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Evaluating the Effects of Feeding a Concentrated *Saccharomyces cerevisiae* Fermentation Product on the Performance and Stress Susceptibility of Broiler Chickens

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Abstract: This study evaluated the effect of a concentrated yeast fermentation product on the performance and stress response of broiler chickens. Day-old Cobb 500 male broiler chicks were randomly allocated to one of two dietary treatments: Control (CON) or concentrated yeast fermentation product (CSCFP, 0.625 kg/MT). On d18, simultaneous feed withdrawal and heat stress challenges were performed for 12 h. Blood was analyzed for plasma corticosterone (CORT) and heterophil-to-lymphocyte ratio (HL) on d19 and d42. Performance parameters were collected throughout the trial: body weight (BW), feed consumption (FC), and feed conversion ratio (FCR). On d19, the CSCFP birds had lower ($p \leq 0.05$) CORT (5320.3 ng/mL) and HL (0.14) than the CON birds (9049.6 ng/mL and 0.21). On d42, the CSCFP birds had lower ($p \leq 0.05$) CORT (1623.8 ng/mL) and HL (0.74) than the CON birds (2920.2 ng/mL and 1.05). No differences were observed in mortality ($p > 0.05$). The CON birds had a higher ($p \leq 0.05$) FCR than CSCFP throughout all phases. The CON birds consumed more feed than the CSCFP birds throughout all phases ($p \leq 0.05$). In conclusion, CYFP reduced stress and improved feed conversion when compared to CON, making it a viable feed additive to improve welfare and production.

Keywords: *Saccharomyces cerevisiae*; postbiotic; broiler; stress; production

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1. Introduction

Broiler chickens are often exposed to many stressful situations when reared under field conditions. A typical grow out period exposes broilers to stressors like vaccination, used litter, growth, and, in some cases, heat stress. When exposed to these conditions, it is not uncommon for the birds to experience a loss of appetite, lethargy, reduced body weight gain, a loss of feed efficiency, and increased mortality. Minimizing stress is not only an important factor for production efficiency but also for animal welfare.

In response to stressors, the activated hypothalamic–pituitary–adrenal axis ultimately secretes corticosterone into the bloodstream [1]. Corticosterone is the primary stress hormone in poultry, and prolonged high concentrations are detrimental to bird health due to their ability to alter the immune system [2]. Increases in corticosterone production have been shown to slow growth rate [3] and negatively affect the microbial balance of the cecal microflora [4]. When a chicken becomes stressed, lymphocyte cell numbers decrease, while the number of heterophils increases as a response to the increasing levels of corticosterone [5]. Corticosterone levels have long been used to measure the severity of exposure to physiological and environmental stresses [6,7]. Gross and Siegel [5] found that as dietary corticosterone increased, heterophil/lymphocyte ratios increased as well—thus, validating the idea that increases in corticosterone elevate the heterophil/lymphocyte ratio. Heat stress, even if acute, in poultry can have lasting effects on poultry production. Altan et al. [8]

found that broilers exposed to heat stress had increases in the heterophil/lymphocyte ratio in addition to longer periods of tonic immobility (an indicator of fear).

Saccharomyces cerevisiae fermentation products (SCFPs) have been shown to be effective in reducing the negative consequences observed in poultry subjected to potentially stressful conditions [9–14], while also improving the overall performance of a flock. *Saccharomyces cerevisiae* fermentation products are composed of a plethora of biologically active substances such as proteins, small peptides, oligosaccharides, vitamins, minerals, enzymes, and numerous 'unknown growth factors' coming from the yeast biomass, fermentation metabolites, and the residual growth medium [15]. However, the types of yeast used, fermentation medium, and fermentation conditions impact the composition of the final product. Nelson et al. [10] found that the inclusion of SCFPs in the feed or water reduced stress in poultry subjected to heat stress, vaccine stress, reused litter, and feed/water withdrawal. This was demonstrated by the decreased corticosterone levels and heterophil/lymphocyte ratio and the improved asymmetry scores when compared to non-supplemented treatments in the study. Additionally, SCFPs have been shown to be effective in reducing stress indicators in turkeys [16] and broilers subjected to short-term heat stress [9–14]. Although one study [17] found in effect on some blood parameters associated with stress, it has been shown in cattle that SCFP can help reduce the negative effects of heat stress [18–20]. Furthermore, SCFPs have also been shown to be beneficial toward improving growth performance by way of feed conversion and body weight gain [21] even in heat-stressed broilers reared on reused poultry litter [22]. SCFPs have been shown to reduce *Salmonella* [23–26] and *Campylobacter* [27] loads in poultry and even reduce antibiotic resistance [28] and decrease intestinal damage [29]. However, a study [30] found no effect of SCFPs on cecal microbiota populations, although poultry under different pathogen challenges have seen increased growth when supplemented with SCFP as well [31,32].

