Nigerian J. Anim. Sci. 2021, 23 (2): 51-59

Effect of replacement levels of Red Finger millet-based diets on growth performance of broiler chickens fed with and without phytase enzyme supplementation

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Target Audience: *Poultry farmers, Researchers, Nutritionists, Feed millers*

Abstract

An experiment was conducted to evaluate the effect of feeding red finger millet variety as replacement for maize with and without phytase (Ronozyme®) enzyme supplementation on the growth performance of broiler chickens. A total of 600 chicks were allotted in to 10 treatments, each treatment had 3 replicates containing 20 chicks each with and without enzyme supplementation at the rate of 100g/100kg diet in a completely randomized design (CRD). Red finger millet was included at 0,25,50,75 and 100% with phytase supplementation and at 0,25,50,75 and 100% without enzyme supplementation. This represents treatments (T) 1 2,3,4,5,6,7,8,9 and 10 respectively where 0% inclusions are the controls at both the starter and finisher phases. Result showed significant (P<0.05) differences across the treatments with and without enzyme supplementation. The highest final weight (766.20) in the starter was recorded in the control with enzyme, all the others had similar lower weights, and the same control recorded the best FCR (1.70). At the finisher phase there was no significant (P>0.05) differences recorded in final weight, weight gain and FCR. The highest final weight (2534) was recorded in 75% replacement with enzyme and the least FCR appeared in diets with enzyme. Therefore, it can be concluded that finger millet based-diets with enzyme supplementation can enhance and give better growth performance without any adverse effects in broiler chickens.

Keywords: *Finger millet, Enzyme, broiler chickens, Replacement levels and growth performance*

Description of Problem

Poultry enjoys a relative advantage over other livestock in terms of its ease of management, high turnover, quick return to capital investment and wide acceptance of its products for human consumption (1) Poultry production has an unquestionable propensity to close the existing gap in protein consumption in Nigeria (2). According to (3) the ability of poultry to close the existing gap in animal protein consumption is because of their short generation intervals, large number, fast growth, greater affordability, easy raising, absence of taboo and barrier to consumption of production in anticlimatic zone in the country. FAO, (4) reported that poultry has contributed to improving human nutrition and food security by being a source of high-quality protein, economic, social and cultural significance in small societies. According to Oluyemi and Roberts (1) various studies have revealed that broilers

fed with high quality rations perform better than their counterparts reared on low quality feeds.

There is a need to expand the ingredient base to provide an array of alternative feedstuffs for poultry feed formulation (5; 6). The frequent collapse of many commercial poultry farms in Nigeria have been attributed to high cost of poultry feeds (7). Conolly, (8) reported that feed cost is expected to continue in the upward swing. Maize is a major ingredient used in livestock feed but competition between man and livestock for maize has resulted in high cost of the cereals, which has consequently resulted in high cost of feed and livestock production (9). This was no news because it was witnessed in Nigeria at the worst stage from the year 2020 that the price of maize went beyond the reach of many farmers and was not available in the market which consequently caused many poultry farmers to shut down their farms.

Exogenous enzymes reduce the amount of nutrients voided in faeces thereby reducing pollutants in the environment (10). The benefit of using enzymes in poultry diets includes not only enhanced performance and feed conversion but also less environmental problems due to reduced output of excreta. Feed enzymes have the potential to reduce effects of anti-nutritional factors, render nutrients more available for digestion and absorption, increase energy value of feed ingredients and allow for greater flexibility in feed formulation, thus reducing formulation cost and modulating or stabilizing gut micro flora.

Eleusine coracana popularly known as finger millet is an annual herbaceous plant which is widely grown as a cereal crop in the arid and semi-arid areas in Africa and Asia. It is a tetraploid and self-pollinating species probably evolved from its wild relative *Eleusine Africana* (11). *Eleusine coracana* is called *kpana* by the Beroms, *tamba* in Hausa, (12). *Ragi* by the Indians, in Ethiopia it is called *dagussa* in Amharic, *tokuso* in Soddo, *barankiya* in Oromo and Bulo in Uganda (13). (14) reported finger millet to be a native of East Africa-Ethiopia and Ugandan highlands. The crop is generally considered as a high drought tolerant and has a very long storage time which may be up to 50 years. The long storage capacity makes finger millet an important crop in risk-avoidance strategies as a famine crop for poor farming communities.

