



Nano-Curcumin as a Functional Feed Additive for the Nile Tilapia: Impacts on Growth, Health, and Gene Expression

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ABSTRACT

This study aimed to evaluate the effects of dietary supplementation with nano-curcumin at levels of 0, 50, 100, and 150mg/ kg of feed (G1, G2, G3, and G4, respectively) on the growth performance, feed efficiency, blood biochemical parameters, and gene expression of the Nile tilapia. A total of 120 fingerlings were used in the experiment, distributed evenly among the treatment groups. They were acclimated and then randomly allocated and distributed across 12 aquariums with 10 fries each, having an initial average weight of 251.75±0.494g per aquarium. Experimental diets seemed to be iso-caloric and nitrogenous among the four tested diets. Values of FW, TBWG, ADG, SGR, RGR, FI, CPI, and PER were significantly increased when fish group received diets containing 50, 100, and 150mg nano-curcumin/ kg diet in comparison with the control group. In addition, FCR was significantly improved. Serum protein, albumin, and globulin levels were significantly ($P<0.05$) increased in all nano-curcumin treated groups. Values of ALT, AST, uric acid, and creatinine showed non-significant ($P>0.05$) changes, while glucose and cholesterol exhibited a significant decrease ($P<0.05$) with a 150mg/ kg diet (G₄). Nano-curcumin supplementation modulated the hepatic GH–IGF axis in the Nile tilapia in a dose-dependent manner. A moderate level (50mg nano-curcumin/ kg diet) enhanced IGF1 expression and growth potential, whereas higher doses (100 and 150mg nano-curcumin/ kg diet) reduced IGF1 but sustained elevated GH expression, suggesting a shift toward metabolic or stress-adaptive functions. Practically, a diet of 50mg nano-curcumin/kg appears optimal for promoting growth-related gene expression, although higher doses may still support resilience. It can be mentioned that, under the condition that it is available, the incorporation of nano-curcumin at different levels enhances growth performance, total protein, albumin, and globulin values, has no hazardous effect on liver and kidney functions, and improves gene expression.

INTRODUCTION

Aquaculture has become one of the fastest-growing food production sectors worldwide, with the Nile tilapia (*Oreochromis niloticus*) representing a key species due to growth rates, adaptability, and economic importance.

However, achieving optimal growth and maintaining health in intensive aquaculture systems requires innovative nutritional strategies that can enhance growth performance and immune function while reducing reliance on synthetic additives. In this context, functional feed additives derived from natural compounds, such as curcumin, have attracted considerable attention (**Abdel-Tawwab *et al.*, 2018**).

Global tilapia production reaches around 4.5 million tons each year (**FAO, 2022**). This species is known for its rapid growth (**Abdel-Tawwab *et al.*, 2006**), ability to accept a variety of alternative protein sources (**Ng & Romano, 2013**), and efficient feed utilization (**Mengistu *et al.*, 2020**).

Tilapia also shows strong resilience to stress (**Sutthi & Thaimuangphol, 2020; Wardani *et al.*, 2021**) and can tolerate less-than-ideal water conditions (**Ai *et al.*, 2022; Zidan *et al.*, 2022**). Due to these characteristics, tilapia is considered a highly adaptable and promising species for global aquaculture (**Prabu *et al.*, 2019**).

Boyd *et al.* (2022) and **Jiang *et al.* (2022)** highlighted that, in order to satisfy the growing demand for aquaculture products, farmers are increasingly adopting intensive farming practices to boost fish growth and health. However, these high-density systems can introduce stressors that compromise fish welfare, leading to higher susceptibility to disease, increased mortality, and economic losses (**Tian & Dong, 2023**).

Recent advances in nanotechnology have shown considerable promise in addressing such challenges. **Parveen *et al.* (2023)** reported a rapid expansion of nanotechnology applications in biomedical research, reflected by the rising number of related publications. Furthermore, studies by **Moniruzzaman and Min (2020)**, **Kumar *et al.* (2023)** and **Parveen *et al.* (2023)** indicate that nanomaterials such as nano-emulsions of essential oils can overcome the limitations of conventional approaches by offering enhanced structural properties and surface characteristics that effectively combat pathogenic bacteria.

Moreover, **El Basuini *et al.* (2024)** stated that curcumin or diferuloylmethane [1, 7-bis (4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-Dione] originated from turmeric rhizome (*Curcuma longa*) at 3–6%, is a polyphenol highly vigorous botanical product with bioactive properties.

Furthermore, many published works have confirmed the beneficial effects of curcumin on fish growth, productivity, immunity and health, as demonstrated by **Fagnon *et al.* (2020)**, **Moniruzzaman and Min (2020)** and **Alagawany *et al.* (2021a)**. These

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include the rainbow trout (*Oncorhynchus mykiss*), as mentioned by **Yonar et al. (2019)**, the snakehead fish (*Channa argus*), as noted by **Li et al. (2022)**, and the red tilapia (*Oreochromis* sp.), as shown in the study of **Eissa et al. (2023b)**.

Curcumin, the bioactive polyphenolic compound extracted from *Curcuma longa* (turmeric), is well known for its antioxidant, anti-inflammatory, antimicrobial, and growth-promoting properties (**Hewlings & Kalman, 2017**).

Nevertheless, its application in aqua feeds is limited due to poor bioavailability, rapid metabolism, and low water solubility. To overcome these drawbacks, nano-curcumin formulations have been developed, which significantly improve curcumin's solubility, stability, and absorption, thereby enhancing its biological activity (**Prasad et al., 2014; Salehi et al., 2020**).

