

THE INFLUENCE OF BETEL LEAF EXTRACT ADMINISTRATION IN ENHANCING NON-SPECIFIC IMMUNITY TO COMBAT DISEASES IN THE AQUACULTURE SECTOR (REVIEW)

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ABSTRACT

Received : 2023-11-30

Accepted : 2023-12-30

Keywords :
Betel Leaf,
Immunostimulant, Non-specific Immunity,
Aquaculture

This review aims to investigate the impact of betel leaf extract administration in enhancing non-specific immunity in fish within the context of aquaculture. A literature review was conducted to evaluate previous studies, analyze the mechanisms of action of active compounds, and provide practical recommendations for field implementation. The review results indicate that betel leaf extract has antimicrobial potential that can inhibit the growth of bacteria, viruses, and parasitic agents causing diseases in cultured fish. The administration of this extract also stimulates non-specific immune responses, including increased production of immune cells such as macrophages and lymphocytes. The antioxidant effects of compounds in betel leaves provide protection against oxidative stress, enhancing fish resilience to unfavorable environmental conditions. Despite these positive findings, further research is needed to deeply understand the mechanisms of action of active compounds, taking into account environmental factors in betel leaf extract administration. Integration with other disease management strategies and strict monitoring of environmental safety are crucial aspects of practical implementation. In conclusion, the administration of betel leaf extract can be a promising alternative to enhance fish resistance to diseases in aquaculture. Administering betel leaf extract in feed and water can improve survival rates and egg hatching. Collaboration among researchers, farmers, and other stakeholders is necessary to optimize the practical application of these findings, with the goal of enhancing productivity and sustainability in the aquaculture sector as a whole.

INTRODUCTION

Aquaculture, as an integral part of the fisheries sector, has an important role in meeting global protein needs (Triani & Novani, 2023). However, the main challenge in developing fish farming is the problem of disease which can cause significant losses (Muahiddah et al., 2023; Muahiddah & Dwiyantri, 2023). Improving the fish immune system can be an effective strategy

to reduce the impact of disease in aquaculture (Novriadi, 2014). One interesting approach is the administration of betel leaf extract, which has long been known to have antimicrobial and immunomodulatory properties (Kurniawati, 2023).

Diseases in aquaculture can be caused by a variety of pathogens, including bacteria, viruses, and parasites. Non-specific immunity, which involves natural defense responses without specificity against certain pathogens, is a key aspect in fighting disease attacks (Alhakim et al., 2021). One plant whose extract can fight disease attacks in the aquaculture sector is betel leaf

Betel leaf plants grow in tropical areas, including Southeast Asia and parts of East Africa. In Indonesia, betel leaves can be found on various islands, and their adaptation to tropical climate conditions allows them to grow in various environments. Betel leaves (*Piper betle*) have been proven to contain bioactive compounds such as flavonoids, polyphenols and terpenoid compounds which can increase non-specific immune responses in various organisms (Pasaribu & Djonu, 2021). Betel leaf extract is known to have antimicrobial properties which can inhibit the growth of bacteria and viruses. This can help prevent infections in fish that are susceptible to microbial pathogens (Tjahjani & Lestari, 2022). The bioactive compounds in betel leaves can stimulate the production of immune cells, such as macrophages and lymphocytes, which play a role in the non-specific immune system. The antioxidant content in betel leaves can help protect fish cells from oxidative damage caused by free radicals, increasing fish resistance to disease (Sumarya, 2020).

This review will investigate previous studies that have been conducted to evaluate the effect of administering betel leaf extract on the non-specific immune system of fish in the context of aquaculture. Through this review, we will try to understand the mechanism of action of the compounds in betel leaves which are responsible for increasing non-specific immune responses in fish. Based on the review findings, practical ways of administering betel leaf extract in aquaculture cultivation systems will also be suggested to increase disease resistance. By digging deeper into the influence of betel leaf extract on the non-specific immune system of fish in aquaculture, it is hoped that effective strategies can be found to increase productivity and resistance to disease in this sector.

RESULTS AND DISCUSSION

The use of betel leaf extract can reduce the prevalence of bacterial and viral infections in farmed fish (Febrianto, 2022). By reducing the burden of microbial infections, administering betel leaf extract can play a role in preventing disease, reducing fish mortality, and improving the overall health of fish populations (Syahida et al., 2013). Compounds in betel leaves have been shown to stimulate the production of immune cells, including macrophages and lymphocytes. This contributes to increased non-specific immune responses in fish (Mutahhara, 2020).

