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Phytochemistry and Anti-Inflammatory Properties of *Muntingia calabura* L. as a Medicinal Plant: A Review

Nadila Fauziah Rezeki[1]; Rezlie Bellatasie[1]; Ifora Ifora*[1]
[1]Departement of Pharmacology and Clinical Pharmacy, School of Pharmaceutical Science Padang (STIFARM Padang), West Sumatera, Indonesia, 25147
*For correspondence; Tel. +(62) 85266031448, Email: iforafo03@gmail.com

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Abstract:

Inflammation is a normal protective response to tissue injury caused by physical trauma, damaging chemical or microbiological agents. *Muntingia calabura L.* contains flavonoid compounds that have activities such as anti-inflammatory and antioxidant. This article aims to present the knowledge of the phytochemicals and anti-inflammatory activity of *Muntingia calabura* L. This review collects various articles related to the phytochemicals and in vitro or in vivo anti-inflammatory activity of *Muntingia calabura* L. An article search was conducted on electronic databases such as PubMed, Science Direct, and Google Scholar which were published from 2013 to 2023. The keywords "Phytochemistry", "Phytochemical", "Anti-inflammatory" and "*Muntingia calabura* L.*"*. A total of 19 articles for phytochemicals from *Muntingia calabura* L. and 12 articles provide anti-inflammatory activity *Muntingia calabura* L. *Muntingia calabura* L. inhibits the formation of edema, inhibiting the formation of granulomatous tissue, hypotonicity lysis, protein denaturation, lysosomal enzymes and stabilizing lysosomal membranes. This activity exists because of the phytochemical compounds contained in it *Muntingia calabura* L. is spread in leaves, stems, fruit, and stem bark such as tannins, flavonoids, terpenoids, coumarins, saponins, phenolic compounds, alkaloids, steroids.

Keywords*:* Phytochemistry, Anti-inflammatory, Pharmacology, *Muntingia calabura* L.

1. Introduction

Inflammation is the protective response that normally occurs when our body encounters microbial attack, tissue injury, cancer, and cell death[1], [2]. Immune cells such as macrophages, dendritic cells, lymphocytes, and neutrophils play an influential role in the development of the inflammatory response[3]. Interferons, interleukins, tumor necrosis factor, prostaglandins, and leukotrienes are some of the mediators of the inflammatory response. Free radical accumulation, activation of complex enzymes, and release of inflammatory and pro-inflammatory mediators can lead to the advancement of an acute inflammatory response. Cyclooxygenase (COX) enzymes play a major role in the inflammatory process by synthesizing prostaglandins, prostacyclins, and thromboxane which cause inflammation, pain, and platelet aggregation [4].

Muntingia calabura L. of the family Elaeocarpaceae is a common roadside tree locally called the Jamaican cherry tree. In Peruvian folk medicine, the leaves, flowers, and bark are considered to have various therapeutic uses such as antiseptic activity, relieving colds, headaches, and stomach ulcers, reducing swelling of the prostate gland, and anti-spasm activity. Boiled bark *Muntingia calabura* used is to reduce swelling of the lower extremities [5]. This article aims to present the knowledge of the phytochemical constituents and anti-inflammatory activity of *Muntingia calabura* L.

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2. Methods

Plant names are verified using www.theplantlist.org. This review gathers various articles for evidence from the literature review regarding the phytochemicals and in vitro or in vivo anti-inflammatory activity of *Muntingia calabura* L. Article searches were conducted on electronic databases such as PubMed, Science Direct, and Google Scholar which were published in 2013 to 2023. The keyword used is "Phytochemistry", "Phytochemical", "Anti-inflammatory" and "*Muntingia calabura* L.*"*. The articles reviewed in this research are original articles or research articles published in Indonesian and English. Articles in the form of books, review articles, systematic reviews, meta-analyses, brief communications, bulletins, and expert opinions are not included in this review. Complete articles are collected, checked, summarized, and concluded. The most relevant articles were selected for screening and inclusion in this review.

