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Stimulating effect of dietary Na butyrate for controlling of contracecum infection in Nile Tilapia

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ABSTRACT

The purpose of this study was to find out how sodium butyrate affected the Nile tilapia's defenses against *Contracaecum infections*. In the preliminary phases of the experiment, we established certain subsets of tilapia which met specific inspection requirements. For this, 100 tilapia fish were examined for *Contracaecum larvae* and their infection status determined. The parasites were found mainly in the body cavity. The fish were separated into two primary groups with subcategories .**Gp.1** comprised fish that were seemingly healthy and parasite-free and were maintained on a standard diet yielding a 1:3 (-ve control). On the other hand, **Gp.2 :**This set of contaminated fish was then separated into four subgroups, each consisting of ten fish: Gp. (1) Infected fish fed a normal diet without treatment (+ve control), Gp. (2) Infected fish fed a diet supplemented with sodium butyrate, Gp. (3) Infected fish treated with mebandazole and fed a normal diet, and Gp. (4) Infected fish treated with both sodium butyrate and mebandazole. For four weeks, weekly parasitological assessments were conducted. Hematological and biochemical analyses, such as intestinal histophotometry, antioxidant enzyme activities (SOD, MDA), immunological parameters (MPO, C3 complement), and liver function markers, were performed on blood samples. The findings showed that dietary sodium butyrate enhanced intestinal structure, immunological response, and growth performance while successfully lowering the parasite burden, particularly when paired with mebandazole.

INTRODUCTION

Although aquaculture offers a viable substitute for marine feed ingredients, the addition of sodium butyrate to diets impairs gut health and increases susceptibility to infections. **(Piazzon et al. 2017; Mougin et al. 2021 and Sarker et al. 2021).**

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The modern aquaculture industry has led to fish diseases in many parts of the world, which in turn, induces human illnesses **(Ruiter, 1995).** The life cycle of many immature parasites, is either a solitary host or one of several hosts **(Hart and Reynolds, 2002)**. *Contracaecum* species are from the genera *Ascaridoidea* and within the *Anisakidae* family. The adult stage of *Contracaecum spp.* can be located within the intestines of carnivorous birds, while the larvae reside in the visceral cavity and mesenteries of fish **(Anderson, 2000) .**

Immunostimulant therapy is more difficult to treat because aquatic fish parasites cannot be effectively treated with drugs. Numerous studies have demonstrated the effectiveness of albendazole (ABZ) as an anthelmintic.Mebendazole (methyl{5-(benzoyl)-1H-benzimidazole-2} carbamate) is a broad-spectrum anthelmintic. By upsetting the microtubules in the parasites' intestinal epithelium, it causes damage to their ability to absorb glucose, paralysis of their muscles, and ultimately, the death of the parasite **(Barbara, 2007 and Kim et al. 2024).** Parasites cause physiological and behavioral changes in their hosts **(Timi and Poulin, 2020).** As ectoparasites, fish have produced an outer layer of mucus that acts as a physical and chemical barrier. Mucus contains immunological components such as immunoglobulins and antioxidant enzymes that reduce oxidative damage from the infectious process **(Clarkson and Thompson, 2000).** Indicators of the oxidative state in mucus and immunological measures can provide information about the infection and the host's capacity to react. As the infection level increased, a decrease in the body condition index was observed. The antioxidant enzymes glutathione peroxidase, superoxide dismutase, and catalase in the mucus became more active as the illness got worse. Even though the antioxidant defenses were turned on, the group with the highest infection rate saw an increase in malondialdehyde levels, which is a sign of oxidative damage. In the same way, as the infection got worse, mucus levels of immunological markers, alkaline phosphatase, myeloperoxidase, and immunoglobulins (C3 complement) rose **(Amanda et al. 2023).** The dietary supplement SB changed *Oreochromis niloticus's* hematological profile, blood proteins, immunological indices, and antioxidant capacity, which led to higher levels of erythrocytes, leukocytes, hemoglobin, hematocrit, and total albumin **(Abdel–Latif et al. 2022).**

Fish and other aquatic species that were ill were long treated with chemicals and antibiotics **(Kovalakova et al. 2020).** According to **Singh et al. (2020),** the overuse of chemical medications and antibiotics can result in drug residues and microorganisms that are resistant to them. Finding strategies to reduce medication use and strengthen aquatic animals' immunity is therefore crucial.