In Nigeria it is popularly grown in some parts of Plateau and parts of Kaduna states, it contains appreciable quantities of essential nutrients including amino acids and minerals that make it a useful food supplement for the people of northern Nigeria (12). These attributes make this crop a very good source of feed for the livestock especially poultry birds that have capacity to reciprocate the good nutritional value of the cereal.

Materials and methods

Location of the study area

The study was conducted at the Poultry Section of Federal College of Animal Health and Production Technology (FCAH&PT), in Livestock Investigation Division (LID), National Veterinary Research Institute (NVRI), Vom, Nigeria. Vom is located in the Guinea Savannah zone of Nigeria, with geographical location on longitude 8^{o} 45` E and latitude $9^{o}$ 44` N on an altitude of 4200 feet (1280 m) above sea level, relative humidity ranges from 22 % in January to 78 % July/August. The daily average environmental temperature ranges between 17^{o}C – 28.6^{o}C with mean monthly sunshine hours range of 177– 288.30 (15).

Source of finger millet

The grain which is popularly called finger millet or *tamba* locally was purchased

from Ganawuri local markets which is located in Riyom Local Government Area of Plateau State and Manchok in Kaura Local Government Area of Kaduna State.

Table 1: Composition of Broiler chicken (0-4 weeks)

	With enzyme					Without enzyme				
Ingredient (%)	**0 (1)**	**25 (2)**	**50 (3)**	**75 (4)**	**100 (5)**	**0 (6)**	**25 (7)**	**50 (8)**	**75 (9)**	**100 (10)**
Maize	57.00	42.75	28.50	14.25	0.00	57.00	42.75	28.50	14.25	0.00
Finger millet	0.00	14.25	28.50	42.75	57.00	0.00	14.25	28.50	42.75	57.00
Groundnut cake	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00	15.00
Soya bean meal	24.00	24.00	24.00	24.00	24.00	24.00	24.00	24.00	24.00	24.00
Bone meal	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
Lime stone	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20
*Premix	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Lysine	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10
Methionine	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20
Common salt	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Enzyme	0.10	0.10	0.10	0.10	0.10	0.00	0.00	0.00	0.00	0.00
Total	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**
Calculated analysis										
Crude Protein (%)	23.00	23.40	23.70	24.10	24.50	23.00	23.40	23.70	24.10	24.50
ME (kcal/kg)	2926	2893	2860	2827	2794	2926	2893	2860	2827	2794
Ether Extract (%)	3.96	3.96	3.87	3.83	3.79	3.96	3.96	3.87	3.83	3.79
Crude fibre (%)	3.61	4.19	4.77	5.35	5.93	3.61	4.19	4.77	5.35	5.93
Calcium (%)	1.24	1.27	1.31	1.34	1.37	1.24	1.27	1.31	1.34	1.37
Av. P (%)	0.81	0.80	0.79	0.78	0.77	0.81	0.80	0.79	0.78	0.77
Lysine (%)	1.33	1.32	1.32	1.31	1.30	1.33	1.32	1.32	1.31	1.30
Methionine (%)	0.53	0.57	0.64	0.65	0.69	0.53	0.57	0.64	0.65	0.69
Feed cost (? /kg)	112.38	127.38	142.38	157.38	172.28	112.38	128.13	143.88	159.63	175.38

*Vitamin-mineral premix provides per kg of diet: vit. A, 13,340iu; vit. D3, 2680iu; vit. E, 10iu; vit. K, 2.68mg; calcium pantothenate, 10.68mg; vit. B12, 0.022mg; folic acid, 0.668mg; choline choride, 400mg; chlorotetrcycline, 26.68mg; manganese, 13mg; iron, 66.68mg; zinc, 53.34mg; copper, 3.2mg; iodine, 1.86mg; cobalt,0.268mg; selenium, 0.108mg; ME- Metabolizable Energy, Av. P- Available Phosphorus

Diet 1-Maize based+enzyme; Diet 6–Maize based; Diets 2, 3, 4 and 5–finger millet+enzyme Diets 7, 8, 9 and 10–finger millet

***Source of* experimental birds**

The broiler chicks used for this experiment were of arbor acre breed purchased fromPierodex hatchery/company in Barikin Ladi local government area, Plateau State.

