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Review Article

Phytochemical and Anti-Inflammatory Potential of *Anredera cordifolia* (*Ten*): A Review

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Abstract

Objective : Inflammation is a manifestation of the immune response to eliminate antigens from the body. This process will occur until the antigen is eliminated from the body. This inflammatory process can occur locally or systemically. *Anredera cordifolia* (*Ten*) has been used as a traditional medicine as a therapy for inflammation, diabetes, kidney failure, hypertension, hyperlipidemia, and others. Therefore, this review aims to provide current information and obtain a comprehensive review of the anti-inflammatory activity of *Anredera cordifolia (Ten)*.

Methods : This review provides evidence in the literature for the phytochemical and anti-inflammatory activity of *Anredera cordifolia* (*Ten*), from August 2011-August 2021. Three bibliographic databases were used as the main sources of information (Pubmed, ScienceDirect, and Google scholar). The keywords used in this research are as follows: "Phytochemical", "anti-inflammatory", "Bioactive compounds", "Pharmacology" and "*Anredera cordifolia*".

Results: A total of 10 studies were included in this review according to the required criteria, 5 of which were concerning phytochemical and 5 were concerning anti-inflammatory. *Anredera cordifolia* (*Ten*) contains many secondary metabolites such as essential oil, saponins, phenolics, rauninflammatory activity of *Anredera cordifolia* (*Ten*) occur mainly through several mechanisms including a decrease in the volume of paw edema, inhibition of hemolysis, inhibition of the inflammatory mediators TNF-α, IL-1β, IL-6, and NO, and a decrease in the number of neutrophil PMNs.

Conclusions: Recent interest in the traditional treatment of the *Anredera cordifolia* (*Ten*) plant both in vitro and in vivo has shown potential anti-inflammatory activity attributed to the presence of natural bioactive compounds.

Keywords : Anti-inflammatory, *Anredera*, Phytochemical, Pharmacology

INTRODUCTION

Inflammation is an essential immune response as a strategy to protect tissue damage caused by microbes, injury and other harmful conditions [1]. In general, inflammation is classified into acute inflammation and chronic inflammation. Acute inflammation is a very useful process in helping to immobilize the injured area and allowing the immune system to heal the wound. On the other hand, chronic inflammation becomes a problem for wounds. Inflamed tissue stimulates immune cells from the bloodstream to amplify the inflammatory response [2].

Anti-inflammatory drugs such as Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) are the most successful drugs used in the world by a large number of patients [3]. However, NSAIDs can cause various side effects including gastrointestinal (GI), cardiovascular (CV) disturbances, high blood pressure, kidney toxicity, worsening of congestive heart failure, and hepatotoxicity [4–7].

Plants have played an important role in maintaining human health and improving the quality of human life for hundreds of years and serve as highly valuable medicines [8,9]. Natural medicines have been increasingly used in recent years as alternative treatments for inflammation due to their relatively mild side effects [10,11] Previous studies have found that various plants have different pharmacological activities, including anti-inflammatory activity [12–14]. One of the plants known to have many benefits, including Binahong or which has the Latin name of *Anredera cordifolia (Ten)* [15].

Classification of *A. cordifolia (Ten)* plant is as follows: Kingdom: *Plantae*. Subkingdom: *Tracheobionta*, Division: *Spermatophyta*, Subdivision: *Angiospermae*, Class: *Magnoliopsida*, Order: *Caryophyllales*, Family: *Basellaceae*genus: *Anredera* and Species: *Anredera cordifolia (Ten)* [16].

A. cordifolia (Ten) has been shown to have activities such as antidiabetic [17], antibacterial [18–20], anti hematoma [21], antihyperlipidemic [22], antioxidant [23], analgesic [24,25], and treatment of kidney failure [26].

However, there is no complete literature regarding its phytochemical content and its use as an anti-inflammatory. Therefore, it is important to develop knowledge related to drugs that are sourced from natural ingredients that are useful in drug discovery efforts in the future. This review aims to

provide up-to-date information and obtain a comprehensive review of the anti-inflammatory activity of *A. cordifolia (Ten)*.