Feed additives, often known as non-antibiotic growth boosters, improve the nutrition and health of aquatic animals **(Salah et al. 2017).** Dietary acidifiers, such butyrate, are readily available feed additives used in fish aquaculture **(Refstie et al. 2000 and Abdel-Latif et al. 2020).** The intestinal barrier is the result of complex interactions between the gut microbiota, immune cells, and the epithelial barrier **(Storebakken et al. 1998, Buttle et al. 2001, and McCracken and Lorenz 2001).**

Sodium butyrate (SB) is used in the feed business instead of butyric acid because of its stability, low odor, and high solid phase properties **(Guilloteau et al. 2010).** SB's ability to stop mucosal apoptosis has drawn special interest due to its antioxidative, antimicrobial, anti-inflammatory, and immunomodulatory properties **(Mentschel and Claus, 2003; Liu et al. 2014; Zhang et al. 2015).** A range of farmed fish feeds also contain SB to improve intestinal absorbency, gut health, and ultimately growth performance **(Owen et al. 2006; Gao et al. 2011; Liu et al. 2014, 2019 and Ullah et al. 2020).**

An aquatic animal's digestive tract is one of the primary areas of contact between its body and the external environment. Intestinal health, one of the most crucial factors in guaranteeing proper growth, is connected to the intestinal

barrier activities of aquatic animals **(Xiao et al. 2017).** Aquatic species' endogenous microbiome, epithelial immune system, and physical barrier shield their gut tissue from potentially harmful pathogens (**Guilloteau et al. 2010 and Niklasson et al. 2011).** The intestinal immunological barrier can stop the spread of infections by causing intestinal inflammation and inflammatory-induced apoptosis, but the physical barrier is primarily composed of tight junctions, intestinal epithelial cells, and peritrophic membrane **(Chen and Tang, 2013; Suo et al. 2017).** Furthermore, the host's immunological homeostasis and metabolic processes are both regulated by the gut microbiota **(Qiao et al. 2019).** Ultimately, the synchronization of all three intestinal barrier types maintains intestinal homeostasis.

MATERIALS and METHODS

The present inquiry was conducted within the Aquaculture Diseases Unit of the Animal Health Research Institute-Zagazig.

Fish sampling:

A total of 100 tilapia fish, weighing an average of 60 to 70 grams, were acquired at the start of the experiment, acclimated to laboratory conditions, and checked for parasites and *Contracaecum nematode larvae* in *Oreochromis niloticus* fish. Through the body cavity, the larvae were collected. The fifty fish were split up into two major groups: Gp. (1): Seems to be healthy and parasite-free, but Gp. (2): *Contracaecum nematode-infected*. In the meantime, Gp.(2) subdivided into four treatment groups, each of which contained ten fish. The following are the groups:

	Groups		No. of fish	Type of treatment	Time of blood sampling
The experimental groups (N = 50)	Experimental Groups with have parasitic infection	Group 1	10	Healthy fish feeding normal ration with ratio 1:3 kept as control (-ve control).	Blood samples was collected from the caudal vein from 5 fish per aquarium at the 7 th , 14th day from the beginning of the treatment using sterile clean tubes per fish.
		Group 2	10	Infected with *Contracaecum* and feeding normal ration & not treated with Mebendazole (+ve contr vccccccccol) .	
		Group 3	10	Infected with *Contracaecum* and feeding normal ration containing Na butyrate (2gml/kg) .	
		Group 4	10	Infected with *Contracaecum* and feeding normal ration without Na butyrate (2gm/kg) & treated with Mebendazole feeding normal ration.	
		Group 5	10	Infected with *Contracaecum* and feeding normal ration containing Na butyrate(2gml/kg) & treated with Mebendazole .	
Total number			50		

Parasitological Examination:

At the start of the current study, 100 seemingly healthy tilapia fish were taken from Sharkia Governate. By applying mild pressure to the abdomen with the thumb and forefinger, starting in line at the front of the pelvic fins and ending at the anus, the NO. of fifty fish were inspected. According to **Scott and Pamela (2015),** feces are collected in a petri plate.

