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

Rosidah and Skalalis Diana

DOI: https://doi.org/10.22271/fish.2021.v9.i5b.2571

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 Nees 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 Nees, 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 ± 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 tripterpenoids, with ethyl acetate solvent, steroids and tripterpenoids 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 tripterpenoids. 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-19β-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 (andrographide D), homoonandrographolide, andrographan, andrographone, andrographosterine and stigmastanol [15].

| Solvent extract | Plant parts | Alkaloids | Flavonoids glycosides/ flavonoid aglycone | Saponins/ Tanins | Steroids | Phenols | Tripterpenoids | Ref |
|-----------------|-------------|-----------|------------------------------------------|-----------------|----------|---------|----------------|-----|
| Methanol        | leaf        | -         | -                                        | -               | +        | +       | +              | 10  |
| Etil acetat     | leaf        | -         | -                                        | -               | +        | -       | -              | +   |
| n-hexan         | leaf        | -         | -                                        | -               | +        | -       | -              | 10  |

| Methanol 90%    | leaf        | -         | +/+                                      | +/+             | +        | -       | -              | 11  |
| Methanol 90%    | Leaf       | +/++      | +/++                                     | +/+             | -        | -       | -              | 11  |
| Methanol 90%    | Leaf       | +/++      | +/++                                     | +/+             | -        | -       | -              | 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 is 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 2g/40mL has the ability to inhibit the growth of Staphylococcus aureus bacteria with an inhibition zone diameter of 7.4 mm [10]. 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 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]. Tripterpenoids 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 andrograpolids, 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 extract the IC50 value is 402.50 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 [31].

**Effect of Andrographis paniculata ness 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 IFNγ 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 57x105 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 107 cells/ml through intramuscular injection, the number of leukocytes decreased to 31.70x105 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 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.

**Competing Interests**

Author has declared that no competing interests exist.

**References**

1. Warditiani NK, Larasanty LPF, Widjaja INK, Juniari NPM, Nugroho AE, Pramono S. Identification of the Chemical Content of the Purified Extract of Sambiloto Herb. Udayana Journal of Pharmacy 2014;3(1):22-25.
2. Rachmuni EPN dan Suhesti TS. Antioxidant Activity of Sambiloto (Andrographis paniculata) Herba Extract and Fraction. Media Pharmaceutica Indonesiana 2016;1(2):100-105.
3. Shrestha PM, Dhillon SS. Medicinal plant diversity and use in the highlands of Dolakha district, Nepal. Journal of Ethnopharmacology 2003;86(1):81-96.
4. Asase A, Kokubun T, Grayer RJ, Kite G, Simmonds MSJ, Oteng-Yeboah AA et al. Chemical constituents and antimicrobial activity of medicinal plants from Ghana: Cassia sieberiana, Haematoxistis barteri, Mitragyna inermis and Pseudocedrela kotschyi. Phytotherapy
Research 2008;22(8):1013-1016.

5. Ministry of Health RI. Indonesian Pharmacopoeia. Edition IV. Jakarta: Ministry of Health of the Republic of Indonesia 1995.

6. Rao YK, Vimalamma G, Rao CV, Tzeng YM. Flavonoids and andrographolides from Andrographis paniculata. Phytochemistry 2004;65(16):2317-21.

7. Chao WW, Lin BF. Review isolation and identification of bioactive compounds in Andrographis paniculata (Chuanxianin). Growth. 2010;10:44.

8. Hossain MS, Urbi Z, Sule A, Rahman KM. Andrographis paniculata (Burm.f.) Wall. ex Nees: A Review of ethnomedicine, phytochemistry, and pharmacology. The Scientific World Journal 2014, 1-28.

9. Kumar A, Dora J, Sigh A, Tripathi R. A Review on King of Bitter (Kalmeheh), International Journal of Research in Pharmacy and Chemistry 2012;2(1):116-124.