METHODS

This review is based on a search of data on scientific literature databases, namely Pubmed, ScienceDirect, and Google scholar. This literature review search was conducted to find evidence in the literature on the phytochemical and anti-inflammatory activity in vitro and/or in vivo of *Anredera cordifolia (Ten)*. In this study, the search for articles was carried out using online media with the keyword being "Phytochemicals", "Anti-inflammatory", "Phytochemicals", "anti-inflammatory", "Bioactive compounds", "Pharmacology" and "*Anredera cordifolia (Ten)*". Inclusion criteria include original articles or research articles published starting from August 2011-August 2021 which can be accessed online, and articles that are written in English and Indonesian. Meanwhile, the exclusion criteria are as follows: review articles, systematic reviews, meta-analytic reviews, short communications, news letters, editorials, case reports and expert opinions. All abstracts and complete articles were collected, examined, summarized, and concluded. The most relevant articles were selected for screening and included in this review. The plant taxonomy has been verified from the "Plant List" database (www.theplantlist.org).

RESULT AND DISCUSSION

The literature study regarding the phytochemicals and anti-inflammatory activity of *A. cordifolia (Ten)* used 10 literatures of which there are 5 studies on the phytochemical of *A. cordifolia (Ten)* and 5 literatures on its anti-inflammatory activity.

Phytochemical

Phytochemical activity in *A. cordifolia (Ten)* plants has been proven by research from several researchers. A total of 5 studies have been conducted and the results of these studies will be summarized in table 1 below.

Tabel 1. ***Summary on Phytochemical of Anredera cordifolia (Ten).***

Compounds	Parts	Country	References
Saponins, triterpenoids and steroids	Leaves, stems and tubers	Malaysia	(27)
Flavonoids	Leaves	Indonesia	(28)
Essential Oil	Leaves	Brazil	(29)
Phenolic, steroids, alkaloids, saponins	Leaves	Indonesia	(30)
Saponins, tannins, flavonoids	Leaves	Indonesia	(31)

Phytochemical tests of binahong plants using the TLC method conducted by Astuti, M, S found the presence of saponins in the leaves, stems, and tubers of the *A. cordifolia (Ten)* plant. Saponin levels contained in the leaves of *A. cordifolia (Ten)* are (28.14±0.22), while in stems (3.65±0.11), tubers (43.15±0.10) mg/g dry sample [27].

Phytochemical activity was evaluated by Selawa *et al.,* this study showed the identification of flavonoids using (Thin Layer Chromatography) TLC and color reaction. The types of secondary metabolites obtained from the isolation and identification of fresh powder and dry powder of ethanol leaf extract from *A. cordifolia (Ten)* are flavonoids. Flavonoids contained in the leaf extract of *A. cordifolia (Ten)* from fresh samples (7.81 mg/kg) and dry samples (11.23 mg/kg) [28].

Phytochemical tests conducted by Souza *et al.,* qualitatively using GC & GC-MS identified essential oil in *A. cordifolia (Ten).* The results were 19 compounds, namely 1-Tetradecene, n-Tetradecene, 2,6,10- Trimethyl-dodecane, 2- Dodecenal, n-Pentadecane, trans-Cyclohexane, 6-Methyl-a-ionone, 2-Hexyl-1-decanol, 1,10-Decanediol, n-Hexadecane, Tetradecanal, n-Heptadecane, n-Pentadecanol, 1-Octadecene, n-Octadecane, n-Hexadecanol, n-Nonadecane, n-Eicosene and n-Eicosane [29].

