



A Mini-review: Potential of *Andrographis paniculata* Ness as Immunostimulator in Fish Aquaculture

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Abstract

Fish is one of the fishery commodities that have economic value, both as consumption fish and ornamental fish. In addition, fish is also a source of animal protein that contains essential nutrients. One of the factors that harm the fish farming business is the presence of disease. Disease control must be carried out as early as possible, so that disease outbreaks do not occur that cause economic losses. One of the efforts to control the disease is to increase the fish's immune system. Immunostimulants are compounds that can be used as alternative therapies to increase the fish's immune system against pathogenic infections, because they are able to increase the work of the immune system through the activity of white blood cells and other phagocytic cells. Several research results have proven the effectiveness of various types of plants as immunostimulants, one of which is *Andrographis paniculata* Nees. Deoxyandrographolide, andrographolide, 14-deoxy-11, neoandrographolide, 12-didehydroandrographolide, homoandrographolide, diterpenoids and flavonoids are compounds contained in *A. paniculata* Nees which act as immunostimulants. So the purpose of this article is to explain *A. paniculata* as an immunostimulant in cultured fish that can increase the fish's body resistance to disease attacks. Based on the above studies, *Andrographis paniculata* Nees Potential to be used as an alternative immunostimulant that can increase the body's resistance of *Pangasius hypophthalmus*, *Oreochromis mossambicus*, *Pangasianodon hypophthalmus* fish against bacterial pathogens such as *Edwardsiella tarda*, *Aeromonas hydrophila* and *Streptococcus agalactiae*.

Keywords: fish, *Andrographis paniculata* Nees, Immune system, disease.

1. INTRODUCTION

The increase in fish farming business occurs due to increasing public awareness to consume fish as a source of animal protein which contains essential nutrients and is very beneficial for human health [1]. The main problem in cultivation activities is the presence of disease [2]. Disease control must be addressed as early as possible to avoid large economic losses, due to

death and failure of fish harvests. One of the efforts to prevent fish from getting sick is to increase the fish's immune system. Immunostimulant is a compound that can be used as an alternative therapy to increase fish resistance to disease, through the mechanism of increasing the work of the immune system. Therefore, the immune system plays a role in protecting the body from foreign objects that enter, so that the body's physiological condition is not disturbed [3]. The *Andrographis paniculata* Ness plant can be used as a source of natural immunostimulants that can increase the body's immune system [4]. *Andrographis paniculata* contains deoxyandrographolide, andrographolide, 14-deoxy-11, neoandrographolide, 12-didehydroandrographolide, homoandrographolide, diterpenoids and flavonoids [5]. Pharmacological effects of *A. paniculata* as an immunostimulant, because it contains an active compound, namely andrographolide which 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 [6]. 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 [7]. The mechanism of *A. paniculata* as an immunostimulant is to stimulate the body's immune system in the form of a specific antigen response and 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 [8]. This article will review the potential of *A. paniculata* which can be developed as an alternative therapy in increasing the fish's immune system.

2. CLASSIFICATION AND MORPHOLOGY OF *Andrographis paniculata* Ness

The *Andrographis paniculata* (Figure 1) is local to Taiwan, Mainland China, and India. It is likewise normally discovered withinside the tropical and subtropical Asia, Southeast Asia, and a few different international locations along with Cambodia, Caribbean islands, Indonesia, Laos, Malaysia, Myanmar, Sri Lanka, Thailand, and Vietnam [9,10 and 11]. This plant is likewise discovered in distinctive phytogeographical and edaphic zones of China, America, West Indies, and Christmas Island [11]. The classification of *A. paniculata* is as follows:

Division : Angiosperma,
Class : Dicotyledonae
Subclass : Gamopetalae,,
Series : Bicarpellatae,
Order : Personales,
Family : Acanthaceae
Subfamily : Acanthoideae,
Tribe : Justiciae
Subtribe : Andrographideae,
Genus : Andrographis
Species : *A. paniculata* (Burm. f.) Nees [12]