The primary objective of this experiment was to determine the effects of the supplementation of a concentrated *Saccharomyces cerevisiae* fermentation product (CSCFP; XPC Ultra, Diamond V Mills, Cedar Rapids, IA, USA), a more concentrated version than previously investigated in poultry, subjected to multiple stressors commonly observed in the commercial poultry industry. Our hypothesis was that the inclusion of CSCFP would result in reduced stress susceptibility and improve body weight as well as FCR.

2. Materials and Methods

All procedures were carried out in accordance with the guidelines established by the Texas A&M Institutional Animal Care and Use Committee (AUP #IACUC 2019-0056) and adhered to the ethical and humane use of animals for research. The live animal research was conducted at the Poultry Science Research, Teaching, and Extension Center in College Station, TX, USA.

2.1. Animals and Husbandry

For the experiment, Ross 708 male broilers were acquired from a commercial hatchery (n = 750). All chicks were vaccinated with a Coccidiosis Vaccine (COCCIVAC-B52, Merck, Rahway, NJ, USA) on the day of placement. After vaccination, the chicks were randomly allocated to one of 30 pens, measuring 0.9 × 1.8 m. The chicks were stocked 25 birds/pen, allowing for 0.275 m^2/bird. All pens were lined with 8 to 10 cm of used pine shavings. The chicks were randomly allocated to 1 of 2 dietary treatments, each with 15 replicates, and treatments were block-replicated equally throughout the barn. Treatments consisted of either a control diet or the control diet with 0.625 kg/metric ton of CSCFP added during all phases.

All birds were provided with ad libitum access to both feed and water through the duration of the study. All birds were fed a three-phase diet consisting of a starter (days 1–18, crumble), grower (days 19–28, pellet), and finisher (days 29–42, pellet). All diets were mixed at the Texas A&M Poultry Research Center Feed Mill. The broilers were allowed ad libitum access to feed and water throughout the trial, except on day 18 during the 12 h

fasting stress. The birds were housed in a tunnel-ventilated house that was maintained at 35 °C from placement to day 7 and then reduced to 31 °C to day 14. On day 14, the house temperature was reduced to 29 °C and further reduced by 5 °C weekly until the ambient temperature was reached. Broilers received 24 h of light for the first three days, and then 20 h of light and 4 h of darkness for the remaining duration of the trial.

2.2. Performance Parameters

Mortalities were collected, recorded, and weighed daily. Group pen weights were recorded on day 0 and 28 and individually on days 18, 19, 35, and 42 to determine body weight gain (BW). Body weight gain was determined by subtracting the day 0 weight from the day 42 weight. The feed was weighed before its addition to the feeder in each pen, and the remaining feed was weighed on feed transition days so that the total feed intake could be calculated. The feed conversion ratio (FCR) was calculated by dividing the total feed intake per pen by the total body weight gain per pen and corrected for mortality. On day 0, all birds were weighed on a per-pen basis using a platform scale (UFM-F120, UWE Scales, Cape Town, South Africa). On day 28, the birds were weighed as a pen using a platform scale (UFM-F120, UWE Scales, Cape Town, South Africa). On days 35 and 42, the birds were weighed individually using a hanging scale with shackles (RPBS-1, Rotem, Petach-Tikva, Israel). Uniformity was determined on day 42 by two methods. The first method was by calculating the coefficient of variation (% CV) using the following formula: standard deviation of the average bird weight per pen/average bird weight per pen. The second method was by calculating the percent of individual weights which occurred within 10% of the pen average [14].

