

Mesobiliverdin-Enriched Feed Supplement Benefits Rabbit Gut Health



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Abstract

Mesobiliverdin is an analog of biliverdin, an innate anti-inflammatory and metabolic product of heme degradation. Recent studies show that farm-raised chicken broilers have improved gut health and lower levels of the inflammatory cytokine IL-6 in blood serum when fed antibiotic-free feed containing mesobiliverdin. The purpose of this study was to determine if similar beneficial health effects occur with laboratory-bred rabbits fed a diet containing an microalgal extract enriched with mesobiliverdin. Body weights, blood chemistry panels, and serum IL-6 levels were analyzed. Cecotropes were also recovered for gut microbiome analysis. Rabbits fed mesobiliverdin-containing feed for 18 days had slight body weight gains (1.5%, P-value 0.045) but lower serum IL-6 levels (16%, P-value 0.078) compared to rabbits provided feed without mesobiliverdin. The results show that a rabbit diet containing mesobiliverdin-enriched microalgae extract lowers serum IL-6 levels with minor body weight gain suggesting health benefits for rabbits. Gut microbiome profile analyses of collected cecotropes are currently in progress.

Background

Biliverdin is a metabolic product of the breakdown of erythrocytes and heme. It and the close structural analog, mesobiliverdin have anti-inflammatory and anti-oxidative properties that reduce the mal-effects of cellular inflammation. Biliverdin provides cytoprotection against numerous inflammatory conditions including ischemic reperfusion injury, sepsis, wound-healing, lung damage, and intestinal bowel diseases (Takemoto et al. 2019). IL-6 is an inflammatory cytokine having central and regulatory roles in innate immunity. Rapid overproduction of IL-6 creates pathological effects associated with chronic inflammation and autoimmunity (Tanaka et al., 2014). Antibiotics fed to livestock are used widely to promote animal growth and to increase the yield of meat products as a consequence of inhibition of pathogenic gut bacteria. However, along with increased nutrient absorption and weight gain, antibiotics inhibit beneficial gut bacteria and promote inflammation. Continual use of antibiotics in feed leads to proliferation of antibiotic resistant bacteria in both livestock and humans. Recent studies show that feeding broilers with mesobiliverdin-supplemented feed without antibiotic administration promoted growth, gut health and populations of beneficial gut microbes. A reduction of cytokine IL-6 levels in serum was also observed indicating lowered gut inflammation (Chang et al., 2021).

Research Question: Will rabbits that consume feed containing mesobiliverdin have reduced serum IL-6 levels and improved health?

Methods

Twelve laboratory-bred New Zealand white rabbits (6 males and 6 females) were labeled rabbits 1 through 12. They were provided a diet of commercial rabbit feed (Sherwood Pet Health, Logan, UT) (Normal Feed) for 7 days. Then rabbits 1,3,5,7,9 and 11 were fed daily for 11 days with Normal Feed supplemented with microalgae extract containing 0.1% mesobiliverdin IXalpha (MB Feed) (Chang et al., 2021) and rabbits 2, 4, 6, 8, 10 and 12 were fed Normal Feed. Blood sera were obtained on day 1 and then daily on days 8 to 18 for blood chemistry profiles and determination of IL-6 levels. Cecotropes were recovered daily throughout for gut microbiome analysis. Rabbits were weighed at days 8 and 18. and blood sera were collected again at day 18. Comparisons of serum IL-6 levels at days 8 and 18 and of rabbits fed MB Feed and Normal Feed were done with an enzyme-linked immunosorbent assay (ELISA) kit (NOVUS). Blood chemistry profiles were performed by the Utah Veterinary Diagnostic Laboratory, Utah State University and Utah Department of Agriculture, Logan Utah.

Results

MB Feed lowered serum cytokine IL-6 values (16%, P-value 0.078) (Figures 1 and 2) and a slightly elevated rabbit average body weight gain (1.5%, P-value 0.045) (Figures 3 and 4) compared to Normal Feed. IL-6 levels in all rabbits increased over the course of the feeding trial, but the increase was less with rabbits fed MB Feed. Effects of MB Feed on blood chemistry profiles are shown in Table 1.