After a week, we check the fish for helminth parasites using the same method as before. Each fish was examined inside for helminth infections after four weeks. The fish's skin, fins, gills, buccal cavity, and digestive tract were all investigated. The fish were placed in a petri dish with saline solution, opened, scraped, and studied under a dis-

secting microscope **(Lucky, 1977).** Using the typical keys found in the literature for nematodes, the parasites were identified under a light microscope **(Vernon, 2006).**

Collection of samples:

Intestinal microvilli morphology was investigated through the collection of hindgut samples from three fish per tank, conducted under aseptic conditions, followed by their transfer to the laboratory for subsequent measurement via transmission electron microscopy (TEM) and scanning electron microscopy (SEM) in accordance with the methodologies established by **Ran et al. (2015).** The images acquired from either TEM or SEM were subjected to rigorous analysis to derive data pertaining to microvilli length or density, in alignment with the previously documented procedures **(Ran et al. 2015).**

Blood samples were gathered from the caudal vein from 5 fish per aquarium on the 7 th , 14 th day from the beginning of the treatment utilizing sterile clean tubes for each fish. The initial blood sample was collected into heparinized tubes as an anticoagulant and used to determine hemoglobin concentration (Hb%), packed cell volume percentage (PCV) **Dacie and Lewis (1991),** red blood cells (RBCs), and white blood cells (WBCs) counts **(Toghyani et al. 2010),** whilst the second blood sample was gathered from the tail vein into a sterile clean centrifuged tube without anticoagulant, left to coagulate at room temperature, and at once centrifuged at 4000 rpm for 10 min to obtain serum. The obtained serum was transferred to dry sterile screw -capped tubes (Eppendorf) and stored in a deep freezer (− 20 °C) to perform subsequent biochemical tests. The subsequent biochemical parameters were assessed: serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, and uric acid using a commercial kit. Activities of AST and ALT were assayed following **Reitman and Frankel (1957).** Serum content of total proteins (TP) was measured according to **(Gornall et al. 1949),** albumin (ALb) was measured according to **(Doumas et al. 1971).** Alkaline phosphates (ALP) was measured according to **(Kind and King 1954).** All serum biochemicals were measured spectrophotometrically at wavelength (560- 630 nm) utilizing commercial kits. Furthermore, the serum immune and antioxidative parameters and their serum samples were prepared via centrifugation (3000 g for 15 min) and stored at -80 c prior to analysis. The serum profile of SOD, MDA, MPO and C3 complement were measured by the commercial kit **(Nanjing Jiancheng Institute, Jiangsu, China)** according to the methods of the operation instructions **(Han et al. 2011).**

Histopathological examination:

Once cleaned using a physiological saline solution (0.9% NaCl), intestinal tissue specimens were removed from each fish and blotted on filter paper prior to being buffered in 10% formalin. A standard paraffin embedding method was utilized to process the fixed samples. Hematoxylin and eosin (H&E) was applied to dye 5-mm thick slices of the ready paraffin blocks for light microscopic examination **(Culling 1983).**

Histomorphometric analysis:

The crypt depth was measured from the crypt-villus junction to the base of the crypt, the villus height was measured from the tip of the villus to the villus-crypt junction, and the villus width was measured from the mid of the villus. The histomorphometric analysis was carried out using Image J analysis software **(National Institutes of Health, MD, USA).**

Statistical analysis:

The statistical analysis was carried out using SPSS for Windows (Version 18.0; SPSS Inc., Chicago, IL). Using one-way analysis of variance (ANOVA), the significance of the differences between the experimental groups was evaluated. Individual group differences were measured using the post hoc Fisher's least significant difference (LSD) test if the one-way ANOVA revealed a significant difference. In the results, the mean ± standard error of mean was shown. It was considered significant if the *P-value* was less than 0.05 **(Kinnear and Gray, 2006).**

Experimental drugs:

Mebendazole (Albendazole 2.5%) ® produced by Pharma Swede company and used in form of bath at dose of 500 mg/L for 24 h.