In addition, the phytochemical analysis conducted by Basyuni *et al*., qualitatively using a color reaction, showed that the leaf extract of *A. cordifolia (Ten)* contains phenolic secondary metabolites, which was proven positive when reacted with 1% FeCl3 marked by a change in color to blackish, positive for steroids/terpenoids when reacted with 1% FeCl3. libermann-bouchard that was indicated by a turquoise color, positive for alkaloids when reacted with dragendorff that was indicated by the formation of a precipitate, and positive for saponins when tested with distilled water-HCl [30].

Another study by Hanafiah et.al., phytochemical conducted a test on *A. cordifolia (Ten)* leaves using the TLC method for saponin testing, and spectrophotometers method for tannins and flavonoids testing, the result showed that *A. cordifolia (Ten)* leaves contain saponins, tannins and flavonoids [31].

Anti-inflammatory Activity

Anti-inflammatory activity in *A. cordifolia (Ten)* has been proven by experimental studies both in vitro and in vivo. A total of 5 studies have been conducted and the results of these studies will be summarized in table 2 below.

Table 2. Anti-inflammatory activity of *Anredera cordifolia (Ten)* plants *(in vitro and in vivo)*

Type of Extract/ Formulation	Plant part used	Dose/ Concentration	Experimental model	Animal/ test cell	Reported activity	Region	Ref
Binahong leaves extract	Leaves	25.2, 50.4, 100.8 mg/200 g BW	Carrageenan induced paw edema (in vivo)	Sprague Dawley Male Rats	Binahong leaves extract provides an anti-inflammatory effect. Characterized by a decrease in the volume of hind paw edema	Indonesia	(32)
Ethyl Alcohol Extract	Leaves	100, 200, 400, and 800-ppm	Hypotonicity induced human red blood cell (HRBC)) membrane stabilization	Human Red Blood Cell (HRBC) (in vitro)	Ethyl alcohol extract of binahong leaves showed anti-inflammatory activity through inhibition of hemolysis	Indonesia	(33)
Ethanol Extract	Leaves	100, 200 and 400 mg/kg BW	Carrageenan induced paw edema (in vivo)	Wistar rat	Ethanol extract provides an anti-inflammatory effect. Characterized by a decrease in the volume of hond paw edema	Indonesia	(34)
Ethanol extract	Leaves	10, 50, 75 µg/mL	LPS-stimulated RAW264.7 macrophage cells (in vitro)	RAW 264.7 macrophage cells	Binahong ethanol extract showed anti-inflammatory activity through the inhibition of inflammatory mediators TNF-α, IL-1β, IL-6, and NO	Bangladesh	(35)
Ethanol extract	Leaves	10%, 20%, 40%	Injection of ketamine (in vivo)	Sprague dawley white male rat strain	Binahong leaf extract showed an anti-inflammatory effect by reducing the number of PMN neutrophils	Indonesia	(36)

Kurniawan *et.al,* tested the anti-inflammatory activity of binahong leaves extract by dividing the male rats into five groups, each group was given a different dose as follows: group 1 (5ml aquadest), group 2 (mefenamic acid 12.6mg/200g BW), group 3 (*A. cordifolia (Ten)* extract 25.2mg/200g BW), group 4 (*A. cordifolia (Ten)* extract 50.4mg/200g BW) , group 5 (*A. cordifolia (Ten)* extract 100.8mg/200g BW). The leaf extract of *A. cordifolia (Ten)* has anti-inflammatory properties as indicated by a decrease in the volume of hind paw edema of rats. The anti-inflammatory properties of each dose were 25.2 mg/200 g BW, 50.4 mg/200 g BW, and 100.8 mg/200 g BW respectively by 5.17%, 10.12%, and 1.92% [32]. In line with previous studies using the method of induction of carrageenan on rat paws, the research of Yuziani *et al.* examined the anti-inflammatory effect of the ethanolic extract of the leaves of *A. cordifolia (Ten)* (EEDB) orally was carried out on 5 treatment groups, group 1 was given 1% CMC suspension (SCMC), group 2 was DSS (diclofenac sodium suspension) at a dose of 2.25 mg/kg BW as for comparison, groups 3, 4, and 5 were given EEDB doses of 100 mg/kg BW, 200 mg/kg BW, and 400 mg/kg BW. The ethanol extract of binahong leaves showed effectiveness against anti-inflammatory by decreasing the volume of hind paw edema [34].

