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A Mini-review: Effect of *Andrographis paniculata* nees on fish health

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Abstract

The use of medicinal ingredients derived from plants as a substitute for antibiotics needs to be done. Plants contain many secondary metabolites and other phytochemical compounds that have antibacterial, antiviral, antioxidant, anti-inflammatory, immunostimulant effects. The main advantage of herbal ingredients is that they are safe for consumption for humans and animals and are also safe for the environment. *Andrographis paniculata* Nees is one of the medicinal plants that has many benefits for human health. Based on the results of phytochemical tests, the main components contained in the plant *A. paniculata* are diterpenoids, flavonoids and polyphenols. The main bioactive compound contained in *A. paniculata* plants is andrographolide. Some of the pharmacological activities of *A. paniculata* are useful for human health, including anti-inflammatory, antibacterial, antipyretic, antioxidant, antiparasitic, hepatoprotective, antidiabetic and stimulating the immune system. Based on the pharmacological activity of the bitter plant, the purpose of this article is to explain *A. paniculata* and the effect of *A. paniculata* health of fish. Based on the above studies, *Andrographis paniculata* Ness has the potential to be used as an alternative supplement for the health of various fish, because it has antibacterial, antioxidant and immunostimulant effects.

Keywords: *Andrographis paniculata* Ness, antibacterial, antioxidant, immunostimulant medicinal plants

Introduction

Medicinal plants have been used for thousands of years as traditional medicine by people in various parts of the world. This traditional medicine is widely used by the community not only for treatment (curative), but also used as an effort to prevent disease, for health recovery (rehabilitation) and also to increase endurance and health^[1]. Therefore, until now traditional medicine is still being used from generation to generation^[2]. As many as 60% of the world's people still use plants as the main medicine to maintain health and about 80% of people in developing countries in doing treatment still depend on medicinal plants^[3].

In addition to the benefits that are quite varied, plants are chosen by the community as ingredients for traditional medicines based on several reasons, including easy to obtain, cost-effective, because the price is relatively cheaper than chemical drugs (modern medicine), safer because it has side effects minimal and environmentally friendly^[4].

Andrographis paniculata Nees is one of the medicinal plants that has many benefits for human health. *A. paniculata* belongs to the Acanthaceae family, is an upright herb that grows naturally in lowland areas to an altitude of \pm 1600 above sea level. *A. paniculata* has oppositely crossed leaves, lanceolate in shape, brittle, thin, hairless, leaf margins flat, with dark green or brownish green upper surface and pale green underside. Stem hairless, 2 mm to 6 mm thick, upper stem often with slightly ribbed angle. The flower petals consist of 5 petals. The fruit is oblong, the base and the tip are sharp. The seeds are rather hard, the outer surface is light brown with bumps^[5].

Based on the results of phytochemical tests, the main components contained in *A. paniculata* plants are andrographolides and flavonoids. Andrographolide is a diterpene compound that has been widely studied and has pharmacological activity, while flavonoids have polyhydroxy and polymethoxy groups^[6-8]. Several pharmacological activities of *A. paniculata* are useful for human health, including anti-inflammatory, antibacterial, antipyretic, antioxidant, antiparasitic, hepatoprotective, and antidiabetic, stimulating the immune system^[9].

Other pharmacological activities of the bitter plant are medicine for itching, vaginal discharge, diuretic, diabetes and rheumatism [2].

Based on the pharmacological activity of the *A. paniculata* plant as antibacterial, antioxidant, antiparasitic and as an immunostimulant, the plant can be used in aquaculture. This article aims to review the benefits of the bitter plant (*Andrographis paniculata* Ness.) in aquaculture, especially to maintain the health of the fish body.

Phytochemistry of *Andrographis paniculata* Ness

Based on the results of qualitative phytochemical screening of *A. paniculata* leaf extract using methanol as a solvent, several secondary metabolites were detected, namely saponins, steroids and triptenoids, with ethyl acetate solvent, steroids and triptenoids were detected, while with n-hexan only compounds were detected. saponins [10]. While the results of phytochemical screening on the leaves and stems of *A. paniculata* using 90% methanol solvent, the metabolites detected were Alkaloids, Flavonoids glycosides and Flavonoid aglycones, saponins and Tannins. Aglycone

flavonoids are larger in number than flavonoid glycosides [11] (Table 1). From the description above, it can be seen that the bitter plant contains several secondary metabolites, namely alkaloids, flavonoids (g), flavonoids (a), saponins, tannins, steroids and triptenoids. However, the main bioactive component of *A. paniculata* is andrographolide. The leaves contain the most andrographolide compounds, which is 2.39%, while the seeds contain the least andrographolide [12]. The bitter taste of *A. paniculata* plants is caused by diterpenoids, namely deoxyandrographolide-19 β -D glucoside and neo-andrographolide isolated from the leaves [13]. The root contains apigenin-7,4'-di-O-methyl ether, andrographolide and flavone 5-hydroxy-7,8,2',3'-tetramethoxy flavone (C19H18O7, yield, 0.006%). Flavonoid compounds, including 5,7,2',3'-tetramethoxyflavanone, and several other flavonoids, andrographolide diterpenoids, and polyphenols are present in all parts of the *A. paniculata* plant [14]. While *Andrographis* sp. contains the components 14-deoxy-11, 12-didehydroandrographolide (andrographolide D), homoandrographolide, andrographan, andrographone, andrographosterine and stigmaterol [15].