3. Result and Discussion

Literature study on phytochemicals and anti-inflammation *Muntingia calabura* L. used as many as 31 articles, of which 19 articles were about phytochemicals *Muntingia calabura* L. and 12 articles regarding the in-vitro or in-vivo anti-inflammatory activity of *Muntingia calabura L.*

3.1 Phytochemical

Phytochemical activity in plants *Muntingia calabura* L. has been proven in several studies, and the results of these studies will be summarized in Table 1 below.

Table 1. Summary on Bioactive Compounds of *Muntingiacalabura* L.

References	Type of extract/ Formulation	Parts	Compounds	Country
[6]	Ethanol extract	Leaves	Steroids, terpenoids, flavonoids, phenolics	Indonesia
[7]	Ethanol extract	Leaves	Alkaloids, flavonoids, steroids, tannins	Indonesia
[8]	Ethanol extract	Leaves	Alkaloids, flavonoids, saponins, tannins, phenolics	Indonesia
[9]	Fruit extract	Fruit	Saponins, flavonoids, phenols, steroids, tannins	Indonesia
[10]	Ethanol extract	Stems	Alkaloids, flavonoids, tannins	Indonesia
[11]	Ethanol extract	Leaves	Phenolics, flavonoids, tannins, alkaloids, saponins, steroids	Indonesia
[12]	n-Hexane extract	Stems	Flavonoids	India
	Ethyl acetate extract		Alkaloids, flavonoids, phenols, saponins	
	Methanol extract		Flavonoids, phenols, saponins	
[13]	Water extract	Leaves	Phenolics, tannins, saponin, alkaloids, flavonoids	Filipina
[14]	Methanol extract	Fruit	Phenolics	Malaysia
[15]	n-Hexane extract	Ripe fruit	Flavonoids	Malaysia
	Ethyl acetate extract		Alkaloids, flavonoids, tannins	

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	Methanol extract		Alkaloids, flavonoids, tannins	
	n-Hexane extract	Unripe fruit	Flavonoids	
	Ethyl acetate extract		Flavonoids, tannins	
	Methanol extract		flavonoids, tannins, phlobatannins	
[16]	Methanol extract	Leaves	Tannins, flavonoids, saponins, alkaloids	Malaysia
[17]	Petroleum ether extract	Leaves	Polyphenols	India
	Chloroform extract		Alkaloids, flavonoids, saponins, steroids, tannins, polyphenols	
	Methanol extract		Alkaloids, flavonoids, saponins, steroids, tannins, polyphenols	
	Water extract		Alkaloids, flavonoids, saponins, steroids, tannins, polyphenols	
[18]	Ethanol extract	Fruit	Flavonoids (epicatechin, rutin, diosmin, and luteolin)	Taiwan
			Phenolic acid (gallic acid, gentisic acid, p-hydroxybenzoic acid, vanillic acid, p-coumaric acid, ferulic acid, sinapic acid, syringic acid, p-anisic acid, and rosmarinic acid)	
[19]	Ethanol extract	Leaves	Flavonoids, triterpenoids, coumarin	Colombia
[20]	Ethanol extract	Leaves	Steroids, flavonoids, saponins, tannins, alkaloids	Filipina
		Stems	Triterpen, saponins, tannins, flavonoids	
[21]	Methanol extract	Leaves	Flavonoids, tannins, triterpenoids, steroids	Malaysia
[22]	Chloroform extract	Leaves	Tannins, triterpenoids, steroids	Malaysia
[23]	Methanol extract	Leaves	Flavonoids, triterpenoids, tannins, saponins, steroids	Malaysia
[24]	Water extract	Leaves	Alkaloids, steroids, flavonoids, tannins, phenolics	India
		Fruit	Alkaloids, steroids, flavonoids, tannins, phenolics	

The phytochemical test study conducted by Andalia *et al*., 2023 with phytochemical screening reported that the ethanol extract of the leaves *Muntingia calabura* found the presence of secondary metabolites in the form of steroids, terpenoids, flavonoids, and phenolics. Flavonoid compounds were then tested using the infrared spectrum (FT-IR). To determine the composition of the dominant compounds present in cherry leaves, infrared spectrum testing was carried out, it was shown that the ethanol extract of cherry leaves contained flavonoid compounds such as flavones, flavanols, and aurons[6].