Growth in fish is largely regulated by the growth hormone (GH)–insulin-like growth factor 1 (IGF1) axis, which controls somatic growth, protein synthesis, and metabolic regulation (**Reindl & Sherwere idan, 2012**).

Dietary interventions that influence this axis can directly enhance growth performance and feed utilization efficiency. Previous studies have shown that curcumin supplementation can improve growth performance, feed efficiency, and antioxidant capacity in tilapia and other fish species (**Awad et al., 2020; Dawood, 2021**). However, the effects of nano-curcumin on the molecular regulation of GH and IGF1 in the Nile tilapia remain poorly understood.

Therefore, this study investigated the potential role of dietary nano-curcumin in modulating the gene expression of GH and IGF1 in liver tissues of *Oreochromis niloticus*. By assessing the transcriptional responses of these key growth-related genes, we aimed to better understand how nano-curcumin supplementation may improve growth regulation and contribute to sustainable aquaculture production.

Hence, this work aimed to investigate the effect of incorporation of nano-curcumin at different levels in the Nile tilapia fingerlings diets on their performance, feed utilization, blood biochemical parameters and gene expression.

MATERIALS AND METHODS

The experimental study was operated at the Fish Experimental Laboratory belonging to the Animal Production Department, Biological Agriculture Research Institute, National Research Centre, 33 El-Bohouth Street, P.O. Box: 12622, Dokki, Cairo, Egypt, throughout co-operation work with the Department of Cell Biology, Biotechnology Research Institute, National Research Centre, Giza, Dokki, Giza, 12622, Egypt, Hydrobiology Department, Veterinary Research Institute, National Research

Centre, 33 El-Bohouth Street, P.O:12622, Dokki, Cairo, Egypt and the Department of Packaging Materials, National Research Centre, Dokki, Giza, P.O. 12622, Egypt.

Experimental unit

A total of 120 fries were acclimated and then randomly allocated into the experimental aquariums. Fish were distributed across 12 glass aquaria (80 × 40 × 30 cm; 60 L capacity each) at a density of 10 fries per aquarium, having an initial average weight of 251.75±0.494g per aquarium. Fish were obtained from the Abbassa Fish Hatchery, Sharkia Government, Egypt.

Experimental design and diets

Diet preparation

Four experimental diets were prepared to evaluate the effects of nano-curcumin supplementation on fish performance. A basal control diet was formulated to meet the nutritional requirements of the species, and three additional diets were produced by incorporating nano-curcumin at 50, 100, and 150mg kg⁻¹ feed, respectively.

All dry ingredients (Table 1) were finely ground to pass a 500µm sieve and thoroughly mixed in a mechanical blender for 5min. Fish oil and approximately 30–35 % water were gradually added to obtain a homogeneous dough. For the supplemented diets, the required amount of nano-curcumin powder was first premixed with a small portion of the basal feed to ensure uniform distribution, and then blended into the full batch.

The dough was pelleted using a laboratory pelletizer fitted with a 2mm die, producing pellets approximately 2– 3mm long. Pellets were dried in a forced-air oven at 55°C until moisture content was below 10%, then cooled to room temperature. After drying, pellets were stored in airtight, light-proof polyethylene bags at 4°C until use.

Representative samples from each diet were analyzed for proximate composition (moisture, crude protein, lipid, ash, and fiber) following the **AOAC (2019)** procedures. Nano-curcumin inclusion levels were verified by weighing accuracy during mixing, and all diets were prepared from the same basal mixture to ensure comparable nutrient profiles, except for nano-curcumin concentration.

Experimental Nile tilapia fries were divided into 4 groups as follows:

G₁: First group (control group) fed basal diet that did not contain nano-curcumin.

G₂: Second group fed basal diet that contained 50mg nano-curcumin/ kg diet.

G₃: Third group fed basal diet that contained 100mg nano-curcumin/ kg diet.

G₄: Fourth group fed basal diet that contained 150mg nano-curcumin/ kg diet.

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The feeding trial lasted for 56 days and extended approximately from first of June 2024 to the end of July 2024. The composition of the different experimental diets is presented in Table (1)

Table 1. Composition of the different experimental diets

Item	Experimental diets			
	Zero Nano curcumin	50 mg Nano curcumin / kg diet	100 mg Nano curcumin / kg diet	150 mg Nano curcumin / kg diet
	G ₁	G ₂	G ₃	G ₄
Composition of tested diets				
	Basal diet	Tested diets		
Soybean meal (44%)	40	Basal diet	Basal diet	Basal diet
Protein concentration (56%)	17	+	+	+
Ground Yellow corn (8%)	28	50 mg	100 mg	150 mg
Wheat bran (13%)	10	Nano	Nano	Nano curcumin
Vegetable oil	3	curcumin	curcumin	/ kg diet
Vitamin and Minerals mixture*	2	/ kg diet	/ kg diet	

*Vitamin and Minerals mixture: contained Vit. A (E672) (IU) 876.19, Vit. D3 (IU) 1141.39, Vit. E 114.30, Vit. K3 7.55, Vit. B1 13.71, Vit. B2 11.44, Vit. B6 15.33, Vit. B12 0.03, Niacin 60.96, Calpan 30.48, Folic Acid 3.04, Biotin 0.37, Vit. C 11.44, Selenium 0.27, Manganese 19.04, Iron 9.15, Iodine 0.77, Zinc 76.19, Copper 3.04, Cobalt 0.37, Choline Chloride 457.14, and Antioxidant 95.23 (Vit. vitamin; IU international unit).

Parameters of growth performance (NRC, 2001)

Body weight gain (BWG) = Final weight - Initial weight.