Experimental diets

Experimental diets were formulated according to the recommendation of NRC, (16) the starter diets contained metabolizable energy of 2800-2900 Kcal/kg with CP of 23% and fed to birds from day old. The finisher diets contained metabolizable energy of 2900-3000 Kcal/kg with CP of 20% and were fed to the chickens after the starter phase. The experimental diets contained replacement levels of red variety of finger millet *(E. coracana)* as the test ingredient at 0%, 25%, 50%, 75%, 100% and 0%, 25%, 50%, 75%, 100% representing treatments 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 respectively with phytase enzyme supplementation at 100g/100kg in diets 1-5, both at the starter and finisher phases. The composition of experimental diets is presented in Table 1 and 2.

Experimental design

Six hundred (600) day old broiler chicks of arbor acre breed was purchased from a reputable hatchery which was used for this study. The chicks were allotted into ten dietary treatments with each treatment having three replicates and each replicate containing twenty birds for the starter phase. The finisher phase had 540 birds in a Completely Randomized Design (CRD), with and without enzyme supplementation with the same number of treatments and replicates.

Table 2: Composition of Broiler chicken finisher diets (5-8 weeks)

	With enzyme				Without enzyme					
Ingredient (%)	**0 (1)**	**25 (2)**	**50 (3)**	**75 (4)**	**100 (5)**	**0 (6)**	**25 (7)**	**50 (8)**	**75 (9)**	**100 (10)**
Maize	60.00	45.00	30.00	15.00	0.00	60.00	45.00	30.00	15.00	0.00
Finger millet	0.00	15.00	30.00	42.50	60.00	0.00	15.00	30.00	45.00	60.00
Groundnut cake	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00	10.00
Soya bean meal	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00	20.00
Bone meal	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
Lime stone	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.20	0.50
*Premix	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Lysine	0.20	0.20	0.20	0.00	0.20	0.20	0.20	0.20	0.20	0.20
Methionine	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20
Common salt	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Enzyme	0.10	0.10	0.10	0.10	0.10	0.00	0.0	0.00	0.00	0.00
Total	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**
Calculated analysis										
Crude Protein (%)	20.00	20.40	20.80	21.20	21.50	20.00	20.40	20.80	21.20	21.50
ME (kcal/kg)	2950	2915	2880	2845	2811	2950	2915	2880	2845	2811
Ether Extract (%)	3.62	3.58	3.53	3.49	3.44	3.62	3.58	3.53	3.49	3.44
Crude fibre (%)	3.77	4.38	4.99	5.60	6.21	3.77	4.38	4.99	5.60	6.21
Calcium (%)	1.34	1.37	1.40	1.44	1.47	1.34	1.37	1.40	1.44	1.47
Av. P (%)	0.79	0.78	0.77	0.76	0.75	0.79	0.78	0.77	0.76	0.75
Lysine (%)	1.22	1.22	1.21	1.20	1.20	1.22	1.22	1.21	1.20	1.20
Methionine (%)	0.50	0.54	0.62	0.63	0.67	0.50	0.54	0.62	0.63	0.67
Feed cost (? /kg)	116.97	131.22	145.47	159.72	173.97	116.97	131.93	146.89	161.85	176.82

*Vitamin-mineral premix provides per kg of diet: vit. A, 13,340iu; vit. D3, 2680iu; vit. E, 10iu; vit. K, 2.68mg; calcium pantothenate, 10.68mg; vit. B12, 0.022mg; folic acid, 0.668mg; choline chloride, 400mg; chlorotetracycline, 26.68mg; manganese, 13mg; iron, 66.68mg; zinc, 53.34mg; copper, 3.2mg; iodine, 1.86mg; cobalt,0.268mg; selenium, 0.108mg; ME- Metabolizable Energy, Av. P- Available Phosphorus