Figure 1
IL-6 Concentrations Day 8 and Day 18
Rabbits 1,2,7,8

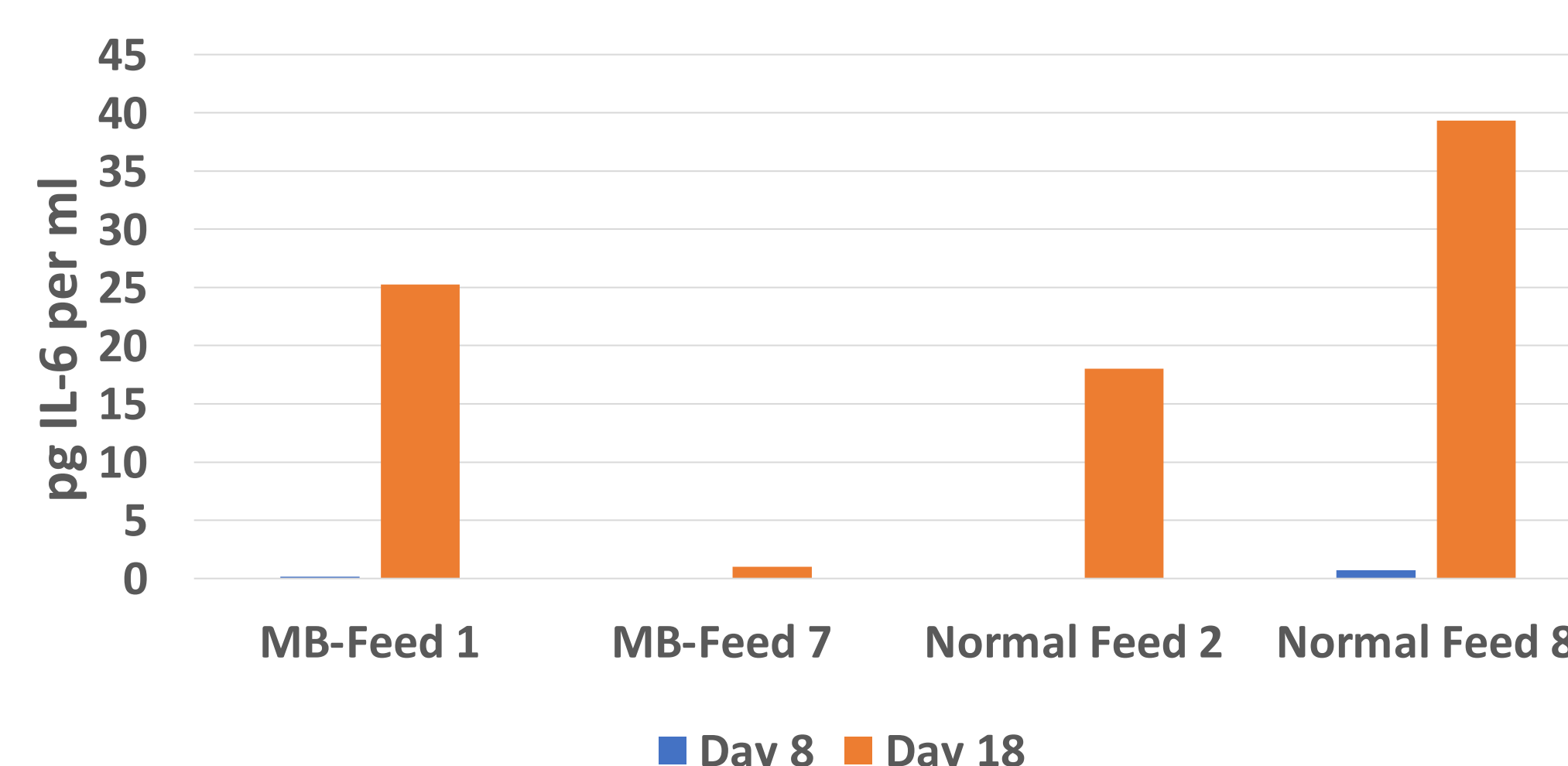


Figure 2
Serum IL-6 Concentrations (Averages for 6 Rabbits)

