Egyptian Journal of Veterinary Sciences

https://ejvs.journals.ekb.eg/

The Impact of Some Natural Alternatives to Antibiotics as Phytobiotic and Nucleotide Supplementation on Growth Performance, Carcass Characteristics, Immune Status and Histopathological Changes in Broiler Chickens Challenged with *Pseudomonas aeruginosa*

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Abstract

PSEUDOMONAS AERUGINOSA (*Ps. aeruginosa)* is one of the main causes of septicemia in broiler chickens, which results in significant losses for the global poultry production industry. The purpose of the current study was to clarify the effects of rationary supplements containing natural feed additives (nucleotides and phytobiotics) on the management of experimentally infected *Ps. aeruginosa* in broiler chickens. The broiler chicks were divided into four groups with five replicates each. The birds in groups 1 and 2 were designated as the positive control (PC) and negative control (NC) groups, respectively, while chickens in groups 3 and 4 were defined as T1 and T2, were fed a feed supplemented with phytobiotic and nucleotides, respectively. On day 3 of life, PC, T1, and T2 groups were experimentally injected with *Ps. aeruginosa* subcutaneously using 0.2 ml of PBS containing 10^6 CFU per bird. The results showed that phytobiotic (1, 0.5, 0.5kg /MT for the starter, grower and finisher rations) respectively, and nucleotides (300 g/MT) supplemented groups had better growth rates, feed efficiency, and European Production Efficiency Factor compared to the PC group. *Ps. aeruginosa* infected and supplemented groups showed lower mortality rates than PC groups. Additionally, the feed additives positively influenced immune organ development, antibody responses, and delayed-type hypersensitivity. Both feed additives reduced the severity of intestinal lesions. Supplemented groups exhibited better carcass yields, breast muscle weight, and intestinal development. Overall, the study demonstrates the potential of phytobiotic feed ingredients and hydrolyzed yeast nucleotides as promising alternatives to antibiotics in poultry production.

Keyword: Broiler chicken, Nucleotides, Phytobiotics, *Ps. aeruginosa.*

Introduction

Poultry is among the most frequent widespread meat types eaten all over the world [1]. Enteric damages by bacterial infections are one of the most important diseases that affect poultry and are continuing to cause high economic losses in the many areas worldwide. Poor enteric health can adversely affect food digestion, gut motility and nutrient absorption by several means [2, 3] . A healthy chicken gastrointestinal tract (GIT) is critical for improved broiler performance and the production of sanitary chicken meat since it is responsible for digestion, food absorption, and immune response. Pathogenic bacteria in the chicken GIT, such as *E. coli*, *Salmonella spp., C. perfringens,* and *Pseudomonas spp.*, compete with the host for nutrients and also damage the intestinal epithelium, impairing the host's digestion and absorption function [4]. *Pseudomonas* infections in poultry are a significant concern because the illness can spread rapidly throughout poultry flocks, leading to increased mortalities at various ages [5]. *Pseudomonas aeruginosa (Ps. aeruginosa*) is an opportunistic pathogen that has caused septicemia, pulmonary, and GIT illnesses in poultry farms [6]. The significance of poultry in transmitting food-borne illnesses and antimicrobial-resistant organisms to human beings was emphasized

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(Received 31 October 2024, accepted 08 January 2025)
DOI: 10.21608/EJVS.2025.331672.2466

[7]. One important method of controlling this disease in poultry is through drug therapy, specifically the use of antibiotics. Hence, there is a worldwide worry about limiting the use of antibiotics in the poultry sector; all nations must safeguard the effectiveness of important antibiotics, particularly those vital for human health. [8]. Moreover; recent research has verified that *Ps. aeruginosa* is resistant to numerous antibiotics due to multiple drug resistance [9]. This could be caused by a non-permeable outer layer and the secretion of extracellular polysaccharides [10]**.** Additionally, the rapid increase in resistance is due to the presence of both intrinsic and acquired antibiotic resistance mechanisms. [11]. Moreover, the high degree of multiple drug resistance in *Ps. aeruginosa* might be also attributed to its opportunistic pathogenic nature, biofilm formation, and ability to induce chronic infections [12]. Accordingly; different approaches other than antibiotic therapy have been the main focus of research in animal science to support animal production. Probiotics, prebiotics, exogenous enzymes, yeast nucleotides, and phytogenics such as plant extracts are the most commonly used alternatives in poultry production. [13,14]. They are used as a viable alternative to antibiotic growth promoters [15] and as safe and efficacious products in combating specific bacteria [16,17].

The present research was conducted to probate the hypothesis that the positive impact of using natural feed additives (phytobiotic and nucleotide) as rationary supplements. Therefore, the main goals were to evaluate using natural feed additives in the control of experimentally infected *Ps. aeruginosa* in broiler chickens and the effects on the broiler performance, carcass yield, breast and thigh meat quality.

Material and Methods

Feed additives

1- A natural phytobiotic feed ingredient (Sangrovit) manufactured by Phytobiotics Feed Additives Co. (Germany) was used. This additive contains 4% Macleaya cordata extract and 96% powdered Macleaya used at a dose of 1kg/MT for the starter ration and 0.5kg/MT for the growth and finishing rations.

2-Hydrolyzed yeast nucleotides (Zymos-N) manufactured by Vaso Biotech Pvt Limited used at a dose of 300 ppm (300 g/MT).

Rations

During the first two weeks of life, chickens were fed a commercial starter ration (23% crude protein and 3000 kcal ME/kg ration), followed by a commercial grower ration (22% crude protein and 3150 kcal ME/kg ration) from 2-4 weeks of age, and finally a commercial finisher ration (19% crude protein and 3200 kcal ME/kg ration) from 4-6 weeks of age. water was provided ad libitum. The water supply and ration were not supplemented with antibiotics.

Chickens

Three hundred; day old Indian River (IR) broiler chickens were used in this study. The birds were divided into 4 groups divided into five replicates with 15 birds each. All birds received Hitchner B1+H120 vaccine via the intraocular and the avian influenza-inactivated H5N2 vaccine by subcutaneous routes at the 7th and 10th day of age, respectively. The intraocular route was used to administer the 228E IBDV and La Sota vaccination on the 14^{th} and 18^{th} day of age respectively. Each group was kept on floor and reared in a separate unit under similar managemental and hygienic condition.

Experimental design

The experiments were carried out in accordance with the National Regulations on Animal Welfare and the Institutional Animal Ethical Committee (IACUC) of the faculty of Veterinary Medicine, Cairo University code no 25122023814.