Survival rate (SR %) = Number of fish at final / Number of fish at start x100.

Specific growth rate (SGR) =

[In final weight (g) - In initial weight (g)] / Experimental days *100

Calculation of feed conversion ratio (FCR)

FCR = Total dry matter intake, (TDMI), g / Total body weight gain (TBWG), g.

Calculation of crude protein efficiency ratio (CPER)

(PER) = Total body weight gain (TBWG), g / Total crude protein intake (TCPI), g.

Blood sampling

Blood samples were obtained from the caudal vein of the fish using a 3mL syringe following anesthesia with clove oil at a concentration of 0.5mL L⁻¹.

The collected blood was transferred into clean, dry centrifuge tubes and was left at room temperature to allow clot formation. After clotting, the samples were centrifuged at 3,000 rpm for 15 minutes. The resulting serum was carefully separated, collected, and stored at -20°C until further biochemical analyses were performed.

Analytical procedures

Analysis of tested diets and fish body composition were analyzed according to **AOAC (2016)**.

Biochemical assays

Serum biochemical parameters were analyzed as follows: Total protein was measured according to **Cannon *et al.* (1974)**; albumin was determined following **Tietz (1990)**; and globulin was calculated by subtracting albumin from total protein. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were assessed according to **Reitman and Frankel (1957)**.

Cholesterol was measured following **Ellefson and Caraway (1976)**, glucose was estimated as described by **Caraway and Watts (1987)**, and uric acid and creatinine were determined according to **Tietz (1990)**. All assays were conducted using commercial biochemical kits (Spectrum-Diagnostics, Egypt). Colorimetric measurements were performed in accordance with the manufacturers' instructions using an Agilent Cary UV-Vis spectrophotometer (100/300 Series).

Gene expression analysis

To assess the molecular responses to dietary nano-curcumin, quantitative gene expression analysis was conducted on liver tissues.

At the end of the feeding trial, three fish per replicate (nine fish per treatment) were randomly selected. Fish were euthanized using an overdose of clove oil (1mL/ L), and liver and head kidney tissues were quickly excised, snap-frozen in liquid nitrogen, and stored at -80°C until RNA extraction.

Total RNA was isolated using TRIzol™ reagent (Invitrogen, Thermo Fisher Scientific) according to the manufacturer's instructions. RNA concentration and purity were evaluated spectrophotometrically (NanoDrop 2000, Thermo Fisher Scientific) by measuring the A260/A280 ratio, and RNA integrity was confirmed on a 1% agarose gel. Complementary DNA (cDNA) was synthesized using the High-Capacity cDNA Reverse Transcription Kit (Applied Biosystems, USA), with 1 µg of total RNA per reaction, following the manufacturer's protocol.

Quantitative real-time PCR (qPCR) was performed on a QuantStudio™ 5 Real-Time PCR System (Applied Biosystems) using SYBR Green Master Mix (Roche). Each 20µL reaction contained 10µL SYBR Green Master Mix, 1µL of each forward and reverse primer, 2µL cDNA template, and 6µL nuclease-free water. The thermal cycling program consisted of an initial denaturation at 95°C for 10 minutes, followed by 40 cycles of 95°C for 15 seconds, 60°C for 30 seconds, and 72°C for 30 seconds.

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The gene panel included growth-related genes, specifically growth hormone (GH) and insulin-like growth factor 1 (IGF1), to evaluate the influence of dietary nano-curcumin on growth regulation. β -actin was used as a housekeeping gene to normalize expression levels. Relative gene expression was calculated using the $2^{-\Delta\Delta C_t}$ method (Livak & Schmittgen, 2001). Primer sequences for all target and reference genes, designed based on GenBank accession numbers, are presented in Table (2).

Table 2. Primer sequences used for gene expression analysis

Gene	Primer Sequences	Accession no.
GH	F: CTGTCTGTCTGTCTGTCAGTCGT R: AGAGGAGACGCCCAAACAC	M97766.1
IGF-1	F: CCCGAACCTTCCTCGACTTGA R: CCTCAGCCAGACAAGACAAAAA	AF033797
β-actin	F: ACCCACACAGTGCCCATC R: CAGGTCCAGACGCAGGAT	EF026001.1

Gross energy calculation and statistical analysis

The gross energy content of the experimental diets and the body composition of the tested fish groups were calculated following the methods of **Blaxter (1968)** and **MacRae and Lobley (2003)**. The energy values used for calculations were: 1g of crude protein (CP) = 5.65 kcal, 1g of ether extract (EE) = 9.40 kcal, and 1g of crude fiber (CF) or nitrogen-free extract (NFE) = 4.15 kcal. All collected data were analyzed using one-way analysis of variance (ANOVA) with SPSS software (version 2020). Significant differences among treatment means were determined using Duncan's multiple range test (Duncan, 1955).

RESULTS

Chemical analysis of different experimental diets

Data in Table (3) show that values of CP% of different experimental diets ranged from 30.66 to 30.79% among the four tested diets. Meanwhile, values of EE% of different experimental diets ranged from 3.44 to 3.46% among the four experimental diets. On the other hand, gross energy fluctuated from 4519 to 4522 kcal/ kg DM among the four tested diets. Furthermore values of different experimental diets considered adequate and suitable to cover the Nile tilapia fish requirements; in addition, the experimental diets seemed to be iso-caloric and iso-nitrogenous.