Andilala *et al*., 2023 conducted a study of phytochemical tests using the phytochemical screening method, stating that the ethanol extract of the leaves *Muntingia calabura* discovered the existence of groups of

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alkaloids, flavonoids, steroids, and tannins[7]. Krisridwany *et al., 2022* tested the phytochemical screening of fruit extracts *Muntingia calabura* and found the presence of secondary metabolites in the form of saponins, flavonoids, phenols, steroids, and tannins[9].

Similar to previous research, Djuwarno *et al.*, 2022 conducted a phytochemical test study by phytochemical screening that stem bark extract *Muntingia calabura* found the presence of secondary metabolites in the form of alkaloids, flavonoids, and tannins [10]. Likewise, the research conducted by Nas *et al*., 2022 reported the identification of phenols, tannins, saponins, alkaloids, and flavonoids water extract of *Muntingia calabura* L. leaves [13]. Cheong *et al.*, 2022 also conducted a similar study by evaluating secondary metabolites from the methanolic extract of the leaves *Muntingia calabura* L., the identified secondary metabolites are tannins, flavonoids, saponins, and alkaloids which were detected [16].

Another study by Pratiwi and Dewi, 2022 used the ethanol extract of leaves *Muntingia calabura* and found the presence of secondary metabolites in the form of alkaloids, flavonoids, saponins, tannins, and phenolics. The phytochemical screening on the N-hexane fraction contained flavonoids and saponins, the ethyl acetate fraction contained alkaloids, flavonoids, saponins, tannins, and phenolic compounds, and the ethanol-water fraction contained alkaloids, flavonoids, saponins, tannins, and phenolic compounds. In this study, This study also used the TLC method with observations under UV light at 254 and 366 nm. TLC results showed that the N-hexane fraction contained flavonoids and saponins, the ethyl acetate fraction contained alkaloids, flavonoids, saponins, and phenolic compounds, and the ethanol-water fraction contained flavonoids, saponins, and phenolics, which were marked with purple spots [8].

The phytochemical test carried out by Anisa and Najib, 2022 stated that the phytochemical screening method was the ethanol extract of the leaves *Muntingia calabura* found the presence of secondary metabolites such as phenols, flavonoids, tannins, alkaloids, saponins, and steroids. In this study, the total phenolic content of cherry leaf extract was determined at 22,389 mg GAE/g extract. The total flavonoid content of the cherry leaf extract was 13,375 mg QE/g extract. The tannin content in cherry leaf extract was 13,715 mg GAE/g extract [11].

Chaudhari *et al*., 2022 proved that the study tested phytochemicals by screening phytochemicals with stem bark *Muntingia calabura* L. found the presence of flavonoids in N-hexane extract, alkaloids, flavonoids, phenols, and saponins from the ethyl acetate extract, flavonoids, phenols, and saponins. Quantitative analysis of total phenolic, flavonoid, and alkaloid from the methanol extract. The amount of phenolic content in ethyl acetate and methanol skin extract *Muntingia calabura was* determined to be 1.074 mg/100 mg and extract 0.859 mg/100mg. The total content of flavonoids in N-hexane, ethyl acetate, and methanol of skin extract *Muntingia calabura* was determined to be 0.456mg/100mg, 0.947mg/100mg, and 0.725mg/100mg. The ethyl acetate extract of the bark has a total alkaloid concentration of 0.694 mg/100 mg [12].

Research by Ariffin *et al.*, 2022 conducted a phytochemical test study by screening phytochemicals with methanol extract from raw fruit of *Muntingia calabura* found the presence of flavonoids, phlorotannins, tannins, and methanol extract of ripe fruit *Muntingia calabura* presence of alkaloids, flavonoids, tannins. Quantitative analysis was also performed to determine the total phenolic content of methanol extract from ripe and unripe fruit showing 94.43 and 47.96 mg GAE/g respectively and the determination of total flavonoid content was found to be highest in methanol extract with 35.38 and 99.74 mg QE /g in ripe and unripe fruit, respectively[15].