The trial lasted for 35 days (from one day of age until the slaughter). Birds belonging to groups 1 and 2 were represented as positive and negative control groups, respectively (denoted as PC and NC). Chicken groups 3 and 4 provided a ration that was supplemented with Sangrovit® and ZYMOS®-N respectively (denoted as T1 and T2). At day 3 of age, *Ps .aeruginosa* was experimentally inoculated subcutaneously into chicken groups 2, 3 and 4 (PC, T1 and T2) using 0.2 ml of PBS containing 10^6 CFU/bird. All groups were operating simultaneously (Table 1).

Measured parameters

Productive performance:

The productive performance of the chickens was determined after [18].Every replicate was monitored for the following variables: weekly individual body weight (Wt.), feed consumption (daily and weekly feed consumption (g/d/bird)), feed conversion ratio (FCR) (cumulative and weekly feed conversion rate (g feed/g live body Wt. gain), and the mortality rate was recorded for each replicate. Weighed dead birds were used to determine feed conversion estimates based on their weights. European Production Efficiency Factor (Production Number) which is estimated after the trial period and equals (kilograms of growth per day * (100–mortality %)/FCR) *100 after [19] , was determined as a measure of productivity.

Carcass characteristics:

Dressing%, front part %, hind part %, breast meat %, thigh drumstick %, carcass meat %, heart wt.%, gizzard wt.%, liver wt.%, and giblet wt.% were measured on randomly chosen 10 birds/group (2 birds/replicate) at the end of the experiment.

Measurements were made on 2 randomly selected birds from each replicate on the 35th day of age to determine Intestinal length; diameter and weight: Intestinal length (duodenum + jejunum + ileum) and diameter (in the middle of the ileum) [20].

Immune status assessment:

An immunoassay was performed to study the possible effect of rationary supplements on humoral immunity. For this purpose, blood samples were collected from the wing veins of 10 randomly selected birds/groups (2 birds/replicate) at weekly intervals (1-5 weeks of age). The serum samples were subjected to a hemagglutination inhibition (HI) test for determining antibody titers against ND vaccination employing 8 hemagglutinating (HA) units [21]. For assessment of the cell-mediated immune response; delayed-type hypersensitivity (DHT) response to bovine serum albumin (BSA) was measured after [22]. The randomly chosen birds in each group were injected at d 28 with 4 mg BSA in 1 ml saline in the back of the neck. At d 35, birds will be re-injected with 1 mg BSA in 1 ml saline into the flat surface of the right wattles. In contrast, the left wattles were injected with 1 ml saline and served as a control. At 24 h post-injection, the thickness of both wattles was measured by a paper thickness micrometer to calculate the differences in the thickness between saline and BSA-injected wattles. The DHT response is calculated as a relative response as the following: Relative response=the thickness of the right wattle (BSA response) - The thickness of the left wattle (saline response) / the thickness of the left wattle (saline response) *100.

Gut Morphometry and Histopathological assays:

Five randomly selected birds from each groups were sacrificed (one bird/replicate) for gut morphometry at the end of the experiment (d 35). The duodenum and jejunum were sampled, with a thickness of one centimeter [the intestinal segmentation according to [23] as jejunum from the bile duct to Meckel's diverticulum]. Routine histological laboratory methods were adopted and villous histomorphometry for recording the histological indices was measured using digital photography and light microscopy. The photos were taken and morphometric analyses were performed. The villous height measured from the apical to the basal region and the crypts from the basis until the region of transition between the crypt and the villous. Five measurements per section were made for each parameter and averaged into one value. For histopathological examination; specimens of the spleen, thymus glands, bursa of Fabricius, and cecal tonsils as well as heart, liver, and lungs, were taken from 5 sacrificed birds/group (one bird/replicate), fixed in 15% buffered formalin and paraffin-embedded sections stained with Hematoxylin and Eosin were made [24] and scored for histopathological lesions according to the method described by [25] .

Statistical Analysis:

One-way analysis of variance adopted using SAS software general linear models' procedure [26]. Sangrovit® TM and ZYMOS®-N as a mean effect were the primary variables. Mean values were assessed for significance using Duncan's multiple-range tests [27]. Statements of statistical significance are based upon $P<0.05$.

Results and Discussion

Due to the recent ban on antibiotics in poultry feed, there is an increasing trend in the use of non-antibiotic feed additives to improve the growth and health of the birds [28]. The most widely accepted alternatives include probiotics, prebiotics, exogenous enzymes, phytogenics, and nucleotides in poultry [13]. In the present study, a natural phytobiotic feed ingredient and hydrolyzed yeast nucleotides were used as alternatives to antibiotics. Phytogenics are derived from Macleaya cordata, with its abundant amounts of sanguinarine, which is suggested to inhibit the growth of some bacteria that cause gastrointestinal upset [29]. Nucleotides are crucial for the body as a cellular energy source (ATP) and play a critical role in protein synthesis, cell mitosis, lipid metabolism, hematopoiesis, immunity, and gut health. They are also a fundamental component in carbohydrate, protein, fat, and nucleic acid metabolism [30].

Experimentally infected chickens with Ps. aeruginosa supplemented with Sangrovit® and Zymos®-N reduced the mortality percentage by 25.33% and 18.65% in the T1 and T2 groups, respectively, vs. the PC group (Table 2). [29] Stated that sanguinarine suppresses the growth of some bacteria that cause gastrointestinal distress by enhancing appetite and feed intake and promoting growth. [31] Reported that sanguinarine effectively controlled Salmonella Enteritis in broiler chickens, indicating that rationary sanguinarine could play an important role in reducing economically important enteric diseases. It is already established that chickens under stress-fed rations containing nucleotides lowered mortality when compared with control birds [32, 33]. [34] Reported that in addition to storing energy, nucleotides perform several vital physiological, gastrointestinal, and immune roles in the organism during rapid growth and development, disease problems, injury, or stress situations like high stocking density or unclean litter.These aforementioned studies confirm our obtained results of supplementation of Sangrovit® and Zymos®-N on mortality post-*Ps. aeruginosa* experimental infection in broiler chickens. The growth performance parameters are illustrated in Tables 2 and 3, including feed intake, body weight, body weight gain, FCR, and production number. Comparatively, the current trial showed significant improvement ($P \leq$

0.05) for growth parameters either in T1 or T2 treated groups vs. the PC group. The improvement in performance in the T1 group accords with results obtained by [35] and [36], which might be due to its influences on gastrointestinal functions such as gut architecture, motility, and fermentation process [37] or due to stimulation of enzyme secretion in the intestine [38]. Contrary to our findings, [39] stated that a rationary treatment of Sangrovit® did not affect the productivity of birds and did not enhance rationary protein utilization. The performance parameters of the T2 group accord with the findings of [32], who verified broiler performance improvement when broilers fed yeast extracts and yeast cell components and attributed the better performance to the beneficial effect of the nucleotides present in the yeast extract. Similarly, this finding is in agreement with [40], who noted that rationary nucleotide supplementation had an important role in improving live body weight and body weight gain. Contrary to our findings, other investigators reported non-significant differences due to the addition of nucleotide or yeast extract products to poultry rations [36, 41]. Both supplemented additives significantly improved weekly and cumulative FCR vs. the PC group ($P \leq 0.05$). About Sangrovit®, our results accord with those reported by [35]**.** Results of Zymos®-N supplementation are in line with those reported by other investigators [42, 43] who demonstrated that nucleotides improved FCR.

