PSX-37-Effects of metformin on body temperature regulation and breast muscle growth in male broiler chickens

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Introduction

- Mechanisms related to mitochondrial UCP-1 independent non-shivering thermogenesis (NST) and the phenomenon known as “browning” of white adipose tissue are a therapeutic target of interest regarding insulin resistance and energy expenditure (1).
- NST utilizes fatty acids and glucose to produce heat instead of ATP via the upcoupling of oxidative phosphorylation, which may be an efficient way to treat obesity (2).
- Recent studies show metformin, a common drug used to treat type II diabetes in humans, can stimulate brown adipose tissue recruitment and the browning of white adipose tissue.
- Chickens provide models for human physiology research, as their normal physiological status mimics mammalian obesity and human Type II diabetes, their propensity overconsume food beyond satiety, lipogenesis occurs only in the liver, lack BAT, and lack UCPI while still possessing skeletal UCP2 and UCP3 (3)
- Metformin effects in the kidney of chickens is similar to humans in the suppression of G6Pase and PEPCK expression and certain enzyme activity (4)
- The objective of this study was to determine if dietary supplementation of metformin can promote NST to reduce body fat mass, increase metabolism, and decrease potential for obesity-related metabolic disorders in broiler chickens.

References

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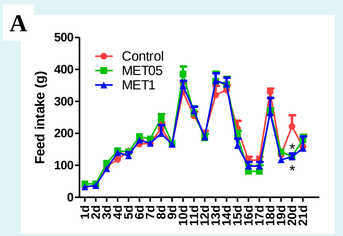
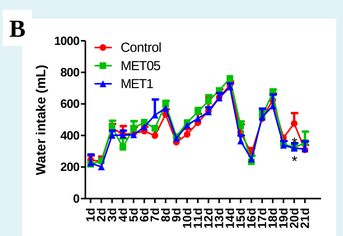
2. Nowack J, Giroud S, Arnold W and Ruf T (2017) Muscle Non-shivering Thermogenesis and Its Role in the Evolution of Endothermy. *Front. Physiol.* 8:889. doi: 10.3389/fphys.2017.00889Nishimura, T.,
3. Katsumura, T., Motoi, M. *et al.* Experimental evidence reveals the *UCP1* genotype changes the oxygen consumption attributed to non-shivering thermogenesis in humans. *Sci Rep* **7,** 5570 (2017). https://doi.org/10.1038/s41598-017-05766-3
4. Sato, T., Toyoshima, A., Hiraki, T., Ohta, Y., Katayama, K., Arai, T., & Tazaki, H. (2011). Effects of metformin on plasma concentrations of glucose and mannose, G6Pase and PEPCK activity, and mRNA expression in the liver and kidney of chickens. *British Poultry Science*, *52*(2), 273-277. doi:10.1080/00071668.2011.560595

Results

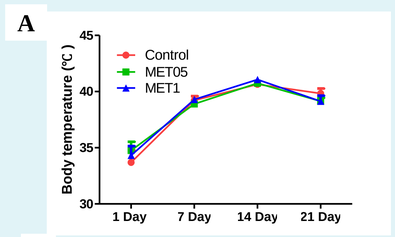




C

Items (g)	CON	MET05	MET1
Day 1-7 ADFI	18.92±1.35^{ab}	20.29±0.96^{a}	18.5±0.75^{b}
Day 8-14 ADFI	62.14±4.73^{b}	68.64±6.65^{ab}	72.07±4.60^{a}
Day 15-21 ADFI	87.13±3.85^{b}	93.82±0.98^{a}	88.69±4.87^{ab}
Day 1-7 G:F	6.51±0.50	6.53±0.31	6.75±0.27
Day 8-14 G:F	4.31±0.35^{a}	4.34±0.17^{a}	3.76±0.25^{b}
Day 15-21G:F	5.61±0.25^{a}	5.66±0.43^{a}	4.81±0.57^{b}

Figure 1 MET05 had the highest average daily feed intake during the first and last week (**A**). There was no difference in water intake during the study (**B**). MET1 group had the lowest ADFI in week 1, but highest in week 2. CON group had the lowest ADFI in weeks 2 and 3. The higher MET1 dosage had a negative effect on the G:F ratio in weeks 2 and 3 (**C**). Values are the least square mean ± standard deviation of the mean. Within a row, means with no superscripts or with a common superscript letter are not significantly different ($P > 0.05$).