Vega max (Na butyrate powder 98%) package 1 kg produced by Biochem company added to fish ration at ratio 1:3.

RESULTS

When comparing fish fed diets supplemented with sodium butyrate to the control group, the number of *contracaecuum larvae* was much reduced. The group that was given 2 grams of sodium butyrate per kilogram had the biggest decrease. Histological analysis revealed improved intestinal

structure in treated groups, with fewer lesions, less inflammation, and regeneration of epithelial tissue. Additionally, the group that got both mebandazole and sodium butyrate had a significant improvement in growth performance, including length and weight gain

Length and weight values of fish:

Table 1. Measurements of the length and weight of Tilapia fish before and after treatment with Na butyrate and Mebendazole during the experimental timeframe

Groups / Parameters	Healthy control fish fed on normal ration (-Ve control)	Infected control fish with contracecum & not treated with mebendazole (+Ve control)	Diseased fish fed normal: Plus Na butyrate (2gml/kg) &treated with mebendazole	Diseased fish fed normal: Without Na butyrate infected with cotracecum & treated with mebendazole	Diseased fish fed normal: Plus Na butyrate infected with cotracecum & treated with mebendazole
Average weight(g)	1.77± 0.095 ^{c}	1.84± 0. 08 ^{d}	1.99± 0.087 ^{d}	2.07± 0.24 ^{b}	3.17± 0.276 ^{a}
Average length(cm)	4.91± 0.099 ^{d}	5.09± 0.80 ^{a}	5.22± 0.061 $^{d e}$	5.41± 0.207 ^{b}	6.28± 0.17 ^{c}

Hematological parameters changes

Table 2. Average values of hematological parameters in tilapia fish before and after treatment with Na butyrate and Mebendazole during the trial duration

Groups / Parameters	Healthy control fish fed on normal ration (-Ve control)	Infected control fish with contracecum & not treated with mebendazole (+Ve control)	Diseased fish fed normal: Plus Na butyrate (2 gm/kg) alone & not treated with mebendazole	Diseased fish fed normal: Without Na butyrate infected with cotracecum & treated with mebendazole	Diseased fish fed normal: Plus Na butyrate infected with cotracecum & treated with mebendazole
Hb gm/dl	8.10± 0.959 ^{e}	12.82± 1.519 ^{a}	10.06± 1.19 ^{c}	11.02± 1.31 ^{b}	9.56± 1.13 ^{d}
RBCs x10^{6}/µl	1.41± 0.01 ^{d}	3.10± 0.021 ^{a}	2.24± 0.016 ^{c}	2.65± 0.019 ^{b}	2.09± 0.015 ^{a}
PCV %	2.20± 0.508 ^{d}	3.61± 0.837 ^{a}	2.42± 0.558 ^{c}	3.03± 0.703 ^{b}	2.14± 0.494 ^{e}
WBCs x10^{3} /µl	7.24± 0.039 ^{e}	9.02± 0.051 ^{a}	7.892± 0.044 ^{c}	8.53± 0.047 ^{b}	7.43± 0.041 ^{d}
Lymphocyte %	50.26± 0.29 $^{d e}$	61.43± 0.37 ^{a}	54.41± 0.31 ^{c}	59.83± 0.33 ^{b}	52.12± 0.30 ^{d}
Monocyte %	3.02± 0.097 ^{a}	1,96± 0.063 ^{e}	2.54±0.081 ^{c}	2.87±0.093 ^{b}	2.23±0.072 ^{d}
Heterophil %	43.16.± 2.88 ^{a}	32.54± 2.01 ^{e}	39.42± 2.63 ^{c}	33.38± 2.23 ^{d}	42.23± 2.82 $^{a b}$
Basophil %	0.99± 0.01 ^{a}	0.99± 0.01 ^{a}	0.99± 0.01 ^{a}	0.99± 0.01 ^{a}	0.99± 0.01 ^{a}
Esinophil %	2.60± 0.29 ^{d}	3.08±0.35 ^{a}	2.64± 0.30 ^{c}	2.93± 0.33 ^{b}	2.43± 0.27 ^{e}