The assessment of broiler performance was conducted using the EPEF (European Production Efficiency Factor), including daily weight gain and survival percentage (Table 3). There was a significant improvement in both the Sangrovit® (T1) and Zymos®-N (T2) groups compared with the PC group ($P \leq 0.05$). The Sangrovit®-supplemented group showed a higher EPEF value, which is similar to [44], who found that the inclusion of extra Sangrovit®, at 5 g/kg broiler feed, improved the EPEF. For the Zymos group, our results agree with [45], who reported that nucleotide enhanced the flock uniformity of broiler chickens.

Furthermore, [46] discovered that adding Sangrovit Extra® at a dosage of 0.15 g/kg had no impact on the production efficiency factor. In addition, [47] discovered that the production efficiency index for the group that received Sangrovit® from one to 21 days of age without facing any challenges was greater than that of the group that was given it from 6 to 21 days of age and exposed to *Salmonella* Heidelberg.

In the present study, experimentally infected broiler chickens with *Ps. aeruginosa* showed dehydration, ruffled feathers, diarrhea, and mild respiratory manifestations with pneumonia, greenish discoloration in lungs, enteritis, and necrotic foci in the liver and spleen. Similar clinical signs in *Ps. aeruginosa*-infected chickens were mentioned by [48]**.** T1 and T2 groups showed a decrease in the severity of clinical signs and lesions where there was a significant improvement in the liver, air sacs, and thymus glands ($P \leq 0.05$) (Table 4). The improvement in kidneys was only recorded in the T1 group (Sangrovit® treated).

Obtained results of the carcass quality illustrated in Tables 5a and 5b were supported by [36], who observed a numerical improvement in carcass yield, drum, thigh, wing, and breast yields in birds fed yeast extract (nucleotide source) as compared to those who did not receive yeast extract. On the other hand, [49] found that nucleotide supplementation did not affect carcass yield % or relatively improve the weight of different organ cut-up sections.Besides, [50] reported that the high dose of nucleotide 1.5 g/kg resulted in a higher weight of breast meat. [36] Attributed this to the fact that yeast extract contains other nutrients in addition to nucleotides, such as amino acids, vitamins, and minerals, which may contribute to increased carcass yield. About Sangrovit® results, [39] observed that broilers fed a ration containing Sangrovit® showed an increase in average carcass and breast muscle weights by 1% and 3%, respectively, and the weight of thigh muscles was found to be 2.44% lower compared to the control group. [51] Reported that incorporating phytobiotics into broiler rations noticeably enhanced carcass characteristics more effectively. In contrast, [39] discovered that supplementation with Sangrovit had no impact on carcass yield, aligning with the results of [52]**.** The effect of Sangrovit and Zymos-N on heart, liver, and gizzard quality showed no significant difference between the infected treated and non-treated groups. Our obtained results are completely in accord with those reported by [53]**.** There was a significant increase in intestinal diameter, weight, and weight % in supplemented groups (T1 and T2) vs. the PC group ($P > 0.05$) (Table 5).

Results of immune status assessment are shown in Tables 6-8. Regarding the weights of immune organs, there was a significant increase in the weight percentage of the bursa and a significant decrease in the weight percentage of other immune organs (thymus and spleen), HI titers against ND vaccination, and delayed-type hypersensitivity test vs. PC group ($P \leq 0.05$). Sangrovit® supplementation enhanced the humoral immune response when compared to the PC group. It is recognized for its ability to modulate the immune system and enhance phagocytic activity, thereby supporting the body's protective responses [54]. [55] Reported that the absorption of exogenous sources of nucleotides is in the intestine and then emigrates to immune organs as bursa, subsequently nucleotides enhance the immunity of broilers. Our results are similar to [32, 43], who reported that nucleotide supplementation had improved the bursa of Fabricius relative weight but had no effect on the spleen. Rationary

nucleotides are capable of increasing cell-mediated immunity and improving host resistance to bacterial infections [55]. This may be attributed to the fact that the inclusion of nucleotides in the ration of broiler chickens might be beneficial for the activation of the local innate immunity of broilers under microbial challenge. Furthermore, nucleotides promote the proliferation of bone marrow cells, stimulate the production and secretion of interleukins and interferon-gamma, and increase the cytotoxicity of the natural killer cells [56]. [57] Demonstrated that the immune system is strengthened by nucleotides when they are added to the ration. In addition, [43] observed an improvement in HI titer against NDV in the nucleotide-supplemented group compared with the control group. [14] Reported that adding yeast nucleotides to birds can boost their immune response to the IBV vaccine, promoting intestinal growth and gene expression related to barrier function while also improving the diversity and abundance of the gut microbiota.

The results of histomorphometric analysis are shown in Table 9. The T1 group showed an improvement in intestinal histomorphology (increasing the villi height/crypt depth ratio) vs. the PC group. This result is in harmony with that recorded by [35], who found that Sangrovit®-fed chickens had decreased relative jejunal weight but increased relative jejunal or ileal length compared with the control group. The group fed on the ration supplemented with nucleotides had the lowest villus height but gained more weight than the PC group. Therefore, a clear relationship between villus height and body weight gain is not established. This result may be attributed to what was said by [32], who observed that nucleotide supplementation raised IgA concentrations in birds at 11 and 21 days of age but had no effect on IgG concentrations in jejunal samples, and that may permit the adverse effect of infection to decrease the villi length.