Diet 1-Maize based+enzyme; Diet 6–Maize based; Diets 2, 3, 4 and 5–finger millet+enzyme; Diets 7, 8, 9 and 10–finger millet

Management of experimental birds

The birds were raised on a deep litter system where wood shaven was used as bedding materials for the birds. Vitalyte was given to the birds to serve as anti-stress and after every vaccine or drug administration. Charcoal was used to provide extra heat and 200 watts' bulbs served as source of both heat and light during brooding. Feed and water were provided to the birds' *ad libitum*, all necessary vaccines were given according to the vaccination schedule as published by National Veterinary Research Institute (NVRI), Vom.

Data collected on growth performance

Feed intake was taken by subtracting left over from feed given, body weight gain was

calculated as the difference between the preceding week and that of the present week weights, and all were recorded on a weekly basis. Mortality was recorded as it occurred and at the end of the experiment feed conversion ratio and cost/kg gain were determined.

Statistical analysis

Data generated from the study was subjected to General Linear Model Procedures of SAS software package (17). Significant differences between the treatment means were separated using Duncan Multiple Range Test (18). The model is as shown below.

$\mathbf{Y}_{ij} = \boldsymbol{\mu} + \mathbf{t}_i + \mathbf{e}_{ij}$

Where:

$\mathbf{Y}_{ij}$= Dependent variable

$\boldsymbol{\mu}$= Overall mean

$\mathbf{t}_i$= i^{th} Effect of treatment

$\mathbf{e}_{ij}$ = Random error

Table 3: Effect of Red Finger millet replacement levels on growth performance of Broiler chickens with and without phytase enzyme supplementation (0-4weeks)

	With enzyme (%)					Without enzyme (%)					
Parameter	**0**	**25**	**50**	**75**	**100**	**0**	**25**	**50**	**75**	**100**	**SEM**
Initial weight (g/bird)	38.18	38.18	38.17	38.17	38.17	38.17	38.21	38.20	38.18	38.17	0.10
Final weight (g/bird)	766.20^{a}	502.80^{d}	524.10^{d}	666.10^{b}	595.60^{c}	534.80^{d}	514.20^{d}	508.20^{d}	525.50^{d}	506.00^{d}	20.66
Total weight gain (g/bird)	728.00^{a}	464.60^{d}	485.90^{d}	627.90^{b}	557.40^{c}	496.60^{d}	475.60^{d}	470.00^{d}	487.30^{d}	467.90^{d}	20.67
Av. daily wt gain (g/bird)	26.00^{a}	16.59^{d}	17.35^{d}	22.42^{b}	19.91^{c}	17.74^{d}	16.99^{d}	16.79^{d}	17.40^{d}	16.71^{d}	0.74
Total Feed Intake (g/bird)	1236^{b}	1074^{c}	1044^{c}	1352^{a}	1326^{ab}	1000^{c}	1001^{c}	1014^{c}	1137^{c}	1102^{c}	44.70
Av. daily Feed Intake (g/bird)	44.15^{b}	38.36^{c}	37.30^{c}	48.29^{a}	47.38^{ab}	35.71^{c}	35.76^{c}	36.21^{c}	40.61^{c}	39.34^{c}	1.60
Feed Conversion Ratio	1.70^{a}	2.31^{b}	2.16^{b}	2.15^{b}	2.39^{b}	2.02^{b}	2.11^{b}	2.16^{b}	2.35^{b}	2.37^{b}	0.15
Feed cost/kg gain (₦)	224^{e}	329^{c}	331^{c}	353^{c}	417^{a}	244^{e}	277^{d}	306^{c}	359^{c}	388^{b}	14.46
Mortality (%)	1.67^{c}	6.67^{a}	10.00^{a}	10.00^{a}	10.00^{a}	8.33^{a}	6.67^{a}	8.33^{a}	10.00^{a}	5.00^{b}	1.64

abcd: Means on the same row with different superscripts differ significantly ($p<0.05$)

