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THE EFFECTIVENESS OF *Cosmos caudatus* IN PREVENTING HYPERGLYCEMIA DUE TO *Aeromonas hydrophila* INFECTION IN *Pangasianodon hypophthalmus*

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ABSTRACT

Cosmos caudatus is a herb that benefits overall health. This study aimed to determine the effect of *C. caudatus* leaf supplementation in feed on blood glucose levels in catfish (*Pangasianodon hypophthalmus*) challenged with *Aeromonas hydrophila*. This study was conducted from March to August 2024 at the Marine Microbiology Laboratory, Faculty of Fisheries and Marine, Universitas Riau. The method used was an experimental design employing a completely randomized design (CRD) with four treatments and three replications: negative control (NC, no supplementation, no infection), positive control (PC, no supplementation, with *A. hydrophila* bacterial infection), supplementation with *C. caudatus* at doses of 10 g/kg (T1), 15 g/kg (T2), and 20 g/kg (T3) of feed, all tested against *A. hydrophila*. The fish fry used weighed 5.00 ± 1.00 g and were reared for 75 days in 100-L tanks integrated with an aquaponics system. The fish were fed the experimental feed for 60 days before challenge with *A. hydrophila* bacteria (10^8 CFU/mL, intramuscular injection) and continued for 14 days after challenge. Blood glucose levels were measured at the beginning (day 1), day 30, pre-challenge (day 60), and post-challenge (day 75). The results showed that adding basil leaves to the feed affected blood glucose ($P<0.05$). The addition of *C. caudatus* leaves maintained glucose homeostasis within the range of 68.33±10.59-79.67±7.77 mg/dL. These findings indicate that *C. Caudatus* supplementation effectively prevents hyperglycemia caused by *A. hydrohila* infection in striped catfish and suggest its potential as a natural immunostimulant and metabolic modulator in aquaculture.

Keywords: Ulam Raja, Striped Catfish, Hyperglycemia, Motile Aeromonas septicemia

1. INTRODUCTION

The striped catfish (*Pangasianodon hypophthalmus*) is a highly valued species in aquaculture due to its rapid growth[1], adaptability to various environmental conditions[2], and high economic value[3]. Pangasius farming faces various challenges, including a bacterial disease caused by *Aeromonas hydrophila*. This bacterium causes Motile Aeromonas Septicemia

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(MAS), which can reduce production and cause mass mortality in fish. Sarker & Faruk[4] stated that *A. hydrophila* infection in striped catfish resulted in mortality rates of up to 100%. The use of antibiotics and synthetic chemotherapeutics is the primary option for treating this disease. However, their unwise use causes various problems such as bacterial resistance, residues in fishery products[6], and negative impacts on the aquatic environment[7].

Bacterial infections in fish trigger a physiological stress response, including an increase in blood glucose levels. Blood glucose is a highly sensitive biomarker commonly used to assess stress levels in fish[8]. When fish experience stress due to a pathogenic infection, the hypothalamic-pituitary-interrenal (HPI) axis is activated, stimulating the release of cortisol from the interrenal tissue. Cortisol then increases gluconeogenesis in the liver and inhibits peripheral glucose utilization, leading to elevated blood glucose levels (hyperglycemia)[9]. Prolonged hyperglycemia can disrupt energy metabolism, reduce immune function, and delay recovery from disease. Conversely, in cases of severe infection or septicemia, hypoglycemia may occur due to impaired liver function, increased glucose consumption by inflamed tissues, or endocrine system depression[10].

Given the problems associated with the use of synthetic antibiotics in aquaculture, the development of environmentally friendly, sustainable alternatives for disease control is crucial. One promising approach is the use of herbal immunostimulants, or phyto-pharmaceuticals, to enhance the non-specific immune system of fish, thereby improving their resistance to pathogenic infections. Herbal immunostimulants generally have low toxicity, leave no harmful residues, are readily biodegradable, and can be produced locally at a relatively affordable cost[11,12]. Various herbal plants have been studied for their potential as immunostimulants in fish, such as kenikir leaves (*Cosmos caudatus* Kunth). *C. caudatus* leaves are a tropical herbal plant that grows widely in Southeast Asia, including Indonesia. *C. caudatus* leaves contain various bioactive compounds, including flavonoids (quercetin, rutin, luteolin), phenolic acids (chlorogenic acid, caffeic acid), saponins, tannins, alkaloids, terpenoids, and essential oils[13,14].