The histopathological lesions of the infected broiler chicken with *Ps. aeruginosa* are shown in Figures 1-6. and Table 10. The results revealed prominent variable changes in the examined organs. The liver showed marked hepatitis, and marked myocardial necrosis, enteritis, and splenitis were recorded. The thymus tissue showed an obvious decrease of lymphocytic cells in the medulla, while the bursa revealed marked bursitis with lymphoid depletion and necrosis. Similar results were observed by [48]**.** The hepatic tissue had severe hepatitis with multiple lymphocytic focal aggregations, congested hepatic sinusoids, and focal hepatic necrosis. These results are supported by [58]. The intestinal tissue showed severe ulcerative enteritis with massive lymphocytic cell infiltration and hyperplastic intestinal glands. Similarly, [59] reported that the intestine in chicks infected with *Pseudomonas* showed epithelial hyperplasia of mucosa with cystic formation of goblet cells. The spleen showed marked splenitis and vasculitis as well as lymphocytic depletion and lymphocytic necrosis. The histopathological lesions in both infected treated groups (T1 and T2) were significantly less severe as compared to the PC group. According to statistical analysis of histopathological scores, there was a significant difference between the treated groups and the PC group ($P \leq 0.05$), although there was no significant difference between the treated groups themselves, which was presented by some improvement in pathological alterations in examined tissues. These results of Sangrovit agreed with [60], who stated that there were improvements in tissues (liver and kidney) in Sangrovit-treated groups.

Conclusion

In conclusion, the use of non-pharmacological feed additives "natural phytobiotics" and "hydrolyzed yeast nucleotides" not only reduced mortality and mitigated the clinical and pathological condition of chickens experimentally infected with *Ps. aeruginosa*, but also enhanced productive performance parameters, carcass characteristics, immune status, gut histomorphology as well as improving the histopathological picture.

Declarations

Ethics approval and consent to participate

This work follows the regulations of IACUC, Faculty of Veterinary Medicine, Cairo University.

Consent for publication

Not applicable

Availability of data and materials

All data generated of analysed during this study are included in this published article.

Competing interests

The authors declare no competing interests.

Funding statement

There is no funding statement to declare.

Conflicts of interest

There are no conflicts to declare.

Authors' contributions

Mohamed, H. H. Awaad conceived the study, designed the experiment, and written the first draft manuscript; Sahar, A. Zouelfakar, Eman, A. Morsy and Ahmed F. Gaber performed the experiment, Ahmed shawky, Heba Badr, Marwa A. Abdelmagid carried out data analysis and histopathology. All authors wrote, revised, and approved the final manuscript.

Acknowledgments

Not applicable

TABLE 1. Experimental design.

Chicken Groups (75 birds /group)	Supplementation		*Ps. aeruginosa* infection
	Sangrovit	Zymos	
PC (Positive control))	-	-	+
NC (Negative control)	-	-	-
T1 (Sangrovit)	+	-	+
T2 (Zymos-N)	-	+	+

TABLE 2. The effect of sangrovit and zymos supplementation on production performance in *Ps .aeruginosa* infected broiler chickens

Mortality Rate						
Gr	1 – 7 days	7 – 14 days	14 – 21 days	21 – 28 days	28 – 35 days	1 – 35 days
NC	1.3%	0%	0%	0%	0%	1.3%
PC	1.3%	5.33%	16%	9.33%	6.66%	38.62%
T1	0%	1.33%	12%	8%	4%	25.33%
T2	0%	1.33%	9.33%	6.66%	1.33%	18.65%
Body Weight						
Gr	1 – 7 days	7 – 14 days	14 – 21 days	21 – 28 days	28 – 35 days	1 – 35 days
NC	37.96±0.3^{a}	159.69±7.2^{a}	389.58±7.2^{a}	676.04±18.3^{a}	1227.31±34.2^{a}	1801.70±63.29^{a}
PC	38.12±0.34^{a}	161.58±2.8^{a}	350.21±7.8^{c}	566.47±18.9^{c}	788.81±30.6^{c}	985.67±30.6^{c}
T1	37.89±0.38^{a}	164.72±2.3^{a}	365.88±9.1^{ab}	615.51±21.1^{b}	844.48±43.5^{b}	1114.07±46.4^{b}
T2	37.83±0.37^{a}	163.60±2.2^{a}	373.61±7.1^{ab}	657.89±18.2^{b}	872.58±37.0^{b}	1154.21±44.7^{b}
Weight Gain						
Gr	0–7 days (g/ bird)	7–14 days	14–21 days	21–28 days	28–35 days	
NC	121.37±2.3^{a}	230.49±7.1^{a}	366.95±15.8^{a}	551.27±13.9^{a}	574.25±8.5^{a}	
PC	123.77±4.9^{a}	188.63±18.8^{ab}	216.26±7.2^{d}	222.34±12.4^{b}	196.86±8.5^{d}	
T1	126.85±3.2^{a}	201.63±11.5^{ab}	249.63±14.97^{c}	229.05±14.4^{b}	269.59±8.3^{c}	
T2	126.24±2.4^{a}	210.49±6.5^{ab}	284.46±18.8^{b}	214.69±15.9^{b}	281.63±4.9^{b}	
Feed Intake (g/d/bird)						
Gr	1 – 7 days	7 – 14 days	14 – 21 days	21 – 28 days	28 – 35 days	
NC	20.56±1.8^{a}	43.08±0.4^{a}	80.30±2.1^{a}	96.19±1.9	111.60±2.7^{a}	
PC	21.55±1.7^{a}	36.59±1.1^{b}	68.95±3.4^{b}	84.35±2.5^{b}	82.13±0.0^{c}	
T1	22.18±0.3^{a}	37.62±1.6^{b}	66.76±4.4^{b}	78.18±5.1^{bc}	84.49±3.7^{c}	
T2	23.18±1.7^{a}	40.57±1.3^{a}	71.75±2.7^{b}	83.13±3.1^{b}	92.35±2.5^{b}	
Weekly FCR						
Gr	1 – 7 days	7 – 14 days	14 – 21 days	21 – 28 days	28 – 35 days	
NC	1.18±0.01^{a}	1.31±0.04^{a}	1.53±0.09^{c}	1.22±0.03^{c}	1.36±.027^{c}	
PC	1.22±0.02^{a}	1.36±0.04^{a}	2.23±0.16^{a}	2.66±0.03^{a}	2.93±0.03^{a}	
T1	1.23±0.03^{a}	1.30±0.04^{a}	1.87±0.05^{b}	2.39±0.05^{b}	2.19±0.05^{b}	
T2	1.28±0.02^{a}	1.35±0.04^{a}	1.77±.0.05^{b}	2.71±0.09^{b}	2.29±0.09^{b}	
Cumulative FCR						
Gr	1 – 7 days	1 – 14 days	1 – 21 days	1 – 28 days	1 – 35 days	
NC	0.91±0.13^{a}	1.14±0.01^{b}	1.49±0.07^{b}	1.37±0.06^{c}	1.37±0.15^{c}	
PC	0.93±0.09^{a}	1.19±0.03^{a}	1.57±0.04^{a}	1.88±0.08^{a}	2.08±0.16^{a}	
T1	0.94±0.15^{a}	1.14±0.05^{a}	1.44±0.03^{b}	1.72±0.09^{b}	1.81±0.09^{b}	
T2	0.99±0.16^{a}	1.16±0.06^{a}	1.44±0.05^{b}	1.75±0.08^{b}	1.89±0.08^{b}	