Figure 1. Plant *Andrographis paniculata* (Burm. f.) Nees

A. paniculata is a shrub with a plant height of up to 90 cm. the stem is dark green, woody, knotty, the young stem is rectangular and the old stem is round and has many branches. The leaves are hairy green, small, 2-12 cm long, 1-3 cm wide, pointed at the base and tip and about 3 cm long on the stalk. *A. paniculata* flower grows at the end of the stalk which is arranged in a bunch. The flowers are compound, the petals are lanceolate, share five with an attached base and are green. The stamens are two, oblong in shape, the anthers are moon-shaped and purple in color. The pistil is short, the white head is purple-brown, the inside of the pistil is purple, while the outside of the hair is red. The flower crown is oval, attached at the base and the ends are broken into four. The fruit is elliptical in shape, with a pointed tip and a grooved center. The fruit is in the form of a valve capsule and contains 3-7 seeds, at the young stage it is green and dark brown after maturity [7,13, 14].

3. THE CONTENT AND BENEFITS OF *Andrographis paniculata* Nees

A. paniculata contains several complete chemical compounds, so it is very beneficial for health. *A. paniculata* leaves contain saponins, steroids and triptenoids [15]. The leaves and stems of *A. paniculata* contain alkaloids, flavonoid glycosides and flavonoid aglycones, saponins and tannins. The content of aglycone flavonoid compounds is greater in number than flavonoid glycosides [16]. However, the main bioactive component of *A. paniculata* is andrographolide. In the leaves, the andrographolide content is higher, which is 2.5-4.8% of the dry weight, while the seeds contain the least andrographolide [17, 18]. In addition to the components of lactones and flavonoids, this bitter plant also contains components of alkanes, ketones, aldehydes, minerals (calcium, sodium, potassium) [17]. The *A. paniculata* taste of bitter plants is caused by diterpenoids, namely deoxyandrographolide-19 β -D glucoside and neo-andrographolide isolated from the leaves [19]. 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 [20]. While *Andrographis* sp. contains the components 14-deoxy-11,12-didehydroandrographolide (andrographolide D), homoandrographolide, andrographan, andrographone, andrographosterine and stigmasterol [21].

The content of andrographolides, essential oils, flavonoids and tannins contained in bitter has several pharmacological activities including anti-bacterial, anti-toxic and anti-infective functions as anti-bacterial, anti-toxin and anti-infection [22, 23 and 24]. Another opinion says

that andrographolides, essential oils and flavonoids function to prevent blood clots, inhibit and destroy cancer nuclei, are anti-bacterial, anti-toxin, and anti-infection, can also be used as antibiotics to fight. Another opinion states that andrographoside and neoandrographolide are glucoside groups that can act as strong antioxidants [25], besides that andrographolide compounds can act as immunostimulants that can improve the work of the immune system [6], able to stimulate both specific and non-specific immune functions. specifically through NK cells, macrophages, and cytokine induction [4]. Therefore, *A. paniculata* can be developed as an alternative therapy in improving the body's immune system [26]. This immune system can detect pathogenic organisms, from viruses to parasites and worms and distinguish them from normal cells and tissues. As a complex organ composed of specific cells, the immune system is also a circulatory system separate from blood vessels that all work together to eliminate infection from the body. The organs of the immune system are located throughout the body, and are called lymphoid organs. Lymph vessels and lymph nodes are part of a special circulatory system that carries lymph fluid, a transparent fluid that contains white blood cells, especially lymphocytes. Lymph nodes contain a network of lymph vessels and provide a medium for immune system cells to defend the body against invading agents [27].