2.3. Stress Challenge

On day 18 at 20:00 h, the broilers were weighed by pen, feed and water were removed, pen space was reduced to induce crowding, and litter temperature was increased to 32–35 °C for a period of 12 h. During the 12 h fasting period, room lights remained on to mimic the correct diurnal pattern of light. Following the 12 h fasting period, at 08:00 h on day 19, five broilers per pen were weighed and euthanized to collect blood for the determination of stress response. After the blood collection, the remaining broilers were weighed by pen, and then feed and water were returned.

Stress Measures

On day 19, blood was collected from five broilers per pen via exsanguination following decapitation. On day 41, blood was collected from five broilers per pen via the brachial wing vein [14]. The area around the vein was sanitized with 70% isopropyl alcohol, and in preparation, the inside of a 3 mL syringe was lined with heparin. Between 2 and 3 mL of blood was collected from each bird on sampling days, and a drop was used to prepare a blood smear slide. Blood smear slides were stained using a hematology staining kit (Catalog #25034, Polysciences Inc., Warrington, PA, USA) and then air-dried. The remaining blood was collected into a vacutainer (BD 368056, BD, Franklin Lakes, NJ, USA) containing a plasma separation gel and lithium heparin. Vacutainers were temporarily stored in an ice water bath. Once all samples were collected, the vacutainers were spun down at 4000 RPM for 15 min (Centrifuge 5804× *g*, Eppendorf, Hamburg, Germany) to separate the cells from the plasma. The plasma was drawn into 2 mL micro centrifuge tubes and stored at −19 °C until further analysis. Plasma corticosterone concentrations were measured using a commercially available ELISA kit (Enzo Life Sciences, ADI-901-097, Farmingdale, NY, USA). The heterophil-to-lymphocyte ratio (H/L) was measured by taking the blood smear slides prepared earlier and observing them under a 40× magnification using an oil immersion lens under microscopy (Cat. #89404-886, VWR International, Radnor, PA, USA). A keystroke counter was used to accurately keep track of the number of cells observed [14].

2.4. Statistical Analysis

All data were analyzed via One-Way ANOVA using the GLM model (Minitab Software 21) with treatment means deemed significantly different at $p \leq 0.05$.

3. Results

3.1. Performance Parameters

The performance parameter data are presented in Tables 1–3. The body weight showed no differences ($p > 0.05$) between treatments on d 14, 28, 35, and 42. Although there were no significant differences, birds supplemented with CSCFP produced numerically heavier body weights at each weigh day, which may result in economically significant improvements. The CSCFP birds had lower ($p < 0.001$) FCRs than the CON birds on d 18, 28, 35, and 42. However, there were no observed differences ($p > 0.05$) in uniformity between treatments on d 35 or 42.

Table 1. Average bird weights (kg) during 42 day grow-out while being fed a control diet (CON) or concentrated *Saccharomyces cerevisiae* fermentation product (CSCFP).

Treatment	d19 wt.	d28 wt.	d35 wt.	d42 wt.
CON	0.758	1.512	2.159	2.782
CSCFP	0.765	1.544	2.166	2.825
SEM	0.003	0.011	0.017	0.031
p-value	0.43	0.14	0.84	0.50

Table 2. Feed conversion ratio of birds being fed a control diet (CON) or concentrated *Saccharomyces cerevisiae* fermentation product (CSCFP).

Treatment	FCR0-18	FCR0-28	FCR0-35	FCR0-42
CON	1.425	1.450	1.565	1.742
CSCFP	1.285	1.361	1.494	1.663
SEM	0.014	0.017	0.012	0.025
p-value	0.001	0.001	0.001	0.001

Table 3. Uniformity score and coefficient of variance (%) of birds being fed a control diet (CON) or concentrated *Saccharomyces cerevisiae* fermentation product (CSCFP).