Serum biochemical analysis:
Table 3. Average values of liver function tests in tilapia fish prior to and following treatment with Na butyrate and Mebendazole during the study period:

Groups / Parameters	Healthy control fish fed on normal ration (-Ve control)	Infected control fish with contracecum & not treated with mebendazole (+Ve control)	Diseased fish fed normal: Plus Na butyrate (2gm/kg) alone & not treated with mebendazole	Diseased fish fed normal: Without Na butyrate infected with cotracecum & treated with mebendazole	Diseased fish fed normal: Plus Na butyrate infected with cotracecum & treated with mebendazole
T.P. g/dl	4.39± 0.798 d	6.57± 1.194 a	5.64± 0.83 c	6.03± 0.88 b	5.06± 0.74 e
Albumin g/dl	1.86± 0.139 e	2.85± 0.215 a	2.14± 0.161 c	2.42± 0.18 b	2.04± 0.154 c d
ALT u/l	18.10± 0.99 e	23.21± 1.28 a	22.15± 1.22 c	22.68± 1.25 b	21.43± 1.18 d
AST u/l	23.94± 0.997 e	26.23± 1.092 a	25.04± 1.04 c d	25.76± 1.07 b	24.40± 1.01 c
ALP u/l	84.09± 7.19 e	151.98± 13.01 a	133.30± 11.409 c	142.52± 12.20 b	118.76± 10.16 d

Groups with varying letters within the identical column are substantially different at P (<0.05).

Serum immune & antioxidant enzymes changes:
Table 4. Average values of C3 complement, MPO, SOD & MDA parameters in tilapia fish before and after administration of Na butyrate and Mebendazole throughout the trial period

Groups / Parameters	Healthy control fish fed on normal ration (-Ve control)	Infected control fish with contracecum & not treated with mebendazole (+Ve control)	Diseased fish fed normal: Plus Na butyrate (2gm/kg) &treated with mebendazole	Diseased fish fed normal: Without Na butyrate infected with cotracecum & treated with mebendazole	Diseased fish fed normal: Plus Na butyrate infected with cotracecum & treated with mebendazole
C3 complement (mg/ml)	62.51± 2.35	106.02± 3.98	81.31± 3.05	91.80± 3.45	77.16± 2.90
MPO (U/L)	91.71± 12.30 e	126.61± 16.98 a	115.51±15.49 c	119.42± 16.02 b	109.43± 14.68 d
SOD (U/L)	155.61± 10.50 e	189.91± 12.81 a	165.05± 11.14 c	171.81± 11.60 b	159.21± 10.75 d
MDA (nmol mg)	9.34± 0.93 a	3.22± 0.32 e	6.16± 0.61 b	4.22± 0.42 d	5.08± 0.51 c

Groups with varying letters within the identical column are substantially different at P (<0.05).