The mechanism of action of herbal immunostimulants includes increased macrophage phagocytosis activity[15], stimulation of respiratory burst production, increased lysozyme activity, and pro-inflammatory cytokine expression. Additionally, bioactive compounds in herbal plants, such as flavonoids, saponins, tannins, and polyphenols, exhibit antioxidant activity that can protect cells from oxidative damage caused by infection[16].

According to Sofia et al.[17]; Rinawati et al.[18], plants rich in flavonoids and phenols have been shown to significantly lower blood glucose levels in diabetic rats. This indicates their potential application in managing hyperglycemia in fish. The potential of *C. caudatus* leaves as an immunostimulant in fish has not been widely explored, so this study is expected to provide scientific information on the effectiveness of *C. caudatus* leaves in increasing striped catfish resistance to *A. hydrophila* infection, particularly in maintaining metabolic homeostasis, as reflected in the stability of blood glucose levels.

2. RESEARCH METHOD

Time and Place

This study was conducted from March to August 2024 at the Marine Microbiology Laboratory, Faculty of Fisheries and Marine Sciences, Universitas Riau.

Method

The method used in this study was an experimental method applying a Complete Randomized Design (CRD) with one factor and four treatment levels. To reduce the error rate, the experiment was repeated three times, requiring 15 experimental units. The treatment doses in this study were based on

Simarmata et al.[19] regarding the application of *C. caudatus* leaves in striped catfish maintenance, with the following treatments:

NC (Negative Control)	:	Feed without *C. caudatus* leaf supplementation, without infection
PC (Positive Control)	:	Feed without *C. caudatus* leaf supplementation, with *A. hydrophila* infection
T1	:	Feed with a *C. caudatus* leaf dose of 10 g/kg feed
T2	:	Feed with a *C. caudatus* leaf dose of 15 g/kg feed
T3	:	Feed with a *C. caudatus* leaf dose of 10 g/kg feed.

Procedures

Feed Preparation

The *C.* caudatus-enriched feed pellets were prepared using a powder-coating method. Fresh *C. caudatus* leaves were procured from local markets in Pekanbaru, Indonesia, and subjected to solar drying, followed by mechanical grinding and sieving to obtain a fine powder. The coating procedure followed the protocol established by Simarmata et al.[19], in which 20 g of tapioca starch was dispersed in 50 mL of distilled water at ambient temperature (25 ± 2°C). Subsequently, 100 mL of boiling water (approximately 100°C) was gradually added to the tapioca suspension under continuous stirring until a homogeneous, viscous, translucent gel was formed. Upon cooling the tapioca gel to room temperature, the predetermined quantity of *C. caudatus* powder was incorporated and thoroughly mixed to ensure uniform distribution. The tapioca-*C.caudatus* mixture was then applied as a coating to 1 kg of commercial fish feed pellets through manual mixing, followed by solar drying until the moisture content stabilized. The enriched pellets were stored in airtight polyethene bags under ambient conditions until use in the experiment.

Experimental Fish and Rearing Conditions

Fingerlings of *P. hypophthalmus* with an initial body weight of 5.00±1.00 g and total length of 5.00 ± 1.00 cm were used in this study. The fish were kept in 100-L circular plastic tanks (60 cm diameter) at a stocking density of 30 individuals per tank. To ensure optimal water quality, an integrated aquaponics system was established in each tank, with 20 *Ipomoea aquatica* plants per unit. A submersible circulation pump with a capacity of 800 L/hour was installed at the tank base to facilitate water flow through the aquaponic units, where plant roots absorbed metabolic waste products before the purified water returned to the rearing tanks.