Mean± SD. Superscript letters in the same column showed significant difference at $p \leq 0.05$

TABLE 3. The effect of sangrovit and zymos supplementation on European Production Efficiency Factor (Production Number) in *Ps .aeruginosa* infected broiler chickens

Groups	Production Number
NC	303.75± 6.85[a]
PC	199.75±13.42[c]
T1	233.53±32.98[b]
T2	224.22±19.31[b]

Mean± SD. Superscript letters in the same column showed significant difference at p≤0.05

TABLE 4. The effect of sangrovit and zymos supplementation on lesion score of internal organs in *Ps .aeruginosa* infected broiler chickens

Groups	Liver	spleen	kidney	intestine	lung	air sac	heart	thymus
PC	2.5±0.31[a]	0	0.5±0.03[a]	1.9±0.32[a]	0.3±0.13	0.7±0.3[a]	0.4±0.31[a]	1.9±0.42[a]
T1	1.3±0.32[c]	0[ns]	0.2±0.02[b]	2±0.41[a]	0	0.4±0.2[b]	0.3±0.13[a]	0.8±0.43[b]
T2	0.9±0.33[b]	0	0	1.4±0.31[b]	0	0.4±0.3[b]	0.4±0.31[a]	0.8±0.41[b]

Mean± SD. Superscript letters in the same column showed significant difference at p≤0.05

TABLE 5a. The effect of sangrovit and zymos supplementation on Carcass characteristics in *Ps .aeruginosa* infected broiler chickens

Gr	Life weight	Carcass		Front Parts		Hind Parts	
	(Kg)	Wt.(kg)	(%)	Wt.(kg)	(%)	Wt.(kg)	(%)
NC	1.802±0.29[a]	1.261±0.16	70.37± 0.17[a]	0.785±0.034	43.57±0.31[a]	0.593±0.13	32.93±0.23[a]
PC	0.926±0.03[c]	0.618±0.21	66.74± 0.51[b]	0.337±0.024	36.43±0.45[c]	0.272±0.262	29.40±0.46[b]
T1	1.014±0.04[b]	0.691±0.13	68.07± 0.02[b]	0.409±0.058	40.34±0.66[a]	0.319±0.34	31.42±0.59[a]
T2	1.071±0.01[b]	0.719±0.09	67.16±0.48[b]	0.417±0.034	38.94±0.67[bc]	0.332±0.25	30.95±0.41[a]

Gr	Carcass Meat		Brest Meat		Thigh Drumstick Meat	
	Wt.(kg)	(%)	Wt.(kg)	(%)	Wt.(kg)	(%)
NC	738.64±49.87	53.57±0.31[a]	438.79±27.02	24.35±0.54[a]	738.64±49.87	53.57±0.31[a]
PC	339.85±58.16	36.43±0.45[c]	206.04±31.48	22.25±0.62[b]	339.85±58.16	36.43±0.45[c]
T1	398.31±57.47	42.35±0.66[b]	237.28±36.51	23.40±0.89[b]	398.31±57.47	42.35±0.66[b]
T2	409.13±34.54	44.52±0.67[b]	252.01±17.42	23.53±0.74[ab]	409.13±34.54	44.52±0.67[b]

Gr	Liver		Heart		Gizzard		Giblets organs	
	Wt. (g)	(%)	Wt. (g)	(%)	Wt. (g)	(%)	Wt. (g)	(%)
NC	52.08±3.65	4.13±0.30[a]	13.17±0.48	1.044±0.042[a]	27.34±5.90	2.168±0.024[a]	92.59±10.03	7.34±0.372[a]
PC	21.07±3.18	3.41±0.11[b]	5.469±0.99	0.885±0.039c[b]	11.96±0.83	1.935±0.056[b]	38.23±5.01	6.24±0.151[b]
T1	27.01±3.44	3.91±0.12[b]	6.26±1.03	0.906±0.031[b]	15.52±1.61	1.817±0.08[b]	45.79±6.080	6.44±0.23[b]
T2	25.74±4.57	3.58±0.23[b]	6.852±0.48	0.953±0.020[b]	16.72±0.99	1.802±0.041[b]	49.31±6.041	6.34±0.47[b]

Mean± SD. Superscript letters in the same column showed significant difference at p≤0.05

TABLE 5b. The effect of sangrovit and zymos supplementation on Intestinal length, diameter, and weight in *Ps .aeruginosa* infected broiler chickens

Groups	Length (cm)	Diameter (cm)	Weight (g)	(%)
NC	190.15±2.23[a]	0.89±0.065[a]	101.77±4.31[a]	8.07±0.65[c]
PC	175.88±7.96[a]	0.66±0.077[c]	79.65±5.05[b]	12.88±0.58[ab]
T1	187.33±5.17[a]	0.82±0.039[ab]	101.22±8.21[a]	14.46±0.35[a]
T2	185.8±6.23[a]	0.87±0.061[ab]	99.07±14.07[a]	13.77±0.28[a]

Mean± SD. Superscript letters in the same column showed significant difference at p≤0.05

TABLE 6. The effect of sangrovit and zymos supplementation on HI Titer against Newcastle Disease Virus in *Ps .aeruginosa* infected broiler chickens

Group	7 days	14 days	21 days	28 days	35 days
NC	2.60±0.16^{a}	1.5±0.22^{a}	3.5±0.22^{a}	4.20±0.44^{a}	4.50±0.37^{a}
PC	2.51±0.27^{a}	1.3±0.16^{b}	2.70±0.30^{b}	3.40±0.47^{b}	3.90±0.45^{b}
T1	2.60±0.26^{a}	1.5±0.22^{a}	3.5±0.22^{a}	4.20±0.44^{a}	4.50±0.37^{a}
T2	2.49±0.39^{a}	1.6±0.17^{a}	3.70±0.30^{a}	4.40±0.47^{a}	4.67±0.45^{a}