Treatment	Uniformity d35	CV d35	Uniformity d42	CV d42
CON	62.600	12.233	50.400	15.033
CSCFP	62.067	13.373	49.600	14.987
SEM	2.59	0.732	3.39	0.62
p-value	0.92	0.45	0.91	0.97

3.2. Stress Susceptibility

The stress susceptibility data are presented in Table 4. On d 19 and 41, the CSCFP birds had lower plasma corticosterone levels ($p < 0.02$) and heterophil/lymphocyte (H/L) ratios ($p < 0.001$) than the CON birds.

Table 4. Corticosterone concentrations (pg/mL of blood) and heterophil/lymphocyte ratios of birds being fed a control diet (CON) or concentrated *Saccharomyces cerevisiae* fermentation product (CSCFP).

Treatment	Corticosterone D19	HL Ratio D19	Corticosterone D41	HL Ratio D41
CON	9049.6	0.21	2920.2	1.05
CSCFP	5320.3	0.14	1623.8	0.74
SEM	838.0	0.011	383.0	0.04
p-value	0.019	0.001	0.008	0.001

4. Discussion

Commercial poultry production often exposes flocks of birds to a number of environmental stressors. Exposure to vaccination, feed withdrawal, previously used litter, and heat stress can trigger stress response, which can impair immunity, reduce growth, and reduce feed efficiency. Exposure to stressors consequently triggers a sequence of events beginning with the increased production of a corticotrophin-releasing factor, followed by the stimulation of the anterior pituitary which produces adrenocorticotropic hormone, which increases the production and release of corticosteroids, predominately corticosterone [1,33]. Corticosterone, as the primary stress hormone in poultry, suppresses the immune system [2] and alters metabolic processes to catabolism in order to increase available energy [1]. This may result in a negative impact on production parameters [34]. Because of these issues, reducing stress susceptibility and mitigating exposure to stressors is extremely important in order to improve broiler performance and welfare.

Stress can also alter the gut microbiota, which can greatly impact bird welfare, growth, and feed efficiency. Alterations to the gut microbiota can affect bird health and increase predisposition to enteric disease. In fact, stress-induced modifications to the intestinal microbiota have been associated with increased cytokine production and the modulation of immune activity [35]. Physiological stress has been shown to lead to the decrease in the abundance of putative beneficial bacteria (e.g., *Lactobacillus* spp.) in the gut [4,36]. Furthermore, stress can also lead to increased colonization by pathogens such as *Escherichia coli* and *Salmonella* spp. [4,37]. These factors further demonstrate the need to reduce the stress susceptibility of poultry and, thereby, maintain optimal gut health that will result in optimum growth and feed efficiency.

There are currently several ways in which the microbiota can be modulated. These include the use of prebiotics, probiotics, synbiotics, or postbiotics. Prebiotics are used to feed microorganisms already existing in the gut by serving as substrates for particular bacteria such as bifidobacteria and lactic acid bacteria [38,39] and can exert beneficial effects. Prebiotics have traditionally been represented by a limited set of carbohydrates and related compounds with fructooligosaccharides (FOS), galactooligosaccharides (GOS), and mannanoligoasacchardes (MOS) being among the more commonly used in animal and poultry research. In contrast, probiotics directly impact the gut microbiome through the selective delivery of beneficial microorganisms to the gastrointestinal tract. The most commonly used probiotics are bacteria of the genera *Lactobacillus*, *Bifidobacterium*, and *Streptococcus*, as well as the yeast *Saccharomyces*. Synbiotics are a combination of prebiotics and probiotics that, through their combination, are thought to have a beneficial impact on gut microbiome. The storage of probioitcs is a concern as they are a living organisime and, therefore, there is increasing interest in the area of postbiotics.

The development of postbiotics is based on the observation that the beneficial effects of the microbiota are mediated by the secretion of various metabolites. According to Tsilingiri et al. [40], postbiotics include any substance released by or produced through the metabolic activity of the microorganism, which exerts a beneficial effect on the host, directly or indirectly. Furthermore, postbiotics are mainly the beneficial metabolites produced by microorganisms and, therefore, are not living organisms, so storing them is not an issue like it is for probiotic.