During weeks 1–3, fish were fed commercial pellets (F999, PT Central Proteina Prima, Indonesia). As the fish developed and their mouth openings increased, the diet was transitioned to larger pellets (HI-provite 781-1). Throughout the 75-day experimental period, fish received feed three times daily (morning, midday, and evening) to apparent satiation. Feed was administered gradually in small portions, with subsequent additions provided only after complete consumption of the previous portion and continued observation of active feeding behavior.

Bacterial Challenge and post-infection monitoring

Following 60 days of feeding with *C. caudatus*-enriched pellets, fish were challenged with *A. hydrophila* on day 61 via intramuscular injection (0.1 mL, 10^8 CFU/mL). Post-challenge, fish continued to receive *C. caudatus*-enriched pellets for an additional 14 days. Survival rates were recorded at least twice daily, with mortalities and uneaten feed removed immediately to maintain tank hygiene.

Blood Sampling and Glucose Analysis

Blood samples were collected at three time points throughout the experimental period: baseline (day 1), pre-challenge (day 60), and post-challenge (day 75). Prior to blood collection, fish were humanely anaesthetized using cold-water immersion at approximately 8°C, following established protocols[20]. Blood was subsequently withdrawn from the caudal vein using a 1-mL sterile syringe and immediately transferred to microcentrifuge tubes for glucose analysis.

Blood glucose concentrations were determined using a portable glucometer (GlucoDr, Allmedicus Co., Ltd.) with a measurement range of 20–600 mg/dL. All glucose measurements were conducted in the morning, prior to the first daily feeding, to minimise postprandial interference. A drop of whole blood was applied directly to a glucose test strip pre-inserted into the glucometer, and readings were recorded immediately upon digital display[21,22].

Data Analysis

Data obtained from blood glucose measurements were collected and tabulated into tables. The data were analysed statistically using SPSS version 26. The data were analysed using a one-way ANOVA, and the results indicated homogeneity. If the analysis showed an effect, further tests using Student-Newman-Keuls (SNK) were conducted.

3. RESULT AND DISCUSSION

Blood glucose is a sensitive biomarker for evaluating stress conditions in fish. Increased blood glucose levels are a normal physiological response to stressful conditions, including bacterial infections. Under stressful conditions, cortisol is released, stimulating gluconeogenesis in the liver and increasing blood glucose levels to meet energy demands. The results of blood glucose level measurements in catfish during the study are presented in Table 1

Table 1. Blood glucose levels of striped catfish (mg/dL

Treatment	Blood glucose			
	Initial	30 days	60 days	Post-challenge
NC		76.00±6.24^{a}	75.00±5.29^{a}	86.67±3.79^{b}
PC		78.67±6.03^{a}	84.67±2.89^{a}	120.33±1.53^{c}
T1	62.00±8.89	83.00±10.54^{a}	80.33±6.11^{a}	68.33±10.59^{a}
T2		72.67±14.98^{a}	78.33±5.51^{a}	79.67±7.77^{ab}
T3		66.67±21.50^{a}	76.67±10.07^{a}	68.67±5.51^{a}

Notes: Different *superscript* letters in the same column indicate significant differences between treatments ($P<0.05$)

Blood glucose level measurements showed interesting fluctuations during the study period. At the initial measurement, all treatments had a blood glucose value of 62.00±8.89 mg/dL, indicating that the catfish were in a normal physiological state before treatment. This value is within the normal physiological range for tropical freshwater fish and indicates that all test fish were in uniform health conditions before treatment. According to Zaki et al.[23], the glucose levels of striped catfish range from 67-92 mg/dL. On the 30th day of observation, an increase in blood glucose levels was seen in all treatments, ranging from 66.67±21.50 to 83.00±10.54 mg/dL. Statistical analysis (ANOVA) showed no significant differences between treatments ($p>0.05$). This increase in blood glucose can be attributed to the physiological adaptation process to the feed given and stress management that occurred during the initial maintenance period. T1 showed the highest value (83.00±10.54 mg/dL), while group T3 with a *C.caudatus* leaf dose of 20 g/kg feed had the lowest value (66.67±21.50 mg/dL).