Mean± SD. Superscript letters in the same column showed significant difference at p≤0.05

TABLE 7. The effect of sangrovit and zymos supplementation on Delayed Type Hypersensitivity Test in *Ps .aeruginosa* infected broiler chickens

Group	Delayed Type Hypersensitivity Test
NC	22.82±6.31^{d}
PC	32.44±6.61^{c}
T1	42.46±7.08^{a}
T2	37.78±7.42^{b}

Mean± SD. Superscript letters in the same column showed significant difference at p≤0.05

TABLE 8. The effect of sangrovit and zymos supplementation on Relative Immune Organs in *Ps .aeruginosa* infected broiler chickens

Groups	Bursa		Spleen		Thymus	
	Weight g)	(%)	Weight (g)	(%)	Weight (g)	(%)
NC	3.57±0.49	0.283±0.03^{d}	1.89±0.29	0.104±0.04^{c}	7.47±0.67	0.592±0.024^{c}
PC	2.07±0.31	0.334±0.11^{c}	2.29±0.27	0.371±0.04^{a}	10.50±0.81	1.696±0.056^{a}
T1	3.31±0.31	0.479±0.10^{b}	1.99±0.18	0.287±0.03^{b}	9.19±1.52	1.278±0.041^{b}
T2	3.73±0.48	0.518±0.02^{a}	1.85±0.27	0.234±0.08^{b}	9.26±1.31	1.299±0.08^{b}

Mean± SD. Superscript letters in the same column showed significant difference at p≤0.05

TABLE 9. The effect of sangrovit and zymos supplementation on Histomorphometry of jejunal intestinal segments in *Ps .aeruginosa* infected broiler chickens

Groups	Villi length	Crypt depth	Villi/crypt ratio
NC	753.94 ± 30.81^{a}	159.6 ± 6.44^{d}	4.86 ± 0.29^{a}
PC	635.81 ± 5.18^{b}	265.5 ± 6.39^{b}	2.42 ± 0.06^{c}
T1	695.68 ± 14.11^{b}	210.03 ± 7.30^{c}	3.39 ± 0.12^{b}
T2	571.68 ± 18.28^{c}	432.27 ± 16.12^{a}	138 ± 0.082^{d}

Mean± SD. Superscript letters in the same column showed significant difference at p≤0.05

TABLE 10. Statistical analysis of histopathological lesion score

Organ/Group	NC	PC	T1	T2
Heart				
Lymphocytic cells infiltration	0.33±0.58^{a}	3.33±0.58^{b}	2.33±0.58^{bc}	1.67±0.58^{c}
Myocardial edema	0.33±0.58^{a}	2.67±0.58^{b}	2.67±0.58^{b}	1.33±0.58^{a}
Myocardial necrosis	0^{a}	3.67±0.58^{b}	1.67±0.58^{c}	1.33±0.58^{c}
Liver				
Hepatic degeneration	0.67±0.58^{a}	3.33±0.58^{b}	2.33±0.58^{b}	2.33±0.58^{b}
Hepatic necrosis	0^{a}	3.33±0.58^{b}	2.33±0.58^{c}	1.33±0.58^{d}
Congested sinusoids	0.67±0.58^{a}	3.33±0.58^{b}	2.33±0.58^{bc}	1.67±0.58^{ac}
Lymphocytic cells infiltration	0.33±0.58^{a}	3.67±0.58^{b}	2.0±0^{c}	1.33±0.58^{c}
Intestine				
Inflammatory cells infiltration	0.67±0.58^{a}	3.33±0.58^{b}	2.67±0.58^{b}	2.33±1.15^{b}
Necrotic or ulcerative villi	0^{a}	3.00±1.00^{b}	3.00±0.00^{b}	2.0±1^{b}

Spleen				
Lymphocytic depletion	0.33±0.58^{a}	3.00±1.00^{b}	1.67±0.58^{a}	1.33±0.58^{a}
Vasculitis	0.33±0.58^{a}	2.67±0.58^{b}	2.0±1^{b}	1.33±0.58^{ab}
Lymphocytic necrosis	0^{a}	2.67±0.58^{b}	1.33±0.58^{c}	1.00±0.00^{c}
Thymus				
Lymphoid depletion	0.33±0.58^{a}	1.67±0.58^{b}	2.67±0.58^{b}	1.67±0.58^{b}
Congestion and hemorrhages	0^{a}	2.67±0.58^{b}	2.33±0.58^{b}	0.67±0.58^{a}
Bursa				
Lymphoid depletion	0.33±0.58^{a}	3.33±0.58^{b}	2.33±0.58^{b}	2.33±0.58^{b}
Edema	0^{a}	3.33±0.58^{b}	2.33±0.58^{c}	2.33±0.58^{c}
Hyperplasia of cortex	0^{a}	3.33±0.58^{b}	2.0±1^{c}	0.33±0.58^{a}

Mean± SD. Superscript letters in the same column showed significant difference at p≤0.05

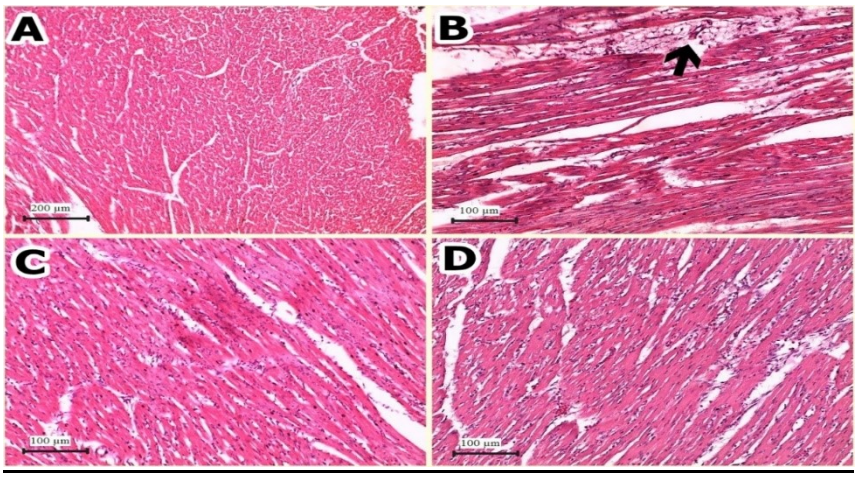

Fig. 1. Photomicrograph of heart (H&E); (A): heart of **NC** group showed normal normal architecture, **(B)**: heart of **PC** group showed heart showed marked myocarditis and myocardial necrosis (arrow), **(C)**: heart of **T1** group showed mild myocarditis with few lymphocytic cells infiltration, **(D)**: heart of **T2** group showed mild myocardial edema.