A study by Muniyappan *et al*., 2022 evaluated secondary metabolites from fruit extracts of *Muntingia calabura* with the Folin-Ciocalteu (F-C) method was used to identify the total phenolic content (TPC) of *Muntingia calabura* based on the formation of a blue colored complex, $(PMoW_{11}TWO_{40})^{-4}$indicating the presence of phenolic compounds. The total phenolic content was calculated based on the calibration curve regression equation (Y = 0.0448x + 0.1637), with a value of R^2= 0.9975 and stated 8.77 ± 0.91 mg GAE/g sample in dry weight[14].

Phytochemical test conducted by Panneerselvam *et al.*, 2020 by phytochemical screening of the leaves *Muntingia calabura* reported that the leaves *Muntingia calabura* found the presence of alkaloids, flavonoids, saponins, steroids, tannins, and phenolic compounds [17]. Pelaez *et al.*, 2018 also reported the content of flavonoids, triterpenes, and coumarins from ethanol extract of the leaves *Muntingia calabura* [19].

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In addition, the phytochemical analysis carried out by Rofiee *et al.*, 2015 showed that the methanol extract *Muntingia calabura* (MEMC) contains flavonoids, tannins, triterpenes, and steroids. Meanwhile, alkaloids and saponins were not detected [21].

The phytochemical activity was evaluated by Krishnaveni and Dhanalakshmi, 2014 this study used the phytochemical screening method. Analysis of the aqueous extract from leaf and fruit extract powders was carried out using different chemical reagents. The result showed that leaf and fruit extract powders contained positive alkaloids, steroids, and flavonoids [24].

Research conducted by Lin *et al.*, 2018 ethanol extract from *Muntingia calabura* L. fruit has a phytochemical content of 35.64 ± 0.72 mg/g extract for total polyphenols and 2.95 ± 0.12 mg/g extract for total flavonoids. In addition, 4 flavonoids were detected (2.43 ± 0.01 mg/g extract), namely epicatechin (0.94 ± 0.04 mg/g extract), rutin (1.05 ± 0.04 mg/g extract), diosmin (0.29 ± 0.01 mg/g extract), and luteolin (0.15 ± 0.01 mg/g extract). Also, there are 11 phenolic acids (30.30 ± 1.24 mg/g extract), namely gallic acid (9.13 ± 0.42mg/g extract), gentisic acid (6.81 ± 0.21mg/g extract), p-hydroxybenzoic (2.18 ± 0.07 mg/g extract), vanillic acid (1.35 ± 0.09 mg/g extract), traffic acid (1.16 ± 0.06mg/g extract), p-Coumaric acid (4.17 ± 0.13mg/g extract), ferulic acid (0.61 ± 0.02mg/g extract), sinapic acid (2.15 ± 0.08mg/g extract), syringic acid (1.43± 0.07mg/g extract), p-Anisic acid (1.12 ± 0.08mg/g extract), and rosmarinic acid (0.19± 0.01mg/g extract) [18].

A study by Buhian *et al.*, 2016 shows the ethanol extract of the leaves was found to contain more secondary metabolites compared to the ethanol extract of the stem. The ethanol extract of the leaves has steroid compounds, flavonoids, alkaloids, saponins, glycosides, and tannins. In the leaves, no triterpene compounds were detected. However, the ethanol extract of the stem contains triterpenes, flavonoids, saponins, glycosides, and tannins. However, the alkaloids and steroids were not detected. The Total phenolic content of leaf extracts is 75.7 ± 5.4mg/g extract and from stem extract 91.5 ± 6.4mg/g extract). The total flavonoid content from leaf extract is 112.8 ± 6.6mg/g extract) and stem extract 55.3 ± 7.5mg/g extract [20].

HPLC analysis of chloroform extract of *Muntingia calabura* conducted by Zakaria *et al*., 2015 found the presence of tannins, triterpenes, and steroids. The HPLC profile of the chloroform extract showed 2 main peaks at a wavelength of 330 nm, namely at retention times of 20.729 and 22.124 minutes. The HPLC analysis of the chloroform extract revealed the presence of flavonoids, namely rutin, fisetin, quercetin, quercitrin, naringenin, genistein, pinostrobin, and hesperetin [22].