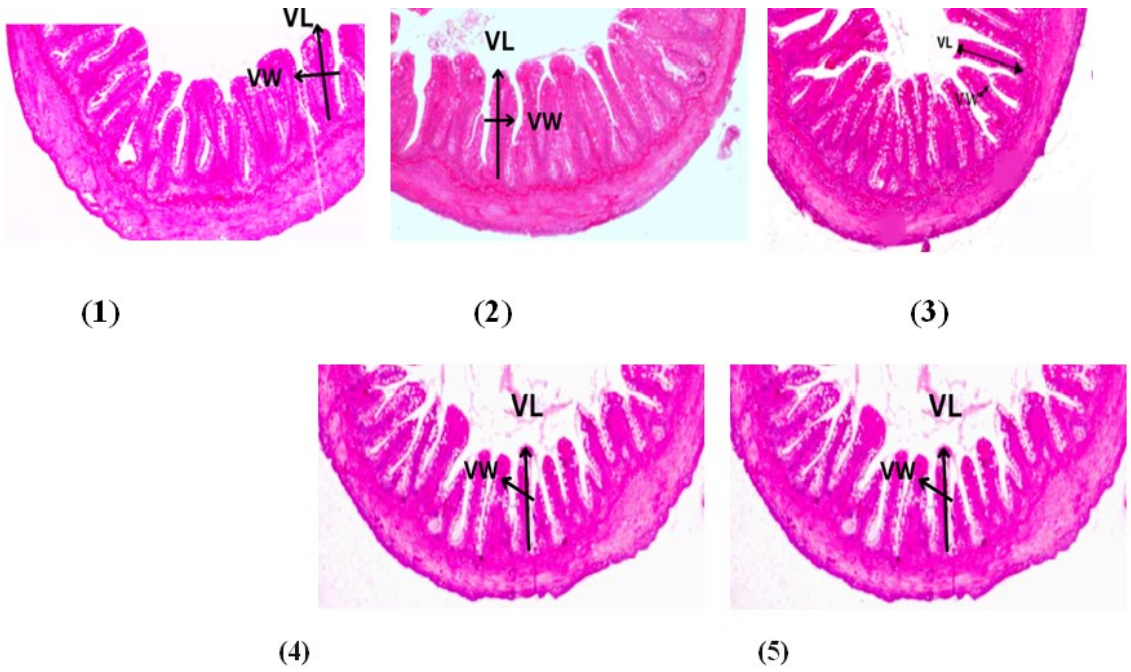
Table 5. Average figures for measurements of intestinal villi length and width in tilapia fish before and after treatment by Na butyrate and Mebendazole throughout the testing period**:**

Groups / Intestial villi portions	Healthy control fish fed on normal ration (-Ve control)	Infected control fish with contracecum & not treated with mebendazole (+Ve control)	Diseased fish fed normal: Plus Na butyrate (2 g m / k g) &treated with mebendazole	Diseased fish fed normal: Without Na butyrate infected with cotracecum & treated with mebendazole	Diseased fish fed normal: Plus Na butyrate infected with cotracecum & treated with mebendazole
Villi Length (VL) µm					
Proximal (PI)	131.51± 0.10 [a]	102.11± 0.078 [d]	112.32± 0.085 [b]	109.21± 0.083 [b c]	144.34± 0.109 [a]
MID (MI)	10.21± 1.38 [b]	7.18± 0.970 [e]	9.31± 1.26 [c]	8.62± 1.17 [d]	11.18± 1.51 [a]
Distal (DI)	30.25± 1.95 [b]	16.65± 1.073 [e]	17.43± 1.12 [d]	21.92± 1.41 [c]	32.51± 2.096 [a]
Villi Width (VW) µm					
Proximal (PI)	20.704± 9.80 [b]	14.62± 6.92 [e]	16.41± 7.77 [d]	18.03± 8.53 [c]	22.71± 10.75 [a]
MID (MI)	12.49± 0.006 [b]	6.41 ± 0.003 [e]	8.60± 0.004 [d]	9.43± 0.005 [c]	14.51± 0.007 [a]
Distal (DI)	7.128± 0.072 [b]	3.29± 0.033 [e]	5.98± 0.060 [c d]	6.72± 0.068 [b c]	9.07± 0.091 [a]

Groups with varying letters within the identical column are substantially different at P (<0.05).