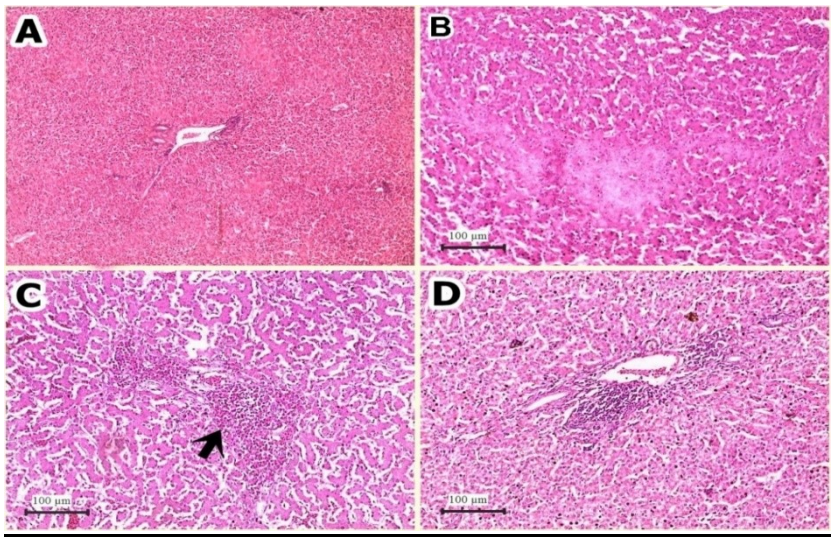

Fig. 2. Photomicrograph of liver (H&E); (A): liver of **NC** group showed normal histologic picture with normal hepatocytic arrangement and portal area, **(B)**: liver of **PC** group showed severe hepatitis, congested hepatic sinusoids, and focal hepatic necrosis, **(C)**: liver of **T1** group with hepatocytic degeneration and focal inflammatory cells infiltration (arrow), **(D)**: liver of **T2** group showed perivascular inflammatory cells infiltration.

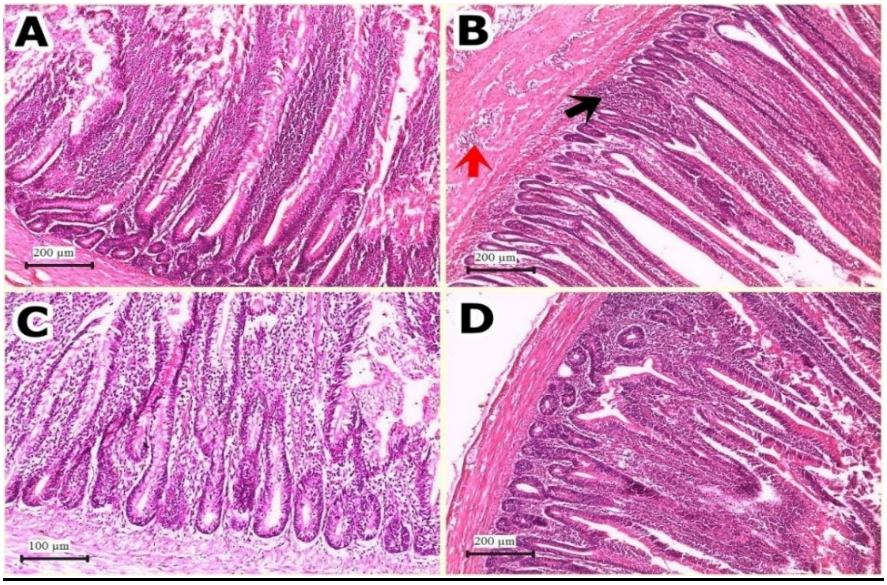

Fig. 3. Photomicrograph of intestine (H&E); (A): intestine of **NC** group showed mild lymphocytic cells infiltration, **(B)**: intestine of **PC** group showed severe ulcerative enteritis (red arrow) with massive lymphocytic cells infiltration (black arrow) and hyperplastic intestinal glands, **(C)**: intestine of **T1** group showed marked enteritis and abundant lymphocytic infiltration within lamina propria, **(D)**: intestine of **T2** group showed massive lymphocytic cells infiltration and ulceration of villi.

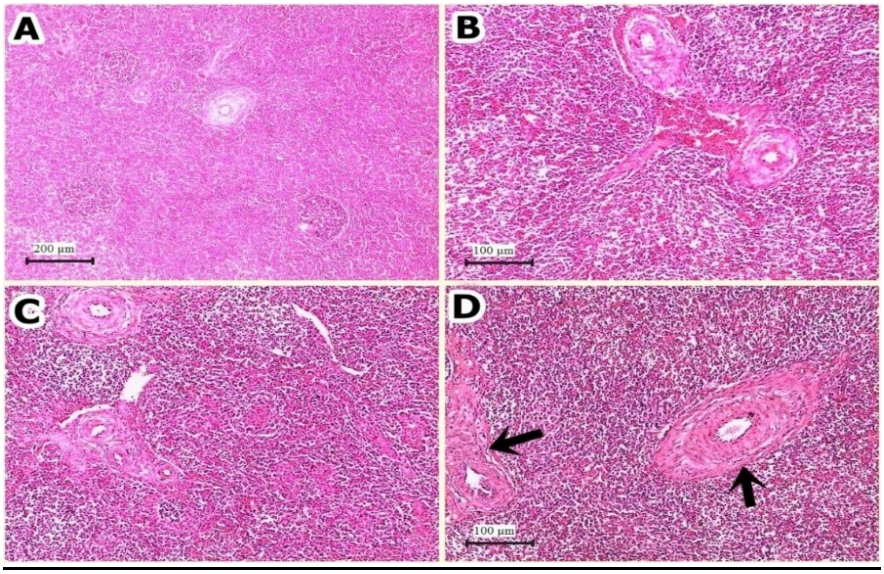

Fig. 4. Photomicrograph of spleen (H&E); (A): spleen of **NC** group showed normal lymphocytic cells and nodules, **(B)**: spleen of **PC** group showed marked spleenitis and vasculitis with lymphocytic depletion and lymphocytic necrosis, **(C)**: spleen of **T1** group showed mild spleenitis and lymphocytic depletion, **(D)**: spleen of **T2** group showed mild lymphocytic necrosis and depletion with vasculitis (arrow).