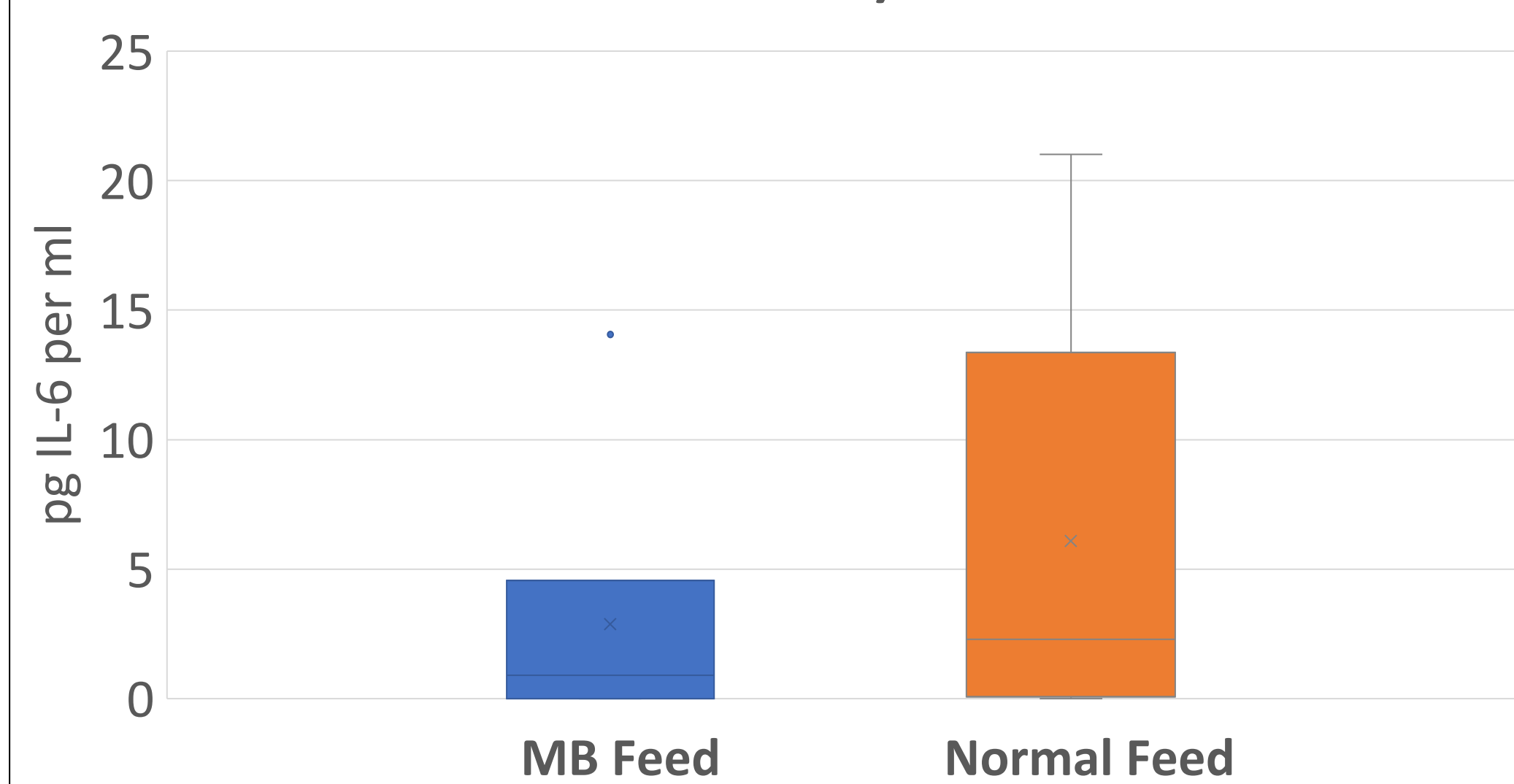


Figure 3
Body Weights

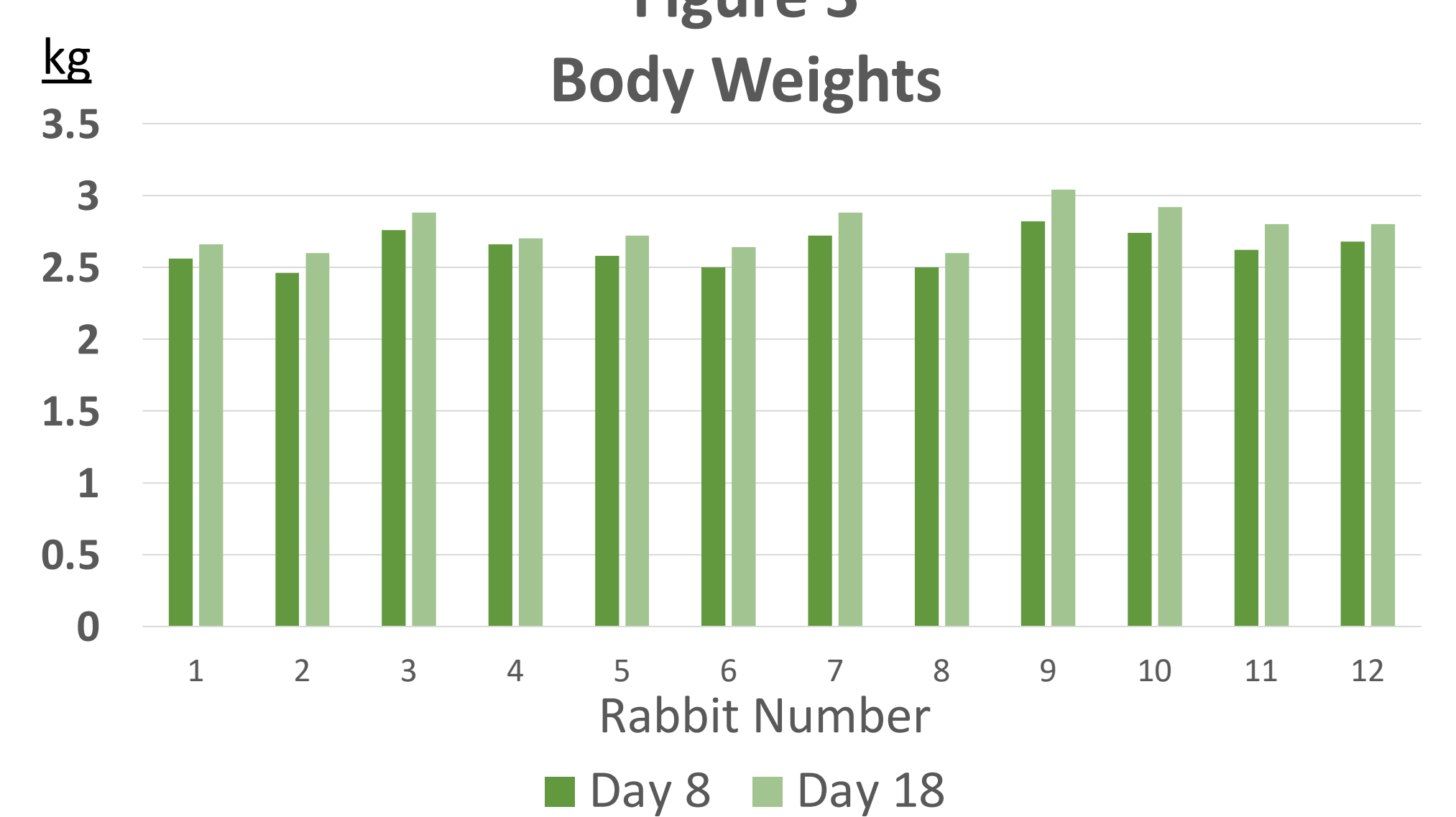


Figure 4
Body Weight Change, Day 18 vs Day 1

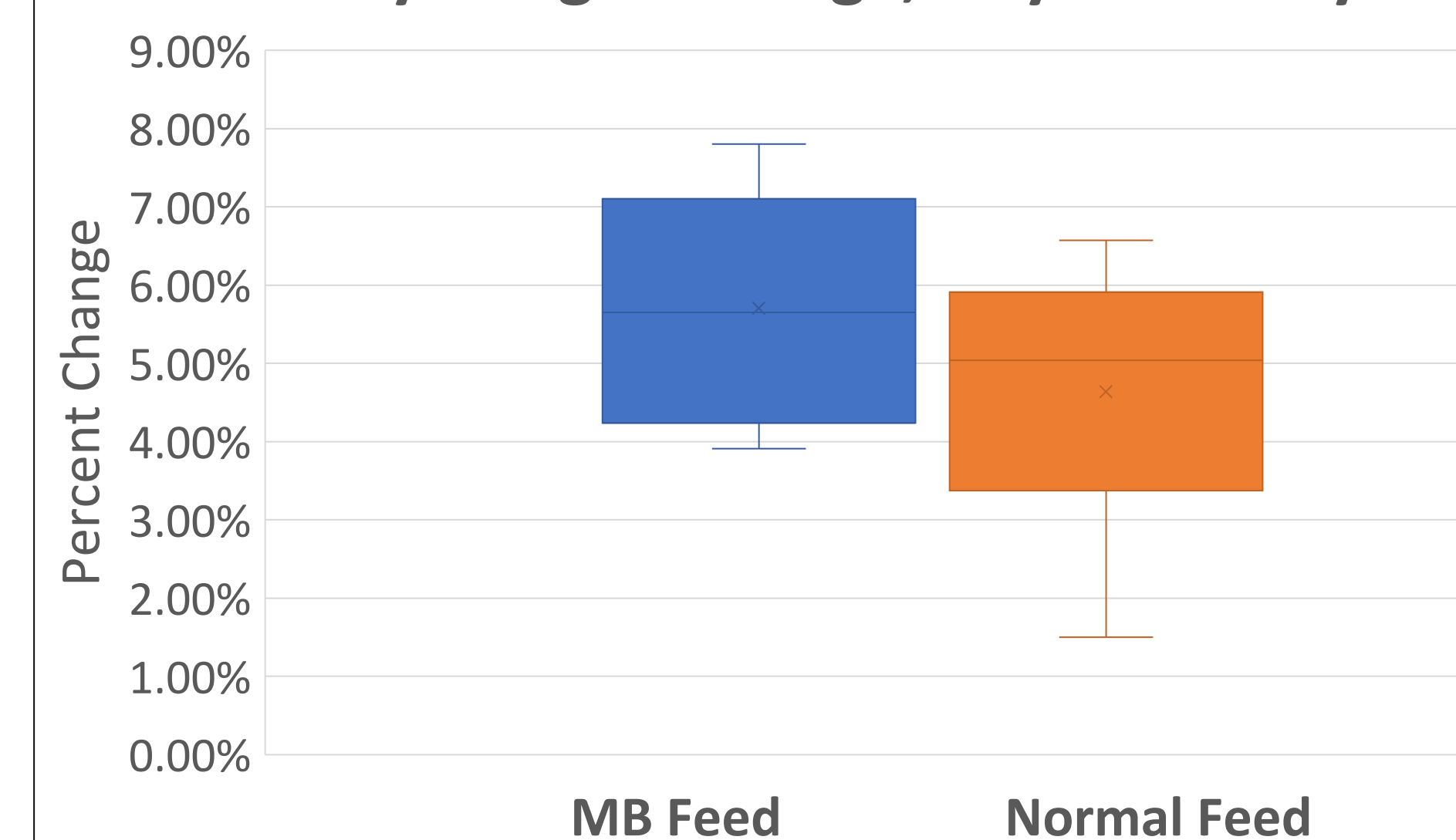


Table 1. Blood Chemistry Profiles (Day 18)

| | (Averages Values, n=3) | | |
|---------------------------|------------------------|-------------|---------|
| | MB Feed | Normal Feed | P-Value |
| Albumin g/dl | 4.2 | 4.2 | .467 |
| Total Protein g/dl | 5.367 | 5.4167 | .439 |
| Globulin g/dl | 1.13 | 1.15 | .44 |
| Total Bilirubin mg/dL | 0.24 | 0.24 | .5 |
| Glucose mg/dL | 172.4 | 162.167 | .434 |
| Bun mg/dL | 20 | 17.83 | .134 |