Intestine Histomorphy:

Means of five measurements from each of the three intestine parts (proximal, mid, and distal) were derived from the histological sections. The intestinal villi on the following plate have become longer



Dietary inclusion of sodium butyrate effect on intestinal morphology in Nile Tilapia (VL: villus length; VW: villus width). (1) -ve control group feeding normal ration; (2) Infected with *Contracaecum* and not treated with Mebendazole (+ve control) . (3) Infected gp.with *Contracaecum* & feeding normal ration containing Na butyrate . (4) Infected gp. with *Contracaecum* and feeding normal ration without S.B.& treated with Mebendazole feeding normal ration.; (5) Infected gp. with *Contracaecum* and feeding normal ration containing Na butyrate & treated with Mebendazole

DISCUSSION

This research demonstrated that feeding Nile tilapia sodium butyrate as a dietary additive substantially reduced the seriousness of their *contraceacum* infection. This aligns with prior research demonstrating the immune-modulating and antibacterial characteristics of short-chain fatty acids, particularly butyrate, in aquaculture animals, the reported decline in parasite load and boost in fish health. Intestinal integrity and pathological markers linked to parasite infection notably improved in the treated groups. These findings align with prior research demonstrating that butyrate supplementation lessens inflammation and promotes intestinal epithelial cell regeneration in parasite -infected fish, also the synergistic impacts of S.B. either alone or coupled with an anti-parasitic drug. **(Hassona et al. 2020; Mohamed et al. 2020; El-Kassas et al. 2020; Abdel-Tawwab et al. 2021).** Our findings showed that fish fed a diet enriched with sodium butyrate had improved, reporting higher final weights and lengths than the control group. The better outcomes were focused on sodium butyrate (S.B.). Similar results were found in Nile tilapia by **Zheng (2009), Abd El -Naby et al. (2019), and Dawood et al. (2020).** Increased feed palatability and physical qualities, as well as improved digestibility and bioavailability of certain minerals including calcium, phosphorous, and zinc, may be the cause of the improvement in fish growth performance observed in response to dietary supplementation with S.B. **(Morken et al. 2012).**

Additionally, S.B. supplements may improve the digestive tract's absorption of some important amino acids, stop them from oxidizing, and increase their bioavailability in the bloodstream **(Ng and Koh, 2019).** Dietary S.B. restored the effects of low dietary fish meal **(Estensoro et al. 2016)** and improved intestinal cell activities **(Hamer et al. 2008)** by supplying energy for the epithelial cells **(Robles et al. 2013).** The high levels of amino acids, vitamins, minerals, phenols, polyphenols, and carotenoids, which may be regarded as either direct nutrients that led to improved growth performance **(Soni et al. 2017)** or indirect nutrients necessary for the growth of beneficial microorganisms in the fish intestine **(Teimouri and Amirkolaie, 2013),** may be the cause of the improved growth performance of fish fed SP in diet. Furthermore, the enhanced growth performance seen in the treated groups provided evidence that S.B. has a function in improving feed efficiency and nutrient absorption in addition to acting as an anti-parasitic agent. In aquaculture, where both disease prevention and growth optimization are essential for long-term financial viability, the dual impact is advantageous. This is in line with the findings of **Clarkson and Thompson (2000),** who noted that fish ectoparasites have developed an exterior mucosal layer that serves as a barrier both physically and chemically. Immune components including immunoglobulins and antioxidant enzymes that lessen oxidative damage from the infectious process are among the mucus's constituents. Additionally, parasites affect the hosts' physiology and behavior, favoring new infections or putting them at risk for predation **(Timi and Poulin, 2020).** According to our findings, fish treated with sodium butyrate either by itself or in combination with mebendazole demonstrated improved hematological parameters and a decreased parasite load. The hematological parameters (RBCs, Hb, PCV, and WBCs) showed a significant increase in RBC count, Hb concentration, and PCV percentage in all treatments, which is consistent with the findings of **Khalafalla et al. (2020).**