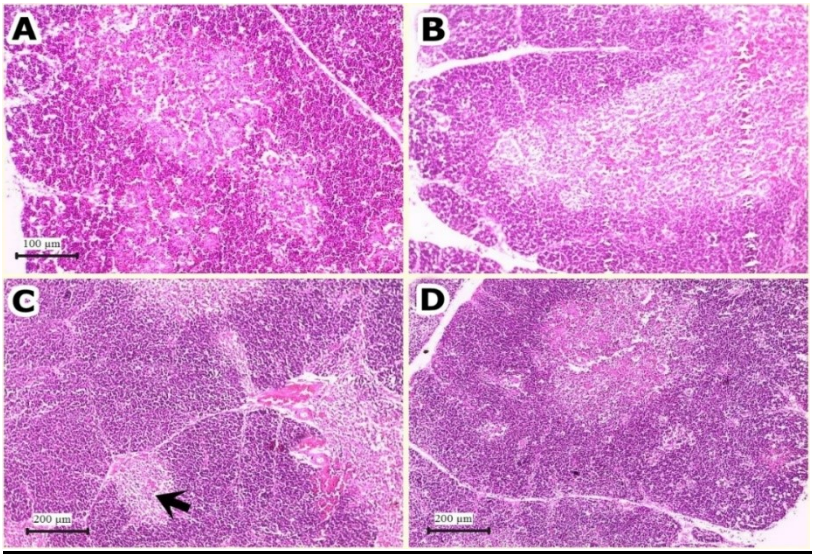

Fig. 5. Photomicrograph of thymus (H&E); (A): thymus of **NC** group showed normal lymphocytic cells within cortex and medulla, **(B)**: thymus of **PC** group showed decrease of lymphocytic cells in the medulla, **(C)**: thymus of **T1** group showed congestion of blood vessels and focal lymphoid depletion (arrow), **(D)**: thymus of **T2** group showed mild lymphoid depletion.

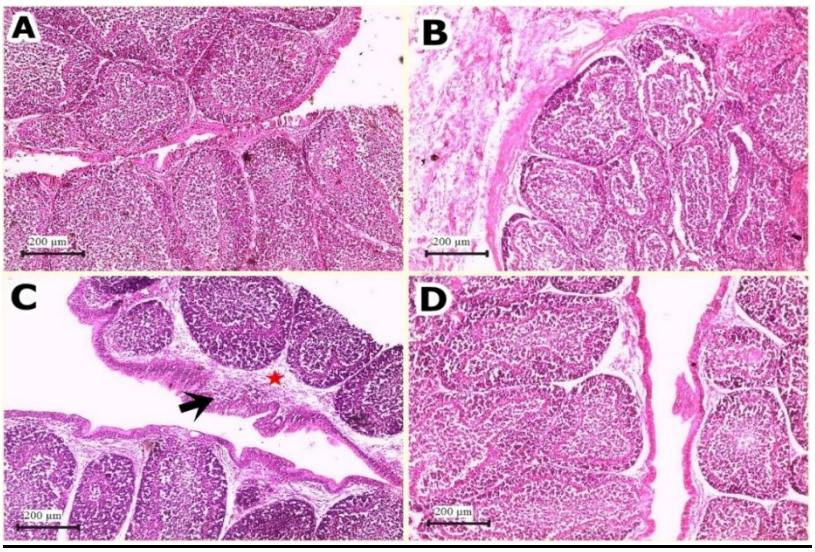

Fig. 6. Photomicrograph of bursa (H&E); (A): bursa of **NC** group showed normal lymphoid follicles and septum, **(B)**: bursa of **PC** group showed marked bursitis with lymphoid depletion and necrosis, **(C)**: bursa of **T1** group showed subcortical edema (read star) and hyperplasia of lining epithelium (arrow), **(D)**: bursa of **T2** group showed mild lymphoid depletion.

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تأثير بعض البدائل الطبيعيه للمضادات الحيويه مثل الاضافات الغذائية النباتية والنيوكليوتيدات على كفاءه النمو وخصائص الذبيحه والحاله المناعيه وتغييرات الهستوباثولوجى في الدجاج اللاحم المعدى بالسودوموناس اريجونوزا

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الملخص

تعد السودوموناس اريجونوزا أحد الأسباب الرئيسية لتسمم الدم في الدجاج اللاحم، مما يؤدي إلى خسائر مالية كبيرة لصناعة الدواجن العالمية. كان الغرض من الدراسة الحالية هو توضيح آثار الاضافات الغذائية التي تحتوي على إضافات غير دوائية (النيوكليوتيدات والنباتات الحيوية) على معالجه السودوموناس اريجونوزا المصابة تجريبياً في الدجاج اللاحم. تم تقسيم فراخ اللاحم إلى أربع مجموعات بها خمس تقسيمات لكل مجموعه. تم تصنيف الطيور في المجموعتين 1 و 2 كمجموعات مراقبة إيجابية (PC) وسلبية (NC) على التوالي . تم تغذية مجموعتي الدجاج 3 و4 (المحددتين بـ T1 وT2) بعلف مكمل بـ (النباتات الحيوية والنيوكليوتيدات) ، على التوالي . تم حقن السودوموناس اريجونوزا تجريبياً تحت الجلد في مجموعات الدجاج 2 و 3 و 4 (PC، T1، و T2) في اليوم الثالث من العمر بجرعه .2 مل يحتوي على 106 CFU / طائر . أظهرت النتائج أن المجموعتين المكملتين (النباتات الحيوية والنيوكليوتيدات) أظهرتا معدلات نمو وكفاءة تغذية وأرقام إنتاج أفضل مقارنة بالمجموعة الضابطة. العدوى التجريبية بالسودوموناس اريجونوزا أدى إلى انخفاض معدلات الوفيات في المجموعات المكملة بهذه الإضافات. أثرت المواد المضافة بشكل إيجابي على نمو الأعضاء المناعية، واستجابات الأجسام المضادة، وفرط الحساسية المتأخر. قلل كل من النباتات الحيوية والنيوكليوتيدات من شدة االتأثيرات المعوية الناجمة عن العدوى. أظهرت المجموعات المكملة بشكل عام إنتاجية أفضل للذبيحة ووزن عضلات الصدر وتطور الأمعاء. بشكل عام، توضح الدراسة إمكانات مكونات العلف النباتي ونيوكليوتيدات الخميرة المحللة كبدائل واعدة للمضادات الحيوية في إنتاج الدواجن.

الكلمات المفتاحية : الدجاج اللاحم، النيوكليوتيدات، النباتات الحيوية، السودوموناس اريجونوزا.

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