| Creatine mg/DL | 2 | 2.2167 | .205 |
| Calcium mg/dL | 11.45 | 11.067 | .349 |
| Phosphorus mg/dL | 6.66 | 6.63 | .428 |
| Cholesterol mg/dL | 42 | 38.83 | .34 |
| Alkaline Phosphatase IU/L | 125 | 111.33 | .35 |
| ALT IU/L | 324.5 | 141.1 | .174 |
| AST IU/L | 600 | 431.167 | .183 |
| GGT IU/L | 19 | 28.67 | .203 |
| CK IU/L | 803.6 | 1363.3 | .35 |
| Sodium mEq/L | 148.8 | 150 | .47 |
| Potassium mEq/L | 8.24 | 17.0167 | .062 |
| Chloride mEq/L | 108.6 | 111.3 | .13 |
| CO2 mEq/L | 20.6 | 17.83 | .098 |
| Anion Gap | 27.84 | 37.85 | .071 |

Conclusions

Supplementing rabbit feed with mesobiliverdin-enriched microalgae extract lowers serum cytokine IL-6 levels when fed to rabbits without affecting body weight.

References

- Chang, C.-W. T.; Takemoto, J. Y.; Chang, P.-E.; Alfindee, M. N.; Lin, Y.-Y., Effects of mesobiliverdin IX alpha-enriched microalgae feed on gut health and microbiota of broilers. **2021**, *Front Vet Sci*, 7, doi: 10.3389/fvets.2020.586813
- Takemoto, J. Y.; Chang, C.-W. T.; Chen, D.; Hinton, G., Heme-Derived Bilins. *Israel Journal of Chemistry* **2019**, 59 (5), 378-386.
- Tanaka, T.; Narazaki, M.; Kishimoto, T., IL-6 in inflammation, immunity, and disease. *Cold Spring Harb Perspect Biol* **2014**, 6 (10), a016295-a016295.

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