Table 1: Phytochemical Test Results of *Andrographis paniculata* Ness Leaf Extrac

Solvent extract	Plant parts	Alkaloids	Flavonoids glikosides/ flavonoid aglikone	Saponins/ Tanins	Steroids	Phenol	Triptenoids	Ref
Methanol	leaf	-	-	+	+	-	+	10
Etil astat	leaf	-	-	-	+	-	+	10
n-hexan	leaf	-	-	+	-	-	-	10
Methanol 90%	leaf- Fresh stems	+	+/+	+/+	-	-	-	11
Methanol 90%	Leaf- Dried stems	+	+/++	+/+	-	-	-	11

++: high content, +: low content, -: no content.

Antibacterial Activity

One of the diseases that often attack fish is bacterial disease. Therefore, natural ingredients are needed as antibacterial which are relatively safer and do not pollute the environment. *A. paniculata* Ness has been used as an object of research, because it has antibacterial activity [16]. Reported in addition to secondary metabolites, andrographolide isolated from the plant *A. paniculata* showed significant antimicrobial activity [17]. Antimicrobial activity depends on the concentration of bioactive compounds it contains [18]. *A. paniculata* has been shown to have antibacterial activity against several types of bacteria that cause disease in fish, including *Staphylococcus aureus* [19], *Pseudomonas aeruginosa* [20], *Aeromonas hydrophila* [21, 10] and *Edwardsiella tarda* [10].

The ethanol extract of sambiloto leaves at a concentration of 2gr/40mL has the ability to inhibit the growth of *Staphylococcus aureus* bacteria with an inhibition zone diameter of 7.4 mm [19]. The ethanol extract of bitter leaf has antibacterial activity against *P. aeruginosa* bacteria with a minimum inhibitory concentration value of 12.5% by weight/volume [20]. In vitro test results from the boiled extract of *A. paniculata* leaf powder have good antimicrobial potential against *A. hydrophila* bacteria. Produced the highest inhibition zone diameter of 14.34 mm (at a concentration of 3000 ppm) and the lowest 10.42 mm (at a concentration of 100 ppm) [21]. Ethyl acetate extract from the leaves of *A. paniculata* can inhibit the growth of *A. hydrophila* bacteria, at a concentration of 10% it produces an inhibition zone diameter of 9.11 mm and at a concentration of 60% it produces an inhibition zone diameter of 10.78 mm. As for the bacteria *Edwardsiella tarda*, the ethyl acetate extract from the leaves of *A. paniculata* produced a smaller diameter of inhibition zone, at a concentration of 10% it produced an

inhibition zone diameter of 6.10 mm and at a concentration of 60% it was 9.50 mm [10].

Here, it can be seen that the extract of *A. paniculata* obtained from boiling resulted in a larger zone of inhibition against *Aeromonas hydrophila* bacteria, compared to the extract using ethyl acetate as solvent.

The mechanism of action of secondary metabolites contained in *A. paniculata* as antibacterial is different. The mechanism of action of alkaloids as antibacterial is by destroying the peptidoglycan constituent components in bacterial cells [22] so that the cell wall layer is not fully formed and bacterial cells will die [23]. The mechanism of action of flavonoids as antibacterial is by inhibiting nucleic acid synthesis, cytoplasmic membrane function, energy metabolism and adhesion and inhibiting biofilm formation, damaging the permeability of bacterial cell wall membranes, microsomes and lysosomes [24]. The mechanism of saponins in inhibiting bacterial growth by reducing surface tension, resulting in increased permeability or cell leakage and resulting in intracellular compounds to come out [25]. Tannins inhibit bacterial growth by binding and precipitation of proteins [26], inhibiting extracellular enzymes and bacterial metabolism by inhibiting bacterial oxidative phosphorylation reactions [27]. Triptenoids can reduce the permeability of bacterial cell walls, by reacting with porins on the outer membrane of bacterial cell walls and forming strong polymer bonds [28].