Another study by Sutrisno *et.al,* reported that the leaf extract of *A. cordifolia (Ten)* showed the ability to inhibit hemolysis of red blood cells in a hypotonic solution. The optimum concentration for the leaf extract of *A. cordifolia (Ten) is* 100ppm with 81% inhibition of hemolysis. The increase in this concentration resulted in a decrease in the ability of the extract to stabilize the red blood cell membrane from hemolysis. The results of this study prove that the leaf extract of *A. cordifolia (Ten)* has anti-inflammatory activity [33].

Laksmitawati *et.al,* proved that the anti-inflammatory potential of *A. cordifolia (Ten)* leaf extract in a pure macrophage cell line was induced by lipopolysaccharide (RAW 264.7). Cell viability test was carried out by MTS test. Parameters that have been measured to determine anti-inflammatory activity are interleukin-1β (IL-1β), tumor necrosis factor (TNF)-α, nitric oxide (NO and IL-6). *A. cordifolia (Ten)* plants with a concentration of 50g/ml can significantly reduce levels of TNF- (250.3 pg/ml), IL-1β (50 g/ml), IL-6 (10 g/ml), and NO (50 g/ml). This study proves that *A. cordifolia (Ten)* has anti-inflammatory potential by inhibiting inflammatory mediator activity, including TNF-, IL-1β, IL-6, and NO [35].

In another study, the anti-inflammatory activity was also tested by Susanti, G. by conducting experiments on the number of (Polymorphonuclear) PMN neutrophils in male sprague dawley rats, which were divided into 5 experimental groups, each group was given an extract of *A. cordifolia (Ten)* with different levels, where in group 1 was given ointment base, group 2 was given povidone iodine ointment, group 3 was given ointment extract (10%), group 4 was given ointment (20%), and group 5 was given ointment extract (40%). Ointment is reported after 4 hours of incision. In testing the effectiveness between groups with independent t-test, it has shown a significant difference ($p<0.05$) except in the positive control group and 40% extract, Post Hoc test showed that there was a difference in effectiveness between the administration of leaf extract ointment of *A. cordifolia*

(Ten) and povidone iodine ointment. From this test, it was concluded that the leaf ointment of *A. cordifolia (Ten)* at 40% level has an anti-inflammatory effect with a decrease in neutrophil PMN by 81.25% in incision but lower than povidone iodine ointment which decreases the number of neutrophil PMN by 84.64% [36].

CONCLUSIONS

The *A. cordifolia (Ten)* plant has an important role in society for medicine, including inflammation. The *A. cordifolia (Ten)* plant also contains phytochemicals that we can use in everyday life. This review describes the importance of *A. cordifolia (Ten)* as an anti-inflammatory agent and has a variety of chemical. Several pharmacological studies reported the potential of *A. cordifolia (Ten)* for the treatment of diseases associated with inflammatory stimuli. This study also confirmed the anti-inflammatory effect in vitro and in vivo, *A. cordifolia (Ten)* showed anti-inflammatory activity by several mechanisms including by decreasing the volume of paw edema, inhibition of hemolysis, inhibition of inflammatory mediators TNF-, IL-1β, IL-6, and NO. , and a decrease in the number of PMN neutrophils.

The chemical content of *A. cordifolia* (*Ten*) has high value and benefits because it has natural phytochemical compounds that have potential, especially in plant parts, namely the leaves. Phytochemical components that have been found include essential oils, saponins, phenolics, triterpenoids, steroids, flavonoids, tannins and alkaloids.

However, further research needs to be done to understand the metabolic processes and the role of metabolites as anti-inflammatory in the body as a prelude to the development of new anti-inflammatory drugs in the future.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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