Table 3. Chemical analysis of different experimental diets

Item	Experimental diets			
	Zero Nano curcumin	50 mg Nano curcumin / kg diet	100 mg Nano curcumin / kg diet	150 mg Nano curcumin / kg diet
	G ₁	G ₂	G ₃	G ₄
Moisture	5.34	5.35	5.33	5.36
Dry matter (DM)	94.66	94.65	94.67	94.64

<i>Chemical analysis on DM basis</i>				
Organic matter (OM)	93.46	93.45	93.47	93.46
Crude protein (CP)	30.66	30.71	30.75	30.79
Crude fiber (CF)	5.61	5.59	5.60	5.62
Ether extract (EE)	3.45	3.44	3.46	3.45
Nitrogen free extract (NFE)	53.74	53.71	53.66	53.60
Ash	6.54	6.55	6.53	6.54
<i>Energetic values</i>				
Gross energy kcal/ kg DM	4520	4519	4522	4522
Gross energy Cal/ g DM	4.520	4.519	4.522	4.522

Gross energy (kcal/ kg DM) was calculated according to (Blaxter1968; MacRae and Lobley 2003).

Where, each g CP = 5.65 Kcal, g EE = 9.40 kcal and g CF and NFE = 4.15 Kcal.

Performance and feed utilization.

Data in Table (4) highlight that incorporation of nano-curcumin at different levels (50, 100 and 150mg/ kg) in the Nile tilapia fingerlings diets caused significantly ($P<0.05$) increasing values of FW, TBWG, ADG, SGR, and RGR. The highest values recorded were when the group of fish received diet containing 150mg nano-curcumin/ kg diet (G₄) compared to the other groups (G₁, G₂ and G₃). Survival ratio recorded 90, 90, 93.33 and 100% for G₁, G₂, G₃ and G₄, respectively, meanwhile, mortality rate % recorded 10, 10, 6.67 and zero % in the four experimental groups (G₁, G₂, G₃ and G₄, respectively). Additionally, as presented in Table (4), the results demonstrated that values of feed utilization that includes FI and CPI were significantly ($P<0.05$) increased when fish group received diets containing 50, 100 and 150mg nano-curcumin/ kg diet in comparison with that received diet containing zero nano-curcumin (G₁).

The highest values of FI and PI were recorded by the group of fish offered a diet containing 150mg nano-curcumin/ kg diet (G₄), with 438g and 134.86g, respectively.

Additionally, FCR significantly ($P<0.05$) improved with fish groups (G₂, G₃ and G₄) that received diets containing 50, 100, and 150 mg nano-curcumin/ kg diet compared to the control group (G₁) that did not receive nano-curcumin in its diet. The best improving value in feed conversion (1.564) was recorded by G₄ that received diet containing 150mg nano-curcumin/ kg diet in comparison with the other three groups (G₁, G₃ and G₂) that were recorded with 4.458, 3.607 and 2.260 for G₁, G₂ and G₃, respectively. Moreover, values of PER significantly ($P<0.05$) increased in fish group when nano-curcumin was added at 50, 100 or 150mg/ kg diet (G₂, G₃ and G₄).

Table 4. Feed utilization of the Nile tilapia fingerlings fed diets containing different levels of nano-curcmin

Item	Experimental groups				SEM	Sign. $P<0.05$
	Zero Nano curcumin	50 mg Nano curcumin / kg diet	100 mg Nano curcumin / kg diet	150 mg Nano curcumin / kg diet		
	G ₁	G ₂	G ₃	G ₄		
TBWG, g	72 ^d	93 ^c	166 ^b	280 ^a	24.642	*
FI, g	321 ^d	335 ^c	375 ^b	438 ^a	13.726	*

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FCR	4.458 ^b	3.607 ^b	2.260 ^a	1.564 ^a	0.358	*
FCP%	30.66	30.71	30.75	30.79	-	-
CPI, g	98.42 ^d	102.87 ^c	115.31 ^b	134.86 ^a	4.271	*
PER	0.7316 ^d	0.9041 ^c	1.4396 ^b	2.0762 ^a	0.160	*

a, b, c and d: Means in the same row having different superscripts differ significantly ($P < 0.05$).

SEM: Standard error of the mean *: Significant at ($P < 0.05$). FI: Feed intake.

TBWG: Total body weight gain. FCR: Feed conversion ratio. FCP%: Feed crude protein percentages.

CPI: Crude protein intake. PER: Protein efficiency ratio.

Biochemical parameters of the different experimental groups

As presented in Table (5), feeding of *O. niloticus* on nano-curcumin revealed a significant increase ($P < 0.05$) in total serum protein, and globulin levels compared to the control. The highest concentrations of protein and globulin were recorded in 150mg nano-curcumin/ kg diet; the corresponding values were 5.83 and 4.78g/ dl, for total protein and globulin, respectively. In addition, albumin values were significantly increased ($P < 0.05$) in both 50mg/ kg diet and 100mg/ kg diet. On the other hand, values of ALT, AST, uric acid, and creatinine showed non-significant ($P > 0.05$) changes in comparison with the control, while glucose and cholesterol showed significant decreasing values ($P < 0.05$) in the fish group that received a diet containing 150mg/ kg (G_4) and non-significant changes ($P > 0.05$) in G_2 that received the lowest nano-curcumin concentration (50mg/ kg).