Antioksidan Activity

Antioxidants are substances that function to protect body organs from oxidative damage [29]. So far, the antioxidants used are synthetic antioxidants such as butylated hydroxyanisole (BHA), butyl hydroxytoluene (BHT), propyl gallate, and tert-butylhydroquinone. Among the synthetic

antioxidants used, some are carcinogenic and have an impact on liver damage, such as BHA and BHT [30]. Therefore, it is necessary to use natural ingredients that have the potential as antioxidants. Several studies have proven that *A. paniculata* has antioxidant activity. Antioxidant compounds contained in bitter leaf are andrographolids, flavonoids, tannins, saponins and vitamin C [31]. *A. paniculata* leaf has a fairly high antioxidant content. The antioxidant activity of *A. paniculata* leaf tea at a drying temperature of 50°C produced the highest value of 83.76%, while the lowest value was found at a drying temperature of 70°C which was 63.82%. It can be seen that the higher the drying temperature, the lower the value of the antioxidant activity produced. This happens because at high temperatures it results in the destruction of metabolite compounds that act as antioxidants, namely flavonoids [31]. The results of the study by Verma and Vinayak [32] showed that the aqueous extract of *A. paniculata* significantly increased the activity of antioxidant defense enzymes such as catalase, superoxide dismutase, and glutathione-S transferase and reduced the glutathione content. The results of the antioxidant test of sambiloto herbs using 2,2-Diphenyl-1-Picrylhydrazyl (DPPH) proved that sambiloto herbs had antioxidant activity. The use of ethyl acetate fraction solvent has the highest antioxidant activity with an Inhibitory concentration (IC)₅₀ value of 402.50 g/ml, while using water extract the IC₅₀ value is 1018.75 g/ml, the chloroform fraction produces an IC₅₀ value of 825, 63 g/ml and a residue of 1648.74 g/ml. Ethanolic extract of bitter herb produces antioxidant activity with an IC₅₀ value of 499.03 g/ml [33]. Based on the results of phytochemical screening, the ethyl acetate fraction of *A. paniculata* contains secondary metabolites of the flavonoid group [2].

Effect of *Andrographis paniculata* nese on health of fish

The pharmacological effects of *A. paniculata* are antibacterial, antioxidant and immunostimulant which of course have a positive effect on fish health. Immunostimulants play a role in increasing the body's immune system. The immune system is a collection of mechanisms in the body that can protect the body from disease or infection by identifying and killing pathogenic substances [34]. *A. paniculata* plants contain Andrographolide compounds which act as immunostimulants that can improve the work of the immune system [35]. The content of andrographolide is able to increase the number of white blood cells as a component that plays a role in the body's defense system to attack pathogenic bacteria and other antigens [36]. Andrographolide compounds can increase the production of peripheral blood mononuclear cells, tumor necrosis factor (TNF)- α , interferon (IFN)- α , and (IFN)- γ , and increase the phagocytic activity of macrophages. Therefore andrographolide can act as an immunostimulant capable of stimulating both specific and non-specific immunity through NK cells, macrophages, and inducing other immune cells, namely cytokines [37]. Alkaloid content in bitter plants can replace the role of IFN γ in maintaining the body's immune response and increase non-specific immune responses in the form of increased levels of leukocytes or specific immune responses, which in turn will activate macrophages to perform phagocytosis against infectious disease agents that infect the body [38]. As according to Puri *et al.* (2013) [39], the mechanism of sambiloto as an immunostimulant is to stimulate the body's immune system in the form of a specific antigen response or a non-specific immune response, which

will then produce phagocytic cells. The specific antigen response produced will cause the production of a high number of lymphocytes, especially B lymphocytes. Furthermore, the B lymphocytes will produce antibodies which are glycoproteins that will bind to antigens and stimulate the phagocytosis process.

Research on *A. paniculata* as an immunostimulant to increase fish resistance to disease attacks has been carried out. The results of research conducted by Lukistyowati (2012) [40] showed that *Pangasius hypophthalmus* fish that had been soaked in a solution of simplicia sambiloto for 10 minutes for 30 days at a concentration of 4 g/L produced the highest total leukocyte value and phagocytic activity, each of 57×10^3 cells/mm³ and 55.50%. The occurrence of an increase in leukocytes as one of the first indicators of fish in a condition infected by a disease [41]. After being challenged with *Edwardsiella tarda* bacteria 10^7 cells/ml through intramuscular injection, the number of leukocytes decreased to 31.70×10^3 cell/mm³ ± 0.577 and survival reached 100%. Leukocytes are one of the blood components that function as non-specific defenses that will localize and eliminate pathogens through phagocytosis [42]. The reduction in the number of leukocytes from normal conditions will affect all systems in the body. Tilapia whose feed is added to dry matter extract) water *A. paniculata* with a ratio of (w/w) 4:36 and 5:35 for 2 weeks was resistant to *Streptococcus agalactiae* attacks, besides that it did not affect the appearance, behavior and response to feed [43]. The results of other studies showed *Pangasianodon hypophthalmus* fish, which was fed with the addition of 2% Andrographis paniculata leaf extract which was tested for 60 days could increase the innate body resistance, as seen from serum lysozyme activity, respiratory burst activity, and globulin levels before and after the challenge with *Aeromonas hydrophila* bacteria produced the highest value. ($P < 0.05$). Likewise, the RPS value after being challenged with *Aeromonas hydrophila* bacteria produced the highest ($P < 0.05$) compared to control and other treatments [44].

Conclusion

Andrographis paniculata Nese has the potential to be used as an alternative supplement for the health of various fish, because it has antibacterial, antioxidant and immunostimulant effects.

Competing Interests

Author has declared that no competing interests exist.

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