4. SOURCE OF IMMUNOSTIMULANT FOR FISH DISEASE PREVENTION

Andrographis paniculata (Burm. f.) Nees is a medicinal plant used in various countries. The main constituents of *A. paniculata* are diterpenoids, flavonoids and polyphenols. Extraction of a single compound from *A. paniculata* showed that andrographolide was the main compound, based on its bioactive properties and abundance [28]. Another pharmacological activity of *A. paniculata* Nees is as a source of immunostimulants that can help prevent diseases, including diseases that attack fish. The use of *A. paniculata* as an immunostimulator is widely recommended, based on its active compound as an immunostimulant, namely andrographolide [29]. Several studies have shown the ability of *A. paniculata* Nees as a source of immunostimulants in several types of fish. *Pangasius hypophthalmus* fish that has 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 values and phagocytic activity, respectively $57 \times 10^3 \text{ cell/mm}^3$ and 55.50%. After a challenge test with *Edwardsiella tarda* bacteria 10^7 cells/ml via intramuscular injection, the number of leukocytes decreased to $31.70 \times 10^3 \text{ cell/mm}^3 \pm 0.577$ and survival reached 100% [30]. In this study, leukocytes were used as observation parameters, because they are one of the cellular immunological indicators that function in the body's defense system against infection. Other cellular immunological indicators are red blood cells and platelets [17, 31]. It was reported that the ethanolic extract of *A. paniculata* can stimulate the proliferation of lymphocyte cells, which causes an increase in the number of leukocytes, because lymphocyte cells are part of leukocyte cells [28] which can modulate innate immunity by regulating macrophage activation, and regulating the production of specific antibodies [32]. *Oreochromis mossambicus* given extract of *A. paniculata* at low concentrations showed a significant increase in cellular immunological indicators including red blood cells, white blood cells, and platelets [31]. Leukocytes act as a non-specific defense against disease by localizing and eliminating pathogens through phagocytosis [33]. Another study reported that *Pangasianodon hypophthalmus* fed with additional 2% *A. paniculata* leaf extract which was tested for 60 days could increase innate body resistance, indicated by increased serum lysozyme activity, respiratory burst activity, and globulin levels, and after being challenged with bacteria

Aeromonas hydrophila, fish produced the highest survival value ($P < 0.05$) and the highest RPS value ($P < 0.05$) compared to control and other treatments [34]. Research on other fish showed that tilapia which had been given extract of *A. paniculata* in its feed ration with a ratio of (w/w) 4:36 and 5:35 given for 2 weeks, was resistant to *Streptococcus agalactiae* attack, and showed behavior, appearance and behavior. good feed response [35]. From the description above, it proves that *A. paniculata* Ness is capable of being an immunostimulant that can increase fish resistance to disease. This is related to the active compound content of the plant, namely andrographolide as an immunostimulant that can improve the function of the body's defense system, including white blood cells to attack bacteria and other pathogens [6]. Andrographolide as an immunostimulant is able to increase the work of the immune system [5], both specific and non-specific immune systems through NK cells, macrophages, and cytokine induction [4]. The resulting specific immune response will cause an increase in the production of large numbers of lymphocytes, especially B lymphocytes. Furthermore, B lymphocytes which are part of leukocyte cells will produce antibodies as plasma glycoproteins that will bind to antigens and stimulate the phagocytosis process [36]. In addition to Andrographolide compounds that act as immunostimulants, flavonoid compounds can also act as immunostimulants. When the activity of the immune system decreases, the flavonoid content in *A. paniculata* will send intracellular signals to cell receptors to increase immune system activity [37]. As an immunomodulatory agent, bitter can be used as an immunostimulator that increases the immune response when the body's immunity is reduced [38]. In addition to andrographolide and flavonoid compounds, the alkaloid content in bitter can replace the role of $IFN\gamma$ in maintaining the immune response and increasing non-specific immune responses in the form of increasing leukocyte responsiveness or specific immune responses to activate macrophages to phagocytize infectious agents that enter the body [39, 34, 40].

CONCLUSION

Andrographis paniculata Ness Potential to be used as an alternative immunostimulant that can increase the body's resistance of *Pangasius hypophthalmus*, *Oreochromis mossambicus*, *Pangasianodon hypophthalmus* fish against attack by pathogenic bacteria including *Edwardsiella tarda*, *Aeromonas hydrophila* and *Streptococcus agalactiae*.

Competing Interests

Author has declared that no competing interests exist.

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