Table 5. Biochemical parameters of the Nile tilapia fingerlings fed diets containing different levels of nano-curcumin

Item	Experimental diets				SEM	Sign. $P < 0.05$
	Zero Nano curcumin	50 mg Nano curcumin / kg diet	100 mg Nano curcumin / kg diet	150 mg Nano curcumin / kg diet		
	G_1	G_2	G_3	G_4		
Total Protein (g/dl)	2.71 ^c	3.78 ^b	4.43 ^b	5.83 ^a	0.25	*
Albumin (g/dl)	0.87 ^c	1.26 ^{ab}	1.36 ^a	1.05 ^{bc}	0.09	*
Globulin (g/dl)	1.91 ^c	2.44 ^{bc}	3.07 ^b	4.78 ^a	0.22	*
Glucose (mg/dl)	108.3 ^a	114.6 ^a	90.9 ^b	97.7 ^b	4.02	*
Total cholesterol (mg/dl)	242.9 ^a	256.5 ^a	280.3 ^a	159.3 ^b	18.59	*
Liver function						
ALT (Unit/l)	106.5 ^a	103.5 ^a	113.4 ^a	101.7 ^a	4.30	NS
AST (Unit/l)	252.0 ^a	245.5 ^a	278.5 ^a	256.4 ^a	8.48	NS
Kidney function						
Uric acid (mg/dl)	25.09 ^{ab}	28.28 ^a	17.55 ^b	29.92 ^a	3.37	NS
Creatinine (mg/dl)	30.21 ^a	21.58 ^b	29.18 ^{ab}	26.99 ^{ab}	2.80	NS

a, b and c: Means in the same row having different superscripts differ significantly ($P < 0.05$).

SEM: Standard error of the mean

NS: Not significant.

*: Significant at $P < 0.05$.

AST: Aspartate aminotransferase (AST). ALT: Alanine aminotransferase.

Gene expression

The relative mRNA expression levels of insulin-like growth factor 1 (IGF1) and growth hormone (GH) in the liver tissues of the Nile tilapia (*Oreochromis niloticus*) following dietary supplementation with nano-curcumin are presented in Fig. (1). For

IGF1, the expression levels varied significantly among treatments. The control group exhibited a low baseline expression level (~1.0 fold). The T1 group (50mg/ kg; 10ml/ kg) showed the highest up-regulation of IGF1, reaching approximately a 2.2-fold increase compared to control. However, IGF1 expression was markedly reduced in T2 (100mg/ kg; 20ml/ kg) and T3 (150mg/ kg; 30ml/ kg), with both showing significantly lower expression values close to or below the control level. Statistical analysis indicated that T1 was significantly different ($P < 0.05$) from the other groups, while T2 and T3 did not differ significantly from the control. In contrast, GH expression exhibited a different trend. The control group again showed the lowest baseline expression (~1.0 fold). A significant up-regulation was observed in all treatment groups supplemented with nano-curcumin. GH expression levels increased progressively from T1 through T3, with T1 and T2 reaching approximately 5-fold increases, and T3 showing the highest expression, nearly 6-fold compared to control. Treatments T1, T2, and T3 were significantly higher than the control ($P < 0.05$) but not significantly different among each other. These results suggest that nano-curcumin supplementation at lower doses (50mg/ kg) enhances IGF1 expression, while higher doses suppress it. In contrast, GH expression responds positively to all supplementation levels, with a dose-dependent trend toward higher expression.

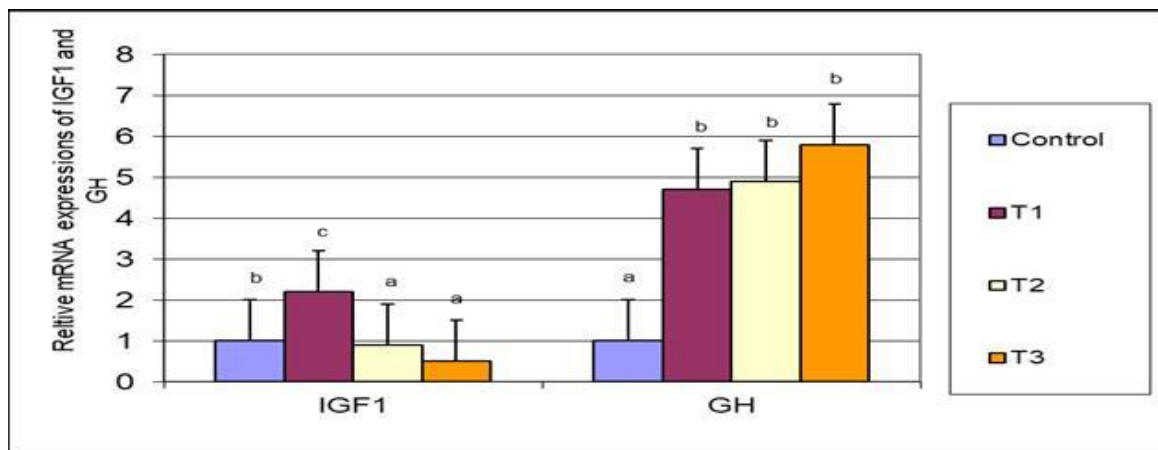


Fig. 1. Relative mRNA expression of IGF1 and GH genes in liver tissues of the farmed Nile tilapia fish after feeding diets with three different nano-curcumin concentrations (50, 100 and 150 mg/kg). Different letters are significantly different at $P < 0.05$

DISCUSSION

Data of chemical analysis of different experimental diets cleared that values of CP% of different experimental diets ranged from 30.66 to 30.79% among the four tested diets. Meanwhile, values of EE% of different experimental diets ranged from 3.44 to 3.46% among the four experimental diets. On the other hand, gross energy ranged from 4519 kcal/ kg DM to 4522 kcal/ kg DM among the four tested diets. Furthermore, values of different experimental diets considered adequate and suitable to cover the Nile tilapia fish requirements; in addition, the experimental diets seemed to be iso-caloric and iso-