The betel leaf plant (*Piper betle*) has long been used as a traditional medicinal plant with various empirically recognized properties. Some of the health benefits of betel leaves include: Betel leaves contain compounds such as estragol, eugenol, and others which have antibacterial and antimicrobial properties (Effa & Puetri, 2015). Therefore, betel leaves are often used to help reduce the growth of bacteria and microbes in the mouth and digestive tract. Several compounds in betel leaves are known to have anti-inflammatory properties, which can help reduce inflammation in several health conditions. Betel leaves contain antioxidant compounds, such as polyphenols, which can help fight cell damage caused by free

radicals in the body. In some cultures, betel leaves are used as a traditional treatment for respiratory problems, such as coughs and colds. These properties may be related to the plant's antimicrobial and anti-inflammatory properties.

Table 1. Use of Betel Leaves in the Field of Aquaculture

No	Fish	Method	Results Improve	Against Disease	Reference
1.	Malay combtail (<i>Belotina hasselti</i>)	Oral (by mixing Chinese betel leaves (<i>Peperomia pellucida</i>) in feed at 0.075 g/kg feed)	<ul style="list-style-type: none"> • Survival Rate • Absolute Growth • Gonad Development 	-	Heru <i>et al.</i> , 2023
2.	Carp (<i>Cyprinus carpio</i>)	Oral (by mixing red betel leaves (<i>Peperomia crocatum</i>) in feed at 5 g/kg feed)	<ul style="list-style-type: none"> • Total Erythrocytes • Lymphocyte Percentage • Phagocytosis Index • Total Leukocytes • Monocyte Percentage 	<i>Aeromonas hydrophila</i>	Syahida <i>et al.</i> , 2013
3.	Milkfish (<i>Chanos chanos</i>)	Soaking eggs in betel leaf extract (<i>Piper betle</i> L.) at a dose of 1.5 ml/L for 20 minutes	<ul style="list-style-type: none"> • Survival Rate • Hatching Rate 	Fungi and bacteria on eggs	Susanti <i>et al.</i> , 2022
4.	Gourami (<i>Osphronemus gouramy</i>)	Soaking eggs in betel leaf extract (<i>Piper betle</i> L.) at a dose of 1.5 ml/L	<ul style="list-style-type: none"> • Survival Rate • Hatching Rate 	<i>Saprolegnia</i> sp.	Susilo & Yusanti, 2022
5.	Bonylip barb (<i>Osteochilus vittatus</i>)	Oral (by mixing betel leaf flour (<i>Piper betle</i> L.) in feed at 6 g/100 g feed)	<ul style="list-style-type: none"> • Survival Rate • Length Growth 	-	Putra, 2022

In research by Heru *et al.* (2023), Chinese betel leaves in feed can increase the survival of Malay combtail and the hatchability of their eggs. This is because Chinese betel leaf extract is known to contain various secondary metabolite compounds such as saponins, alkaloids, tannins, flavonoids and triterpenoids. These compounds often have the potential to exert certain pharmacological effects, such as antimicrobial and antioxidant activity. The alkaloid

and flavonoid compounds in Chinese betel leaf extract are said to act as antibacterial and antioxidant agents. Alkaloids and flavonoids are known to have antimicrobial properties which can help prevent and inhibit the growth of bacteria. In addition, flavonoids also often have antioxidant activity which can help fight free radicals and protect cells from damage. This research also mentions the results of using Chinese betel leaf extract on fish gonads with the aim of reducing potential contaminants. This suggests that Chinese betel leaf extract may have potential applications in microbial control and maintaining the health of organisms, in this case fish gonads.

Syahida et al. (2013) stated the addition of red betel leaf extract seems to affect the number of red blood cells (erythrocytes) and white blood cells (leukocytes) in goldfish. These changes may reflect the immune system's response to exposure to red betel leaf extract. The presence of significant changes in the percentage of lymphocytes and monocytes indicates that red betel leaf extract can influence the composition of white blood cells, which is an indicator of immune system activity. A decrease or increase in the phagocytosis index may indicate changes in the cell's ability to engulf and digest foreign objects or microbes. In this context, red betel leaf extract seems to influence phagocytic activity in goldfish

Soaking milkfish eggs in green betel leaves. Egg hatchability is the percentage of eggs that hatch successfully. In this study, soaking eggs with betel leaf extract at a dose of 1.5 ml/L of water gave HR results of 85.45%. This shows that this treatment is effective in increasing the hatchability of milkfish eggs. Larval survival is the percentage of larvae that survive after hatching. At the same dose, namely 1.5 ml/L of water, larval survival reached 85.52%. This indicates that soaking at this dose also has a positive impact on the survival of milkfish larvae. The statement states that the best dose for soaking betel leaf extract to achieve optimal results is 1.5 ml/L of water. This dose produced the highest hatchability of eggs and survival of milkfish larvae in this study (Susanti et al., 2022).