10. Sinaga L, Suryanto D, Lesmana I. Antimicrobial Activity of Extract of Sambiloto’s Leaf (Andrographis paniculata) to Aeromonas hydrophila, Edwardsiella tarda and Saprolegnia sp. Invitro. Jurnal Aquacostarminae 2016;11(1):13.

11. Syahbirin G, Pradono DI, Rayah T. Inhibition Power of Crude Flavonoid Extracts of Sambiloto (Andrographis paniculata) [Burm. F] Ness) and Temu Putih (Curcuma zedoaria Roscoe) on Tyrosine Kinase Activity In vitro. http://repository.ipb.ac.id/handle/123456789/54047.

12. Sharma A, Krishan L, Handa SS. Standardization of the Indian crude drug Kalmeheh by high pressure liquid chromatographic determination of andrographolide. Phytochemical Analysis 1992;3:129-131.

13. Weiming C, Xiaotiong L. Deoxyandrographolide 198-D-glucoside from the leaves of A. paniculata, Planta Medica 1982;15:245-246.

14. Koteswara RY, Vimalamma G, Venkata RC, Tzeng YM. Flavonoids and andrographolides from Andrographis paniculata. Phytochemistry 2004;65:2317-2321.

15. Siripong P, Kongkathip B, Preechanuokool K, Picha P, Tunsuwan K, Taylor WC. Cytotoxic diterpenoid constituents from Andrographis paniculata, Nees leaves. Journal of the Scientific Society of Thailand 1992;18:187-194.

16. Sasidharan VK. Search for antibiotic and antifungal activity of some plants of Kerala - India. Acta Pharmaceutica (Zagreb) 1997;47:40-47.

17. Burgos RA, Aguila MJ, Santiesteban ET, Sanchez NS, Hancke JL. Andrographis paniculata Nees induces relaxation of uterus by blocking voltage operated calcium channels and inhibits Ca(2+) influx. Phytotherapy Research 2001;15:235-239.

18. Singha PK, Roy S, Dey S. Antimicrobial activity of Andrographis paniculata. Fitoterapia 2003;74:692-694.

19. Arbianti R, Surya T, Hermansyah H, Widyarini S. Extraction of bitter leaf by sonication method and its effect on increasing the refractive index and inhibition of growth of S. aureus bacteria. Journal of Process Technology 2008;7(2):161-166.

20. Mardiana RN, Handayani N. Antibacterial activity of the sambiloto leaf extracts (Andrographis paniculata) to Bacillus cereus and Pseudomonas aeruginosa. Biofarmasi. 2014;14(1):19-24.

21. Taukhid, Suharni I, dan Supriyadi H. The effectiveness of Sambiloto Leaf Extract (Andrographis paniculata) for the Control of Koi Herpes Virus (KHV) on Carp (Cyprinus carpio). Journal of Aquaculture Research 2007;2(3):407-414.

22. Evans CW. Pharmacognosy Trease and Evans 16th Ed. London: Saunders Elsevier. 2009, 263, 356.

23. Darsana, I. Besung, I. Mahatmi, H. The Potential of Binahong Leaves (Anredera Cordifolia (Tenore) Steenis) in Inhibiting the Growth of Escherichia coli Bacteria In vitro. Indonesia Medicus Veterinus 2012;1(3):337-351.

24. Xie Y, Yang W, Tang F, Chen X, Ren L. Antibacterial activities of flavonoids: structure-activity relationship and mechanism. Curr. Med. Chem 2015;22:132-149.

25. Nuria MC, Arvin F, Sumantri. Test of antibacterial activity Jatropha curcas L ethanol extract against Staphylococcus aureus ATCC 25923, Escheria coli ATCC 25922 and Salmonella typhi ATCC 1408. Jurnal Ilmu Pertanian. 2009;5:26-37.

26. Huang Q, Liu X, Zhao G, Hu T, Wang Y. Potential and challenges of tannins as an alternative to in-feed antibiotics for farm animal production. Anim. Nutr 2018;4:137-150.