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nitrogenous. These values are considered sufficient to meet the requirements of the Nile tilapia fish. The present results are approximately in the same range determined in the study of **Abozaid et al. (2024a)**, who found that crude protein percentages ranged from 30.15 to 30.80% among the four tested diets. Gross energy ranged from 4543 to 4559, and metabolizable energy (ME) ranged from 351.37 to 353.94. Additionally, the protein energy ratio varied from 85.18 to 87.66mg CP/Kcal ME among the four tested diets. Data of performance and feed utilization revealed that inclusion nano-curcumin at different levels (50, 100 and 150mg/ kg in the Nile tilapia fingerlings diets caused significantly ($P<0.05$) increasing values of FW, TBWG, ADG, SGR and RGR. The highest values were recorded for the group of fish receiving diet supplemented with 150mg nano-curcumin/kg diet (G_4) compared to the other groups (G_1 , G_2 and G_3). Survival ratio recorded values of 90, 90, 93.33 and 100% for G_1 , G_2 , G_3 and G_4 , respectively, meanwhile, mortality rate % recorded values of 10, 10, 6.67 and zero % in the four experimental groups (G_1 , G_2 , G_3 and G_4 , respectively). **Jastaniah et al. (2024)** revealed that the inclusion of dietary nano-curcumin at varying levels (0, 50, 60, and 70mg/ kg diet) significantly improved the growth indices (final body weight and weight gain, and specific growth rate) of the European seabass fingerlings after 56 days. They also mentioned that when the fish were challenged with *V. parahaemolyticus*, the addition of nano-curcumin in their diets resulted in reduced mortality rates. There is a significant quantity of published works that have been conducted on using curcumin in the diet of aquatic fish. Meanwhile, few investigations have been performed on the use of the nano form of curcumin, as pointed by **Bao et al. (2022)**, **Eissa et al. (2022)**, **Elabd et al. (2023)**, **Mansour et al. (2023)** and **Abozaid et al. (2025d)**. In this context, **Abdel-Ghany et al. (2023)** compared the effects of dietary supplementation with different concentrations of free and nano-curcumin on the growth performance of the Nile tilapia (*Oreochromis niloticus*). They revealed that the highest final weight (FW) and weight gain (WG) were obtained in fish fed 100mg nano-curcumin/ kg diet, followed by 200mg nano-curcumin/ kg diet ($P\leq 0.05$) after feeding for 65 days. While the lowest concentration of 50mg nano-curcumin/ kg diet gave moderate FW and WG. Furthermore, fish fed on 100 and 200mg nano-curcumin/ kg diet showed the highest specific growth rate (SGR), followed by 50mg nano-curcumin/ kg diet and 100mg curcumin/ kg diet ($P\leq 0.05$). Moreover, the highest average daily gain (ADG) was recorded in the 100mg nano-curcumin/ kg diet group, followed by 200mg nano-curcumin/ kg diet and 50mg nano-curcumin/ kg diet and 100mg curcumin/ kg diet groups ($P\leq 0.05$). Groups received 50 and 200mg curcumin/ kg diet showed the lowest values of ADG ($P\leq 0.05$). They finally concluded that the best growth performance (WG, SGR and ADG) and feed utilization (FCR and PER) of the Nile tilapia were achieved at 100mg/ kg, followed by 200mg/ kg diet of nano curcumin. In this respect, **Mahmoud et al. (2017)** elucidated that feeding the Nile tilapia (*Oreochromis niloticus*) with 50 or 100mg/ kg diet of curcumin enhanced growth performance and feed utilization. They linked this improvement in the growth performance and feed utilization to improved

activities of the digestive enzymes (amylase, protease, trypsin and lipase), previously mentioned by **Jiang *et al.* (2016)** and **Midhun *et al.* (2016)**. In general, **Lee *et al.* (2011)** indicated the bio-safety of nano-curcumin utilization, which is consistent with the present results that demonstrated that values of feed utilization, including FI and CPI, were significantly ($P<0.05$) increased when the group of fish received diets containing 50, 100, and 150mg nano-curcumin/ kg diet in comparison with control group that received diet containing zero nano-curcumin (G_1).

The highest values of FI and PI were detected in the group of fish fed diet containing 150mg nano-curcumin/ kg diet (G_4), recording 438 and 134.86 g for FI and CPI, respectively.

In addition, FCR significantly ($P<0.05$) improved with fish groups G_2 , G_3 and G_4 that received diets containing 50, 100 and 150mg nano-curcumin/ kg diet compared to the control group (G_1) that received diet with no nano-curcumin. The best improved value was in feed conversion (1.564) recorded by G_4 that fed diet containing 150mg nano-curcumin/ kg diet in comparison with the other three groups (G_1 , G_3 and G_2) that recorded 4.458, 3.607 and 2.260, respectively. Moreover, values of PER significantly ($P<0.05$) increased in fish groups fed diet with nano-curcumin added at 50, 100 or 150mg/ kg diet (G_2 , G_3 and G_4). Recent studies have highlighted the beneficial effects of nano-curcumin and other dietary supplements on fish feed utilization and growth performance (**Abozaid *et al.* 2025**). **Jastaniah *et al.* (2024)** reported that the European sea bass fingerlings fed diets supplemented with 0, 50, 60, or 70mg/ kg nano-curcumin for 56 days showed an improved feed intake and a reduced feed conversion ratio (FCR, $P<0.05$). Similarly, **Alagawany *et al.* (2021)** outlined several mechanisms by which nano-curcumin enhances fish growth and feed efficiency: it facilitates nutrient assimilation, increases the specific surface area of compounds for higher bioavailability, stimulates the secretion of digestive enzymes for more efficient digestion, and provides additional energy to support body weight gain and overall health.