SEM: Standard Error of Means, Av.– Average

Results and Discussion

There were significant ($P<0.05$) differences in all the parameters measured across the dietary treatments. The final weight and weight gain of birds fed diets containing enzyme in the control gave the best (766.20) performance, followed by birds fed enzyme supplemented diet with 75% inclusion of finger millet. This is an indication that birds fed diets supplemented with enzyme had better feed conversion than birds fed diets without enzyme supplementation. Probably the enzymes helped to make more nutrients available to the birds to utilize by breaking it down into smaller absorbable molecules. (19) stated that when enzymes are added to high fibre monogastric diets they cause the degradation of ß-mannan and 70% non-starch polysaccharides (NSP) into soluble metabolizable products for monogastric. This probably suggest that the birds in the other treatments could not compete with the enzyme supplemented control because they were not able to break down the fibrous materials and make it available for utilization without the aid of an exogenous enzyme. There were significant improvements in growth performance of broilers fed Natuzyme-supplemented diets were achieved by (20) and (21).

The result obtained for feed intake revealed a particular trend that showed birds fed enzyme supplemented diets had higher feed intake than birds fed diets without enzyme supplementation. This can be observed in birds fed diets in the control group and those on 75% and 100% based diets with enzyme supplementation. This result agrees with the findings of (22); (23)

and (24) who reported that the addition of enzyme to the diets of poultry resulted in increase in feed consumption. Probably the exogenous enzymes stimulate appetite which consequently increased feed intake in broiler chickens.

Table 4: Effect of Red Finger millet replacement levels on growth performance of Broiler chickens fed with and without phytase enzyme supplementation (5-8weeks)

	With enzyme (%)					Without enzyme (%)					
Parameter	**0**	**25**	**50**	**75**	**100**	**0**	**25**	**50**	**75**	**100**	**SEM**
Initial weight (g/bird)	744.90	745.20	745.21	745.83	745.53	746.16	745.88	745.51	745.82	745.84	0.74
Final weight (g/bird)	2457.70	2414.527	239.818	2534.23	2505.92	2386.47	2435.56	2342.34	2382.18	2398.65	72.28
Total weight gain (g/bird)	1713.04	1668.57	1654.41	1787.94	1761.13	1641.26	1691.43	1596.85	1636.59	1652.33	73.50
Av. daily weight gain (g/bird)	61.19	59.62	59.07	63.87	62.88	58.60	60.38	57.03	58.45	59.01	2.63
Total Feed Intake (g/bird)	3793.12^{b}	3774.31^{b}	3995.23^{b}	4145.11^{b}	4657.53^{a}	4005.02^{b}	4176.27^{b}	4398.73^{a}	4565.07^{a}	4546.29^{a}	122.98
Av. daily Feed Intake (g/bird)	135.45^{b}	134.78^{b}	142.67^{b}	148.02^{b}	166.34^{a}	143.05^{b}	149.15^{b}	157.12^{a}	163.05^{a}	162.34^{a}	3.98
Feed Conversion Ratio	2.22	2.26	2.42	2.33	2.67	2.44	2.47	2.78	2.79	2.78	0.14
Feed cost/kg gain (?)	267.55^{a}	302.15^{b}	353.65^{c}	369.76^{c}	458.27^{e}	268.18^{a}	303.16^{b}	375.42^{c}	413.05^{d}	446.61^{e}	16.50
Mortality **(%)**	3.71^{a}	1.85^{b}	0.00^{c}	1.85^{b}	1.85^{b}	0.00^{c}	1.85^{b}	1.85^{b}	1.85^{b}	1.85^{b}	0.92

abcde: Means on the same row with different superscripts differ significantly (P<0.05)
SEM: Standard Error of Means, Av.-Average

Generally, the feed conversion ratio in birds fed diets containing enzyme supplementation showed a better performance than the birds fed diets without enzyme supplementation. Birds fed control (1.70) diet with enzyme supplementation gave the best performance and birds fed diets with finger millet included at 50% and 75% with enzyme and finger millet inclusion at 0%, 25%, 50% without enzyme supplementation favourably competed with the birds fed control diet with enzyme supplementation. This observation is probably due to poor utilization of the nutrients by the birds and failure to convert its feed to muscles and may be the presence of antinutrients contributed. The feed conversion ratio range of 1.70-2.39 in this study is lower and better than what was obtained from the findings of (25) who reported feed conversion ratio range for broilers between 2.77-2.99.