Observations on day 60 showed that blood glucose remained stable across most treatments. NC and all treatments with *C. caudatus* leaf supplementation (T1, T2, T3) maintained glucose levels in the range of 75.00-80.33 mg/dL, with no significant differences between groups ($p>0.05$). The upward trend in blood glucose values indicates that the 60-day period represents a phase of metabolic homeostasis, during which blood glucose regulatory mechanisms function optimally, and *C. caudatus* leaf supplementation does not produce significant hyperglycemic or hypoglycemic effects under normal conditions. According to Borski et al.[24], metabolic homeostasis in fish involves a balance between energy intake and expenditure, primarily regulated by glucoregulatory, growth, and stress hormones. Regulating glucose levels is crucial for maintaining energy reserves and ensuring the survival of organisms. Suryadinata[25] found that lime peel extract reduces blood glucose levels in hyperglycemic conditions, indicating its potential as a hypoglycemic agent. Additionally, the addition of FMH to the diet of *P. hypophthalmus* has been shown to improve physiological profiles, including blood glucose levels, indicating that dietary intervention can modulate glucose metabolism[26].

The post-infection response or challenge test with *A. hydrophila* provided a very different appearance and became a crucial point in this study. PC that did not receive *C. caudatus* leaf treatment and was infected showed a drastic increase in blood glucose levels to 120.33±1.53 mg/dL, which was significantly higher ($p<0.05$) than those of other treatments. The hyperglycemia observed in PC was a metabolic stress response to a pathogenic bacterial infection. Infected fish often show an increase in blood glucose levels, a condition known as hyperglycemia. This is a common response to stress and infection, as seen in Nile tilapia infected with *Shewanella putrefaciens*, where glucose levels increased significantly after infection[27]. According to Nissa et al.[28], *A. hydrophila* infection causes significant changes in the host proteome, particularly in liver tissue, which is crucial for glucose metabolism.

Administration of *C. caudatus* leaves demonstrated a remarkable ability to maintain blood glucose homeostasis post-infection. ANOVA results showed a significant effect of treatments ($P<0.05$). This indicates a relatively strong immunomodulatory and antistress effect of *C. caudatus* leaves at that dose. Supplementation with kenikir leaves not only prevents hyperglycemia due to infection stress, but also maintains glucose metabolism at a more efficient level. The bioactive mechanism of *C. caudatus* leaves in modulating blood glucose levels is likely related to the presence of phytochemicals such as flavonoids, polyphenols, and terpenoids, which have been widely reported to have antioxidant, anti-inflammatory, and immunostimulatory activities. Ahda et al.[13]; Curiel-Ayala et al.[29] state that flavonoids and polyphenols in *C. caudatus* have been shown to increase insulin sensitivity, protect pancreatic beta cells, and regulate glucose metabolism, which is crucial for insulin production and helps maintain blood glucose levels. According to Kaur et al.[30], terpenoids in *C. caudatus* enhance insulin secretion and glucose uptake in cells and reduce oxidative stress and inflammation, which are vital for managing diabetes and its complications.

Overall, the results of this study provide strong evidence that supplementing catfish feed with *C. caudatus* leaves can maintain blood glucose homeostasis during *A. hydrophila* infection challenges. This ability indicates the potential of *C. caudatus* leaves as a natural phytobiotic that can enhance fish resistance to disease infection by strengthening the immune response and reducing the impact of metabolic stress.

4. CONCLUSION

Supplementation of *C. caudatus* leaves in the feed significantly affected blood glucose homeostasis in striped catfish challenged with *A. hydrophila*. The positive control (PC) without herbal supplementation showed severe hyperglycemia (120.33±1.53 mg/dL) post-infection, indicating a metabolic stress response. In contrast, fish fed *C. caudatus*-enriched feed maintained blood glucose levels within the normal physiological range (68.33-79.67 mg/dL), comparable to those in the control without infection (KN). This study provides scientific evidence supporting the application of *C. caudatus* as a natural and sustainable alternative to synthetic antibiotics in aquaculture disease management, particularly for controlling metabolic stress associated with *A. hydrophila* infection in striped catfish production.

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