Abdel-Ghany *et al.* (2023) observed that feed intake was at its highest in the Nile tilapia groups receiving 50, 100, or 200mg/ kg nano-curcumin, with 100mg/ kg group yielding the most consistent improvements ($P\leq 0.05$). The lowest FCR values were recorded in the 100 and 200mg/ kg nano-curcumin groups, while higher FCR values were seen in the 50 and 200mg/ kg curcumin groups. Protein efficiency ratio (PER) was also at the highest values in the 100 and 200mg/ kg nano-curcumin treatments, followed by 50mg/ kg, whereas lower PER values were observed in the 50 and 200mg/ kg curcumin groups ($P\leq 0.05$).

In addition, **Abozaid *et al.* (2024a–c)** demonstrated that various dietary interventions improve feed utilization in the Nile tilapia. Incorporation of *Saccharomyces cerevisiae* (4– 12g/ kg) enhanced feed intake, FCR, crude protein intake (CPI), and PER (**Abozaid *et al.*, 2024a**). Supplementing diets with methionine (5, 10, or 15g/ kg)

similarly improved FCR and PER (**Abozaid et al., 2024b**). Furthermore, replacing 5–15% of soybean meal in the control diet with GML significantly increased feed intake, FCR, CPI, and PER ($P < 0.05$) in the Nile tilapia (**Abozaid et al., 2024c**).

Biochemical parameters serve as essential indicators for assessing the health status of fish and their responses to dietary supplements. Nanotechnology has emerged as a promising approach in aquafeed formulations, enhancing the solubility, bioavailability, and efficacy of various feed additives (**Abbas, 2021**). In the present study, dietary supplementation with different levels of nano-curcumin significantly increased serum total protein, albumin, and globulin concentrations. Elevated total protein and globulin levels reflect improved protein metabolism, antioxidant capacity, and immune function in fish.

These findings are consistent with those of **Jastaniah et al. (2024)**, who reported increased total protein, albumin, globulin, and triglyceride levels in the European sea bass (*Dicentrarchus labrax*) fingerlings fed 70mg/ kg nano-curcumin for eight weeks. Similarly, previous studies have highlighted the positive effects of curcumin supplementation on protein and globulin levels in *Clarias gariepinus* (**Abbas et al., 2019**), *Dicentrarchus labrax* (**Jastaniah et al., 2024**), and *Oreochromis niloticus* (**El Basuini et al., 2024**), likely due to curcumin's phenolic compounds, which confer antioxidant, immunostimulatory, and anti-inflammatory properties (**Jastaniah et al., 2024**).

Low total protein levels are considered indicators of hepatic dysfunction (**Sayrafi et al., 2017**), whereas the current study suggests that nano-curcumin supports liver function, consistent with findings in broiler chickens exposed to salinomycin toxicity. Normal liver enzyme activities (ALT and AST) and kidney function markers (uric acid and creatinine) observed here further indicate the safety of nano-curcumin as a feed additive. Similar results were reported by **Yazdani et al. (2023)**, who found no significant changes in ALT levels in nano-curcumin-treated the Nile tilapia. Other studies have also observed reductions in AST, ALT, and ALP in fish fed nano-curcumin-supplemented diets, attributed to curcumin's antioxidant and hepatoprotective effects against pesticide-induced toxicity (**Sow et al., 2022**). Curcumin has also been shown to reduce liver cell degeneration and necrosis, thereby decreasing AST and ALT levels in the bloodstream (**Sayrafi et al., 2017**).

Regarding glucose, lower serum levels observed in G2 and G3 are in line with **Bao et al. (2022)**, who reported reduced glucose in juvenile largemouth bass supplemented with 0.2% curcumin. This effect may be linked to curcumin-induced upregulation of glucose transporter 2 (GLUT2), promoting glucose translocation across cell membranes. Additionally, the reduction in cholesterol was observed in fish fed 150mg/ kg nano-curcumin. The highest dose tested may reflect curcumin's hypocholesterolemic

properties, as reported in previous studies on rats (**Thota *et al.*, 2019; Shamsi-Goushki *et al.*, 2020**), where nano-curcumin improved lipid profiles and alleviated insulin resistance.