Soaking gourami fish eggs in betel leaf juice for 20 minutes resulted in the highest egg hatchability value of 89.33%. This shows that a soaking time of 20 minutes has a significant positive impact on increasing the hatchability of eggs in gourami fish. Treatment with betel leaf juice at 1.5 ml/L for 30 minutes, which may be the control group or treatment without soaking the betel leaves, showed the level of attack by the fungus *Saprolegnia* sp. the lowest was 3.33%. This means that soaking betel leaves has the potential to reduce fungal attacks on gourami fish eggs. Treatment with betel leaf juice at 1.5 ml/L of water also produced the highest larval survival value of 84.00%. This indicates that soaking betel leaf juice for 20 minutes can have a positive impact on the survival of gourami larvae (Susilo & Yusanti, 2022).

Providing green betel leaf flour in the feed of currant fish can increase their survival and growth. There was a significant effect ($P < 0.05$) of the use of betel leaf flour (*Piper betle* L) in feed on the survival and length growth of bonylip barb (*Osteochilus vittatus*). However, there was no significant effect ($P > 0.05$) on the absolute weight growth and daily growth rate of bonylip barb. A dose of betel leaf flour of 6 grams per 100 grams of feed is considered the best treatment to increase the growth and survival of bonylip barb. This indicates that this dose had a significant positive impact on the survival and length growth of bonylip barb. The results of the study showed that the use of betel leaf flour in feed can increase the survival and length growth of bonylip barb. Although there is no significant effect on absolute weight growth and daily growth rate, a positive impact can be observed on survival and length growth (Putra, 2022).

The effectiveness of administering betel leaf extract may be influenced by environmental factors such as water temperature, salinity, and fish population density.

Further research is needed to evaluate the effects of betel leaf extract on a large scale and understand how application in the field can affect overall cultivation results (Rani, 2021). It is important to pay attention to the potential impact of betel leaf extract on the aquatic environment and fish food safety. Administration of betel leaf extract may be part of a holistic disease management strategy, and future research could explore integration with vaccination, probiotics, and other management strategies.

Several studies show that administration of betel leaf extract can increase the phagocytic activity of macrophages, which play a role in engulfing and destroying pathogens (Musdja, 2012). Betel leaves contain antioxidant compounds such as flavonoids and polyphenols (Kopong & Warditiani, 2022). Giving betel leaf extract can provide protection against damage to fish cells due to free radicals (Wardhani, 2014). By increasing the antioxidant capacity in the fish body, betel leaf extract can increase the fish's resistance to oxidative stress which often occurs during disease infections (Widyawati et al., 2021). Further studies are needed to identify the active compounds in betel leaves that are responsible for the positive effects on the fish's immune system. A better understanding of how these compounds interact with fish biological systems can help optimize dosage and administration methods.

Through an in-depth understanding of the mechanism of action and influence of betel leaf extract, it is hoped that this administration can be an effective approach in increasing fish resistance to disease in aquaculture cultivation. There is a need for collaboration between researchers, breeders and policy makers to ensure successful practical implementation in the aquaculture sector.

CONCLUSION

From the results of the review regarding the effect of administering betel leaf extract in increasing non-specific immunity in the field of aquaculture, several important conclusions can be drawn: Betel leaf extract has shown significant antimicrobial potential against aquaculture pathogens, proving its role in controlling the spread of disease in fish farming ponds. Administration of betel leaf extract stimulates non-specific immune responses in fish, including increased production of immune cells such as macrophages and lymphocytes. This can strengthen the fish's body's ability to fight pathogen attacks. The antioxidant content in betel leaves provides protection against oxidative stress in fish, increasing their resistance to disease and unfavorable environmental conditions. Although the positive effects are visible, further research is needed to understand in more depth the mechanism of action of the active compounds in betel leaves and their interactions with the fish's biological systems. There are challenges related to environmental factors and implementation in the field that need to be overcome. However, administering betel leaf extract also offers opportunities as part of a holistic disease management strategy. Increasing the success of administering betel leaf extract in increasing the non-specific immunity of fish requires close collaboration between researchers, breeders and other related parties. Active involvement of stakeholders will ensure optimal knowledge transfer and practical application. By understanding the positive impact of betel leaf extract on the fish immune system in the context of aquaculture, it is hoped that this research can make a valuable contribution to the development of sustainable and effective strategies for managing disease in this sector. Practical implementation of these findings can make a real contribution to increasing the productivity and sustainability of fish farming.

ACKNOWLEDGMENT

Thank you to Sahrul Alim who helped in preparing this article.

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