Postbiotic products like SCFPs have been shown to improve growth performance and instances of enteric infections in multiple species including broilers [41], laying hens [29], turkeys [42], and ducks [43]. The results of this experiment are similar to these previous studies. However, the key difference between this current study and all previous studies is that this study used a much more concentrated SCFP. The concentration of the SCFP allows for it to be fed at lower inclusion rates which will make it more useful for agriculture animal feeding, especially based on the results of this current study, which showed similar results to the previous research with the less concentrated versions of the post biotic.

Stress-indicating parameters observed in this current study suggest that postbiotic products, including CSCFP, which was used in this study, could decrease stress suscep-

tibility and improve the welfare of broilers subjected to husbandry stressors common in the industry. The results of this current study conform to previous studies in that it demonstrated a lowered stress susceptibility in the birds fed CSCFP. Sobotik et al. [14] observed similarly decreased corticosterone and H/L ratios in birds fed SCFP or provided in water. Furthermore, SCFP has been found to decrease the corticosterone and H/L ratio in broilers in numerous studies [9] and also in turkeys [16]. While the exact mechanism for the lowered stress susceptibility is still not known to date, the repeated demonstration of this effect through numerous studies including this current one is very meaningful. Utilizing this product to lower the physiological effects of stress on animals being reared for food will improve their feed efficiency and likely overall health. Having a lower stress susceptibility will likely make animals less likely to be infected with pathogens as well, but this requires further study.

In this current study, supplementing feed with a CSCFP also improved the FCR, demonstrating that the reduced stress susceptibility of the animals resulted in better feed efficiency. While body weights were not statistically different, they could be of meaningful economic importance, as increasing average bird weight by 40 g per bird could result in substantial yearly profits for the poultry industry. The dietary inclusion of *Saccharomyces cerevisiae* postbiotics has been shown to improve growth in broilers [17] in other studies, so it is possible that under a more severe stress, statistical differences would be observed. However, the numerical improvements observed in performance in this current study may be related to the ability of the components of this postbiotic to improve the overall intestinal microflora in poultry species. This, however, needs further investigation. However, Zhang et al. [44] found that similar products derived from *Saccharomyces cerevisiae* improve intestinal mucosal development through an increased villus height and a decreased crypt depth, allowing for a higher villus height/crypt depth ratio. Increasing the length of villus allows for increased nutrient absorption, while a shallower crypt depth allows for increased villus production because of a demand for new tissue [45]. This possible increased nutrient absorption is a likely possible cause of the increased feed efficiency observed in this current study.

The ability of CSCFP to modulate gut microbiome needs further research as it may be one possible mechanism to explain not only the improved feed efficiency but also the reduced stress susceptibility as the gut–brain axis is increasingly being shown to be paramount in many biological phenomena. Cao et al. [46] demonstrated that the microbiota–gut–brain axis was affected by heat stress in chickens. Furthermore, in rodents, the modulation of the gut microbiota by postbiotics has been demonstrated to decrease physiological effects such as corticosterone levels during depression [47].

The dietary inclusion of the CSCFP in this study showed the ability to improve not only broiler performance but also welfare, as demonstrated through a reduction in the stress parameters. Reducing stress susceptibility in poultry is important to their welfare as they are subjected to stressors like heat stress, handling, vaccination, and feed withdrawal. Significant prior research surrounding the non-concentrated SCFP suggests the feed additive as an effective means for improving the welfare and performance of numerous livestock species. A more concentrated SCFP product would allow for low inclusion rates and could be seen as a more economical product allowing for the increased availability of bioactive compounds that may help in improved production performance. The results of this current study clearly demonstrate that the SCFP is a useful feed additive for broilers subjected to stressful environments, especially under heat stress conditions, as it may help reduce adverse effects.

5. Conclusions

The dietary inclusion of CSCFP in the diet of broiler chickens reduced stress susceptibility in this study: H/L ratio and plasma corticosterone. The dietary inclusion of CSCFP in the diet of broiler chickens improved feed conversion. The CSCFP resulted in similar posi-

tive effects as previously observed with higher inclusion rates of less concentrated forms. Allowing for a lower overall inclusion rate in the feed is a desirable trait for feed additives.

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Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy.

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