Dietary nano-curcumin modulated the hepatic GH and IGF1 axis in the Nile tilapia in a dose-dependent but gene-specific manner: IGF1 expression rose significantly at 50mg nano-curcumin/ kg diet and then declined at 100– 150mg nano-curcumin/ kg diet, whereas GH expression increased at all supplemented doses, peaking at 150mg/ kg. This biphasic pattern aligns with the recognized growth-promoting effects of curcumin-based supplements in aquaculture, particularly when provided in bioavailable nano-forms, and is consistent with hormetic responses in which low doses stimulate, but higher doses may attenuate specific growth-related signaling outputs (**Abdel-Tawwab *et al.*, 2022; Shaltout *et al.*, 2023; El-Nokrashy *et al.*, 2024**). Curcumin and nano-curcumin activate antioxidant defenses through Nrf2/Keap1 signaling and suppress pro-inflammatory cascades, thereby improving hepatic anabolic tone and enhancing insulin/GH sensitivity (**Li *et al.*, 2024**). In fish, curcumin supplementation has been shown to increase antioxidant capacity and reduce stress biomarkers under culture stressors. In the present trial, the improved redox status at 150mg/ kg likely facilitated the observed up-regulation of hepatic IGF1 transcription (**El-Nokrashy *et al.*, 2024**). At higher doses, however, antioxidant load may dampen ROS-mediated physiological signaling that normally supports growth-related gene expression, offering a plausible explanation for the IGF1 (**Shaltout *et al.*, 2023; Li *et al.*, 2024**). In vertebrates, GH secretion is classically restrained by hepatic IGF1 via negative feedback. The sustained elevation of GH across all nano-curcumin doses, coupled with reduced IGF1 at higher doses, is consistent with compensatory pituitary output when hepatic IGF1 synthesis falls. Previous teleost studies demonstrate that dietary curcumin can modulate both pituitary GH and hepatic growth factor expression (**Sruthi *et al.*, 2018**). Together with the present data, this supports a model in which moderate nano-curcumin supplementation enhances both hepatic IGF1 and GH, while higher doses shift the axis toward elevated GH but attenuated hepatic IGF1. Nano-curcumin improves solubility, stability, and intestinal uptake, leading to biologically effective tissue concentrations at lower dietary inclusion levels. Studies in tilapia and sea bass confirm that nano-curcumin outperforms free curcumin and that its optimal ranges are comparatively lower (**Abdel-Tawwab *et al.*, 2022; Shaltout *et al.*, 2023; El-Nokrashy *et al.*, 2024**). This matches our finding that 50mg/ kg was the most effective dose for hepatic IGF1 stimulation. Hepatic IGF1 transcription in tilapia is highly sensitive to diet composition and phytochemical load. Reports show that certain dietary manipulations can suppress IGF1 and growth hormone receptor (GHR1) expression (**Ayoola *et al.*, 2024**). In contrast, high levels of nano-curcumin may alter nutrient partitioning or receptor-mediated signaling, which could explain the observed decline in IGF1 levels at 100– 150mg nano-curcumin/kg diet. Comparable findings with selenium supplementation (in both organic and nano forms) demonstrate that antioxidant-focused

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interventions can modulate hepatic IGF1 expression and GH–IGF axis signaling in the Nile tilapia (**Dawood et al., 2024; El-Beltagy et al., 2024; Shaalan et al., 2024**). This broader context strengthens the plausibility that nano-curcumin acts through similar antioxidant and redox-sensitive mechanisms. The findings suggest an optimal nano-curcumin window that supports hepatic IGF1 transcription (~150 mg nano-curcumin/ kg diet under our conditions) and a wider range that maintains elevated GH expression (50–150 mg nano-curcumin/ kg diet). Practically, lower doses may be most effective for augmenting hepatic IGF1-mediated somatic growth, whereas higher doses may prioritize GH-linked metabolic or stress-adaptive outcomes without proportional IGF1 synthesis. Such dose-dependent decoupling of GH and IGF1 has been reported in vertebrates under stress or inflammation and may reflect tissue-specific effects of nano-curcumin on receptor signaling and downstream pathways including JAK/STAT, PI3K–AKT–mTOR, and SOCS feedback (**Li et al., 2024**). **Jastaniah et al. (2024)** reported that dietary supplementation of nano-curcumin at 50, 60, and 70mg/ kg significantly enhanced the expression of growth-related genes (IGF-1 and GH) and the anti-inflammatory cytokine IL-10 in a dose-dependent manner ($P < 0.05$). Interestingly, fish receiving 70mg/ kg exhibited lower expression of the pro-inflammatory gene IL-1 β compared to other groups ($P < 0.05$). These findings suggest that nano-curcumin may act as a natural feed additive that promotes growth, feed utilization, and immune modulation.

To further explore the molecular effects of nano-curcumin, selected genes involved in growth and immune regulation were analyzed. GH and IGF-1 serve as indicators of growth performance in fish, while IL-10 is a key anti-inflammatory cytokine that modulates immune and inflammatory responses (**Iyer & Cheng, 2012**). Conversely, IL-1 β acts as a principal mediator of inflammation (**Lopez-Castejon and Brough, 2011**). In line with these roles, **Jastaniah et al. (2024)** demonstrated that nano-curcumin upregulated GH, IGF-1, and IL-10 expression in the liver of European sea bass, supporting both growth and anti-inflammatory responses. Similarly, **Elabd et al. (2023)** observed a significant enhancement of IGF-1 expression in tilapia following nano-curcumin supplementation. At the same time, the downregulation of IL-1 β confirms the anti-inflammatory potential of nano-curcumin, likely linked to its immunostimulatory and growth-promoting properties.

Vibrio parahaemolyticus is a major pathogen in aquaculture, with its prevalence influenced by environmental factors such as temperature and salinity (**Faja et al., 2019**). **Jastaniah et al. (2024)** highlighted that nano-phytochemicals like nano-curcumin can improve host health by stimulating the immune system, which was reflected in higher survival rates of infected fish (75% and 60% in treated groups vs. 30% in controls). These results are consistent with prior studies on the Nile tilapia challenged with *Aspergillus flavus* (**Eissa et al., 2022; Eissa et al., 2023b**). Collectively, these findings indicate that dietary nano-curcumin enhances growth, immune responses, and disease resistance in

cultured fish. Further investigations using molecular and proteomic approaches are recommended to confirm and expand these observations (**Jastaniah *et al.*, 2024**).

CONCLUSION

Based on the results, it can be deduced that, incorporating nano-curcumin causes an improvement in growth performance, increases values of feed intake, and improves feed conversion ratio. Nano-curcumin also increases total protein, albumin, and globulin levels in serum and has no negative impact on both liver and kidney functions. Furthermore, the present study showed that nano-curcumin supplementation modulates the hepatic GH–IGF axis in the Nile tilapia in a dose-dependent manner. A moderate level (150mg nano-curcumin/ kg diet) enhanced IGF1 expression and growth potential. Practically, 150mg nano-curcumin/ kg diet seems to be optimal for promoting growth-related gene expression, although higher doses may still support resilience.

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