In the meantime, when comparing the infected group to the control group, the WBC count showed a substantial drop in all treatments. Similar outcomes were noted by **Ali et al. (2018), Abdel-Mohsen et al. (2018), and Dawood et al. (2020)** in Nile tilapia fed on various S.B. additions. However, when compared to the control group during the sex reversal stage, Nile tilapia fingerlings fed diets supplemented with SB (0.5%) for 28 days displayed an increase in the RBC count **(Jesus et al. 2018).** On the other hand, fish fed SB-enriched diets had lower WBC counts. These findings did not align with earlier research by **Ali et al. (2018),** which showed that fish fed a diet with various S.B. additions had higher WBC counts. These might result from modifications made to the rearing conditions through-

out the trial. These findings are consistent with the findings of **Caldwell et al. (1999), Li et al. (2009), Astbury et al. (2013), and Xiao et al. (2020),** which reported that butyric acid in the intestine enters the peripheral circulation through the hepatic portal vein and is oxidized in the liver to supply energy following the β-oxidation pathway. The liver function results showed a significant increase in the enzyme activities of AST, ALT, and ALP as well as levels of total protein albumin in serum in all treatments when compared to the control group.

Comparing all treated groups to the control, Complement (C3) showed a substantial increase. Our findings concur with those of **Jin et al. (2023),** who found that C3 is a serum protein having enzymatic and immunity-related activities. It can induce inflammatory responses and antibody formation following activation by substances such as pathogens. Moreover, it is a crucial molecule in the congenital immune defense system. Complement manifests earlier than immunoglobulin in the evolutionary process of fish's immune system. Therefore, the complement system of fish is vital for congenital and acquired immunities. Meanwhile, Myeloperoxidase (MPO) results revealed significant increase in all treated groups when compared with control one.This due to myeloperoxidase is a heme-containing peroxidase, mainly expressed in ne utrophils and, to a lesser extent, in monocytes and have a broad bactericidal ability via catalyzing the reaction of Cl^- with H_2O_2 to produce a strong oxidant, hypochlorous acid (HOCl). However, the excessive synthesis of oxidants produced from MPO has highlighted its harmful impact, particularly in conditions where inflammation is either acute or chronic. The primary way that MPO and its generated oxidants contribute to the pathogenic processes of illnesses is by oxidizing biomolecules, which increases oxidative stress and inflammation **(Amanda et al. 2023 ; Lin et al. 2024).** MPO used the MPO-H_2O_2-iodide system to produce its antibacterial activity **(Klebanoff, 1968).**

Within the feed industry, sodium butyrate (SB) is utilized instead of butyric acid because of its advantageous solid phase characteristics, minimal smell, and stability. **(Guilloteau et al. 2010).** In comparison to the infected group, our results showed a substantial reduction in hepatic malondialdehyde concentrations and a marked increase in hepatic superoxide dismutase enzyme activity across all treatment groups. These conclusions agree with those of **Wu et al. (2006)** who reported that the elevated amounts of polyunsaturated fatty acids and easily generated lipid free radicals in the fish intestine and diet render them susceptible to toxic substances and oxidative stress. **Li et al. (2007)** likewise noted that the antioxidant enzyme SOD can eliminate reactive oxygen species and lessen lipid peroxidation products.

Based on **Onura et al. (2018),** the fish's intestine is the main organ for nutrient absorption. Our results showed that the intestinal microvillus's length and density increased in all treated cohorts compared to the infected group. This is consistent with the findings of **(Mentschel and Claus, 2003; Liu et al. 2014; Zhang et al. 2015 and Fang et al. 2021),** which suggest that SB's antioxidative, antibacterial, anti-inflammatory, and immunomodulatory properties can prevent mucosal apoptosis. Following these results, dietary S.B. can improve microvillus formation, which will increase nutrient absorption effectiveness and boost growth performance **(Abdel-Latif et al. 2021).** Fish intestinal lesions can cause inflammation and some alterations to the intestinal villi, as per **Kowalska et al. (2010).** Hence, according to **Portz (2006),** fish that consume balanced diets are more productive, have enhanced stress responses, and are more resilient to infections. **Mountzouris et al. (2006)** stated that to improve production, strategic nutritional choices are essential. Sodium butyrate is used as a growth booster in the diet of juvenile tilapia because it has a beneficial impact on the gut **(Galfi and Bokori, 1990)** and affects body weight gain **(Kotunia et al. 2004).**

CONCLUSION

Sodium butyrate supplementation noticeably improved fish health and parasite resilience especially when employed with mebendazole.

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