The trend of events showed that as the level of finger millet is increasing the cost of the diets were also increasing in all the treatment groups with and without enzyme supplementation. The feed cost/ kg gain was significantly (P<0.05) lower and better in birds on control diets and diets with finger millet included at 25%, 50% and 75% with enzyme supplementation and those birds fed control diet and diet with finger millet included at 25%, 50% and 75% without enzyme supplementation. The possible reason and explanation to these observations may be that the cost of finger millet added to the cost of diets. The mortality experienced could be probably due to the cold weather prevailing at the experimental station as at the time of carrying out the experiment or may be due to bacterial infection and the presence of antinutritional factors since all the experimental treatments were affected.

The result in finisher phase showed no significant (P>0.05) differences in final weight, weight gain and feed conversion ratio across treatments. However, there is significant (P<0.05) differences in remaining parameters measured across the dietary

treatments. Birds fed diets at 75% level of finger millet inclusion with enzyme supplementation gave the best performance in final weight and weight gain (2534g and 1788g) which is better than the birds on both the control diets. This performance could be attributed to the action of the enzymes on the diets by making the nutrients available to the birds for better utilization. This result is supported by (26) who stated that better availability and efficient utilization of available nutrients in diets is enhanced by the presence of enzymes. The supplemental enzyme must have helped to reduce or eliminate such antinutrients like NSPs which might have been present in the diets and are known to reduce the digestion and absorption of nutrients (27).

However, birds fed finger millet diets in the control group with enzyme supplementation performed ($P<0.05$) better (2.22) than all the remaining treatments in feed conversion ratio. This may suggest that these birds converted consumed feed in to muscles due to the action of exogenous enzymes in the diets. According to (28), better feed conversion ratio signified that more feed was retained in the animal and less waste to the environment.

The result of the feed intake showed that it was increasing as the replacement levels of finger millet increased with and without enzyme supplementation. Birds fed finger millet-based diets with enzyme supplementation consumed less feed than the birds fed finger millet-based diets without enzyme supplementation. This suggests that energy in the feed was made more available to the older birds fed diets with enzyme supplementation than birds fed diets without enzyme supplementation, since birds eat to satisfy their energy requirements. This result agrees with the findings of Freitas *et al*., (29) who reported a decrease in feed intake of birds fed diets containing protease enzyme.

The trend observed in feed cost/kg gain showed that birds fed control diets with and without enzyme supplementation gave the best performance, which were significantly ($P<0.05$) better than those of the other treatments. This was closely followed by birds on diets containing 25% finger millet inclusion with and without enzyme supplementation. The highest cost was observed in birds on diets containing 100% finger millet inclusion with and without enzyme supplementation.

There was mortality across the dietary treatments with and without enzyme supplementation with the highest mortality occurring in the control group with enzyme supplementation.

Conclusion and Applications

Based on the results obtained from this study it can concluded that;

1. The best performances were recorded in birds fed diet containing red finger millet up to 75% replacement level with enzyme supplementation at the starter and finisher phases.
2. At the finisher phase, no significant ($P>0.05$) differences was recorded in final weights of birds fed diets containing finger millet with and without enzyme supplementation.
3. Finger millet based-diets fed broiler chickens with enzyme supplementation had the best FCR.
4. Enzyme inclusion in finger millet based-diets had triggered better performance in birds fed enzyme supplemented diets.
5. Finger millet can serve as an alternative energy resource in broiler chickens' diets with enzyme supplementation for maximum growth performance without any adverse effects.

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