Another study also by Zakaria *et al*., 2014 on methanol extract *Muntingia calabura* (MEMC) shows that methanol contained flavonoids, triterpenes, tannins, saponins, and steroids. However, no alkaloids were found. The HPLC profile of the methanol extract showed five main peaks at 254 and 366 nm. The best isolation of the detected peaks (4 peaks) was observed at a wavelength of 366 nm. Four main peaks appeared on the chromatograph at a wavelength of 366 nm and were tested at retention times of 20.436, 21.26, 22.756, and 23.52 minutes. The HPLC analysis revealed the presence of flavonols, namely rutin and quercitrin [23].

3.2 Anti-inflammatory Activity

Anti-inflammatory activity in *Muntingia calabura* L. has been proven through experimental studies both in vitro and in vivo. A total of 12 studies have been conducted and the results of these studies will be summarized in Table 2 below.

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Table 2. Anti-inflammatory Activity of Muntingia calabura L. Plants (In vitro and In vivo)

Type of extract/ Formulation	Part	Dose/ concentration	Experimental mode	Animal/ test cell	Reported activity	Region	Ref
Ethanol extract	Leaves	100, 200, 400 mg/kg	Carrageenan induced in rat feet (In vivo)	Male rat	Ethanol extract has an anti-inflammatory effect in reducing the volume of leg edema	Indonesia	[25]
Ethanol extract	Leaves	60, 120, 240 mg/kg	Carrageenan induced in mice legs (In vivo)	Mice	Extracts of ethanol, ethyl acetate, and chloroform have anti-inflammatory effects in reducing the volume of leg edema	Indonesia	[26]
Ethyl-acetate extract							
Chloroform extract							
Ethanol extract stick balm	Leaves	5%, 10%	Carrageenan induced in rat feet (In vivo)	Male rat	Balsam stick ethanol extract has an anti-inflammatory effect in reducing the volume of leg edema	Indonesia	[27]
Water extract	Leaves	642mg/kg, 1284 mg/kg	Carrageenan induced in mice legs (In vivo)	albino rat	Leaf water extract *Muntingia calabura* has an anti-inflammatory effect in reducing the volume of leg edema	Indonesia	[28]
Methanol extract	Leaves	100,200 mg/kg	Carrageenan induced in rat feet (In vivo)	Female rat	Methanol extract *Muntingia calabura* has an anti-inflammatory effect by inhibiting induced leg edema	India	[29]

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Ethanol extract	Leaves	50,100 µg/ml	Human Red Blood Cell (HRBC) membrane stabilization assay (In vitro)	Human Red Blood Cells (HRBC)	Ethanol extract has an anti-inflammatory effect in inhibiting lysosomal enzymes or stabilizing lysosomal membranes	India	[30]
Ethanol extract	Leaves	3% b/v, 5% b/v	Carrageenan induced in mice legs (In vivo)	Mice	Ethanol extract has an anti-inflammatory effect in reducing the volume of leg edema	Indonesia	[31]
Methanol extract	Leaves	1000 µg/ml	Inhibition of albumin denaturation (In vitro)	Bovine albumin fraction	Methanol extract and cream formulations of 1% and 5% have deep anti-inflammatory effects and inhibit protein denaturation	Malaysia	[32]
Cream formulation of 1% from methanol extract							
Cream formulation of 5% from methanol extract							
Ethanol extract	Ripe fruit Raw fruit Leaves	50, 100 mg/kg	Carrageenan induced in rat feet (In vivo)	Male rat	Ethanol fruit and leaf extracts have anti-inflammatory activity in reducing the volume of foot edema	Indonesia	[33]