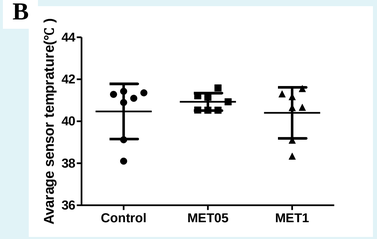
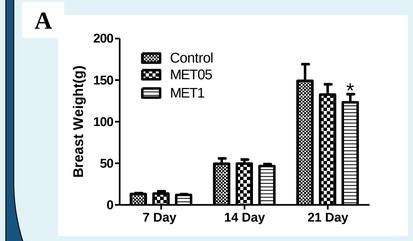
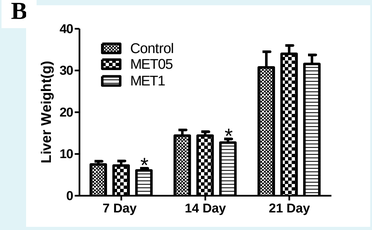


Figure 2 Graph **A** depicts body temperatures measured externally with an infrared camera. Graph **B** depicts internal body temperatures recorded with an Ibutton temperature logger. Although there was no difference ($P>0.10$) in body temperature between groups, data distribution showed less variation in the MET05 group.





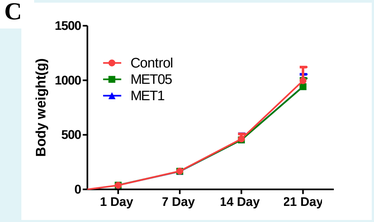


Figure 4 MET05 group had the highest breast weight (**A**) and liver weight (**B**). CON group had the lowest breast weight at week 2 but significantly higher than MET1 group at week 3. MET1 group had the lowest breast weight at week 1 and week 3, and lowest liver weight at week 1 and 2, while CON group had the lowest liver weight at week 3. There was no significant difference of breast/BW ratio or liver/BW ratio at day 7 or 14. However, at the end of week 3, CON group had the highest breast/BW ratio, while MET1 group had the lowest, and both metformin groups had higher liver/BW ration than CON group. Body weight (**C**) was greatest in MET05 for all weeks.

Methods

- Male broiler chicks (n = 72) were assigned randomly to 12 pens (6 chicks/pen) at d1 of age
- Pens were assigned randomly to basal diet (CON), basal diet + 0.5g metformin/kg (MET05), basal diet + 1.0 g/kg metformin (MET1)
- Chicks were allowed ad libitum access to diets and water, with intake of each recorded daily
- Two (2) chicks were harvested from each pen on day 7, day 14, and day 21
- Eternal temperature measured via infrared camera and body weight (BW) were recorded on d1, d7, d14, and d21, or at harvest
- Ibutton temperature loggers were implanted into chicks on d19
- Total breast weight (TBW) and liver weight (LW) were recorded at harvest
- Samples of internal fat, left breast muscle tissue, kidneys, and liver tissue were placed in cryopreservation vials, submerged in liquid nitrogen, then stored at -80ºC for later RT-PCR analysis. Whole blood was collected, centrifuged, plasma transferred to a microcentrifuge tube, and stored at -20C for later analysis.

Discussion

- Metformin dietary supplementation of 0.5g/kg diet significantly increased BW; however, the dosage of 1g/kg diet did not change BW. The lower dosage of metformin increased feed intake and maintained the G:F ratio, but the higher dosage decreased the G:F ration. Breast and liver growth were significantly promoted by metformin in the lower dosage. Higher dosage reduced liver weight in weeks 1 -2 and breast weight in week 3.
- Low dosage of metformin stimulates lean muscle growth and increases metabolism.
- Although UCP1-independent seems unaffected by metformin supplementation, chickens in the low dosage group experienced fewer incidences of low body temperature, indicating that metformin helps to regulate basal body temperature.
- Planned PCR analysis of muscle, adipose, kidney, liver, and analysis of blood plasma may reveal more regarding mechanisms of action and the role of β-androgenic stimuli in NST, energy expenditure, and metabolic function.