayote (Sechium edule) fruit extract can reduce blood serum MDA levels in white rats caused by hypercholesterolemia. This is related to the explanation of the antioxidant content contained in Sechium edule fruit extract and its mechanism of action that was described previously (34).

Potassium
The benefits of potassium in chayote can reduce renin secretion, which causes a decrease in angiotensin II so that vasoconstriction of blood vessels decreases and decreases aldosterone so that absorption of sodium and water into the blood decreases. Potassium also has the effect of a Na-K pump, namely potassium is pumped from the extra cellular fluid into the cells and sodium is pumped out, so that potassium can lower blood pressure. Siamese pumpkin contains saponins, polyphenols and flavonoids (35).

5. Conclusion

The conclusion from writing this systematic review based on the 15 studies reviewed is that chayote is high in antioxidants, so it is needed by the body to reduce free radicals as an endogenous antioxidant. The accumulation of free radicals in the body, one of which is caused by exposure to paraquat, causes oxidative stress. To neutralize free radicals, the body needs a supply of endogenous antioxidants. The approach used in conducting experimental research in general is through 2 experimental methods using statistically based experimental animals and in vitro and in vivo.

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