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Protein isolate	Root	1000 µg/ml	Human Red Blood Cell (HRBC) membrane stabilization assay (In vitro)	Human Red Blood Cells (HRBC)	Root extract protein has anti-inflammatory activity in demonstrating a membrane stabilizing effect by inhibiting the lysis of erythrocyte membrane-induced hypotonicity	India	[34]
Ethanol extract	Stems	100,250,500 mg/kg	Carrageenan induced in rat feet (In vivo)	Rat	Ethanol extract of stem bark *Muntingia calabura* has anti-inflammatory activity by inhibiting induced leg edema	India	[35]
Polyphenolic extract	Fruit	200,400 mg/kg	Carrageenan induced in rat feet (In vivo)	Male rat	Polyphenolic extracts have anti-inflammatory activity by inhibiting induced foot edema and inhibiting the formation of granulomatous tissue.	India	[36]
		100, 200, 400 mg/kg	Cotton pellet-induced granuloma (In vivo)				

A study conducted by Uthia *et al.*, 2023 proved that the ethanol extract of leaves *Muntingia calabura* has an anti-inflammatory effect in reducing the volume of leg edema at a dose of 400 mg/kg [25]. A study conducted by Widyaningrum *et al.*, 2022 reported that the anti-inflammatory activity test observed a decrease in edema with ethanol, ethylene acetate, and chloroform extracts from the leaves of *Muntingia calabura*. Statistical results showed that the ethanol extract had a significant difference with the positive control p-value <0.05 where the 240 mg dose showed a decrease in edema volume that approached the positive control (acetosal = 52.12%) which was 62.51% compared to doses of 60 mg and 120 mg. Furthermore, the reduction of edema by the ethyl acetate extract with doses of 60, 120, and 240 mg were 36.30%, 26.83%, and 24.24% respectively. These results indicate that the average level of anti-inflammatory activity is 22.89%. Lastly, chloroform extract at a dose of 60 mg, 120 mg, and 240 mg had a significance value of p <0.05 compared with the positive control (acetosal) [26].

Sarimanah *et al.*, 2015 also conducted a similar study by testing the anti-inflammatory activity of ethanol extracts of raw, ripe, and leafy fruits *Muntingia calabura*. The results of the anti-inflammatory activity indicated that the ethanol extract of the ripe fruit *Muntingia calabura* at doses of 50 and 100 mg/kg showed a higher anti-inflammatory effect in white Wistar rats compared to ethanol extracts of raw fruit and leaves [33].

Likewise, research conducted by Mondal *et al.*, 2013 in his research reported the ethanol extract of stem bark *Muntingia calabura* with doses used 100, 250, and 500 mg/kg provided a significant reduction of rat foot

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edema. The bark extracts *Muntingia calabura* showed maximum inhibition of 29.57%, 36.57%, and 50.74% at doses of 100, 250, and 500 mg/kg, while standard drugs (diclofenac 12.5 mg/kg, p.o.) showed 57.74% inhibition after 120 minutes of drug administration on carrageenan-induced leg swelling [35]. Another study by Rahman *et al.*, 2017 reported that the ethanol extract and *Muntingia calabura* with concentrations of 3% w/v and 5% w/v had the potential as anti-inflammatory and were not significantly different from the Na diclofenac group as a comparison. [31].

Nugrahaeni *et al.*, 2022 tested the anti-inflammatory activity of cherry leaf extract in topical stick balm preparations. The study was conducted by varying the concentration of cherry leaf extract by 2.5%, 5%, and 10% and testing its anti-inflammatory activity in carrageenan-induced male white rats. Observations were made using a plethysmometer by looking at the volume of edema in carrageenan-induced rat legs. Stick balm with a concentration of 5% and 10% had an inhibition of more than 50% with values of 70.27% and 95.83%, while a concentration of 2.5% had an inhibition of 44.44%. Leaf extract ethanol stick balm *Muntingia calabura* had anti-inflammatory activity at concentrations of 5% and 10% and showed increased anti-inflammatory activity against carrageenan-induced leg edema volume reduction[27].

Bunga *et al*., 2021 proved that the anti-inflammatory potential of the aqueous extract of the leaves *Muntingia calabura* at doses of 642 mg/kg and 1284 mg/kg by testing their anti-inflammatory activity in male rats induced by carrageenan had an anti-inflammatory effect on reducing the volume of induced leg edema. The results showed that the aqueous extract of the leaves *Muntingia calabura* had the highest anti-inflammatory activity at a dose of 1284 mg/kg b/w with a percentage of edema volume of 38.90% and an inhibition of inflammation of 46.83% [28].