27. Scalbert A. Antimicrobial properties of tannins. Phytochemistry 1991;30:3875-3883.

28. Retnowati Y, Bialangi N, Posangi NW. Growth of Staphylococcus aureus Bacteria on Media Exposed to Infusion of Sambiloto (Andrographis paniculata) leaves.Saintek 2011;6(2):1-9.

29. Simic MG. Mechanisms of inhibition of free-radical processes in mutagenesis and carcinogenesis. Mutation Research 1988;202(2):377-386.

30. Sherwin ER, Braren AL, Dayton Wilson LM. Food Additives, Marcel Dekker, New York, NY, USA 1990.

31. Patin EW, Zaini MA, Sulasatri Y. Effect of Drying Temperature Variations on Physicochemical Properties of Sambiloto Leaf Tea (Andrographis paniculata). Pro Food (Journal of Food Science and Technology) 2018;4(1):251-258.

32. Verma N, Vinayak M. Antioxidant action of Andrographis paniculata on lymphoma. Molecular Biology Reports 2008;35(4):535-540.

33. Gani AP, Pramonom S, Matrono S, Widyarini S. Radical Scavenging Activity Combination of Sambiloto (Andrographis paniculata Nees.) and Patikan Kebo (Euphorbia hirta L.) Ethanolic Extracts on 2,2-Diphenyl-1-Picrylhidrazyl (DPPH). Traditional Medicine Journal. 2018;23(3):149-154.

34. Priyani R. Review: Benefits of Sambiloto Plant (Andrographis paniculata Nees) Against the Body's Immune System. Journal of Medical and Health Sciences 2020;7(3):484-490.

35. Muhlisah F. Family Medicinal Plants. Penebar Swadaya Publisher. JakartaEdisi ke halaman 2006;5:84

36. Sumaryono W. Indonesian Traditional Medicine Research and Improvement Strategy. Proceedings of the National Seminar on Indonesian Medicinal Plants XXI. Surabaya 2002, 1-8.

37. Jarukarmjorn K, dan Nemoto N. Pharmacological Aspect Andrographis paniculata on health and its major Diterpenoid Constituent Andrographolide. Journal of Health Sciences 2008;54(23):370-381.

38. Alkandahri MY, Subarnas A, Berbudi. A Review: Immunomodulator Activity of Sambiloto Plant (Andrographis paniculata Nees). Farmaka 2018;16(3):16-21.
39. Puri A, Saxena R, Saxena RP, Saxena KC, Srivastava V, Tandon JS. Immunostimulant agents from *Andrographis paniculata*. Journal of Medicinal Plants Research 2013;7(44):3242-3246.
40. Lukistyowati I. Study of the Effectiveness of Sambiloto (*Andrographis Paniculata* Nees) to Prevent Edwardsiellosis Disease in Catfish (*Pangasius hypophthalmus*). Jurnal Berkala Perikanan Terubuk 2012;40(2):56-74.
41. Chinabut S, Limsuwan C, Kitsawat P. Histology of The Walking Catfish *Clarias batrachus*. Department of Fisheries Thailand 1991, 96.
42. Anderson DP. Immunostimulant, Adjuvant and Vaccine Carrier in Fish: Application to Aquaculture. Annual Review of Fish Diseases 1992;21:281-30
43. Rattanachaikunsopon P, Phumkhachorn P. Prophylactic effect of *Andrographis paniculata* extracts against Streptococcus agalactiae infection in Nile tilapia (*Oreochromis niloticus*). Journal of Bioscience and Bioengineering 2009;107(5):579-582.
44. Maiti S, Saha S, Jana P, Chowdhury A, Khatuaa S, Ghosh TK. Effect of dietary *Andrographis paniculata* leaf extract on growth, immunity, and disease resistance against *Aeromonas hydrophila* in *Pangasianodon hypophthalmus*. Journal of Applied Aquaculture 2021;33(3).