In anti-inflammatory research conducted by Jisha *et al.*, 2019 methanol leaf extracts from *Muntingia calabura* demonstrated anti-inflammatory at the dose of 100 mg/kg and 200 mg/kg with indomethacin as a comparison. The effect of hind leg edema observed on rats at the level of inhibition was 17.42%, 76.18%, and 75.36% respectively [29].

A study by Gomathi *et al.*, 2013 reported on the anti-inflammatory effects of fruit extract polyphenols *Muntingia calabura* using 2 methods, namely carrageenan-induced inflammatory method and cotton pellet-induced granuloma. The model of acute anti-inflammatory activity was carrageenan-induced leg swelling in rat feet with fruit extract polyphenols *Muntingia calabura* showed a significant reduction ($p<0.001$) observed when treated with 400 mg/kg polyphenolic extract as with indomethacin. Different dose groups of extracts (200, 400mg) induced by carrageenan and indomethacin showed standard inflammation inhibition up to levels of 38.55, 68.87, and 81.92% (at 240 minutes). While the model of chronic anti-inflammatory activity is granuloma induced by cotton pellets showed the polyphenol extract at a dose of 400 mg/kg has significant granuloma inhibition ($p<0.001$) (55.64%) which was comparable to the reference drug naproxen (64.28%)[36].

Another study by Chadalawada *et al.*, 2018 stated that the main compound is ethanol extract of leaves *Muntingia calabura* adalah 8-hydroxy-6-methoxyflavone, 3,7-dimethoxy-5-hydroxyflavone, 2',4'-dihydroxychalcone, Galangin, 3-hydroxy-1-(3,5-dimethoxy-4-hydroxyphenyl) propane-1-one, p-nitrophenol. The ethanol extract of M*untingia calabura* leaves with concentrations of 50µ/ml and 100µ/ml against anti-inflammatory activity the human red blood cell membrane stabilization method (HRBC) showed that it was effective against anti-inflammation. The percentage of inhibition of lysosomal enzymes 8-hydroxy-6-methoxyflavone (79.2%) was greater than that of diclofenac (78.9%)[30].

Anti-inflammatory test of root protein isolate *Muntingia calabura* using the Human Red Blood Cells (HRBC) membrane stabilization method carried out by Khan Y *et al.*, 2015 reported that plant root protein showed maximum inhibition, while the diclofenac sodium drug showed a dose of 200µg/ml. [34].

Sekar *et al*., 2017 studied the anti-inflammatory activity of methanol leaf extract of *Muntingia calabura* with concentrations of 1000µg/ml cream formulation 1% and 5% from methanol extract of *Muntingia calabura* leaves using the albumin denaturation inhibition technique. The anti-inflammatory activity showed maximum inhibition on methanol extract 63.93 ± 5.90, 1% methanol extract cream 41.83 ± 5.64, and 5% methanol extract cream 27.20 ± 2.72 observed at a concentration of 1000 µg/ml. Anti-inflammatory activity in leaf methanol extract of *Muntingia calabura* albumin denaturation method showed significant activity at the highest concentration. Protein denaturation is a well-documented cause of inflammation[32].

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4. Conclusions

Plants *Muntingia calabura* L. have many benefits in the community as a traditional medicine. Study of chemical components *Muntingia calabura* showed that plant parts, such as leaves, fruit, stems, and bark contain many active substances, such as tannins, flavonoids, terpenoids, coumarins, saponins, phenolic compounds, alkaloids, and steroids. This study also shows *Muntingia calabura* has benefits as an anti-inflammatory as proven by in-vivo and in-vitro studies, *Muntingia calabura* is reported to have anti-inflammatory activity by inhibiting the formation of edema, inhibiting the formation of granulomatous tissue, inhibits lysis of hypotonicity, inhibits protein denaturation inhibiting lysosomal enzymes or stabilizing lysosomal membranes. It is confirmed that *Muntingia calabura* has potential as an anti-inflammatory.

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