



Introduction

Fortetropin® is a high pressure pasteurized, freeze-dried, fertilized chicken egg yolk powder product that has been studied extensively in human and veterinary clinical trials. In a randomized, double blind, placebo-controlled human clinical study that involved 60-75 year old men and women, daily consumption of Fortetropin led to an increase in the rate of muscle protein synthesis by ~18% when compared to a macronutrient-matched placebo [1]. In an earlier randomized, double blind, placebo-controlled human clinical trial involving 18-21 year old men that involved studying the impact of Fortetropin on gains in muscle mass and thickness, it was found that subjects that consumed Fortetropin on a daily basis experienced significant gains in muscle mass when compared against subjects that received a macronutrient-matched placebo, cheese powder [2]. A study in rodents to elucidate the mechanism of action of Fortetropin revealed that Fortetropin acts by (i) upregulating mTor pathway activity, (ii) downregulating ubiquitin-proteasome pathway activity and (iii) lowering expression of myostatin and the receptor of myostatin, ActRIIB [2].

Fortetropin has also been studied in Veterinary Clinical Trials. In a randomized, double blind, placebo-controlled clinical study that involved 100 dogs recovering from TPLO surgery, it was shown that the daily consumption of Fortetropin® attenuated muscle atrophy when compared to the impact of a macronutrient-matched placebo [3]. In another randomized, double blind, placebo-controlled clinical study that involved 45 geriatric dogs, it was shown that the daily consumption of Fortetropin® led to improvements in mobility and quality of life based on statistically significant reduction in Liverpool Osteoarthritis in Dogs (LOAD) scores [4].

The muscle atrophy that results from syndromes such as sarcopenia and cachexia is of importance to both cats and dogs [5]. However, previous Veterinary Clinical Trials on Fortetropin have only focused on addressing muscle atrophy in dogs. There have been some anecdotal reports of Fortetropin resulting in diarrhea when administered in very high doses to dogs. The recommended dosing range of Fortetropin for cats was unknown prior to this study. The purpose of this study was to evaluate the safety and tolerability of Fortetropin in 12 purpose-bred cats at doses equivalent to the effective Fortetropin dose in people and dogs, ranging from 1 g/day to 4 g/day, over a duration of 2 weeks.

Clinical Study Design

In this study, a cohort of purpose-bred cats was randomized into 3 treatment groups (n=4 in each group) as outlined below. Each cat was treated once daily for 2 weeks one of the following treatment described below.

Treatment Group	Daily Dose (g/day)
Group 1	Placebo (Cheese Powder) – 1 g/day
Group 2	Fortetropin – 1 g/day (~200 mg/kg/day)
Group 3	Fortetropin – 2 g/day (~400 mg/kg/day)

At any given time point, no more than 4 cats were treated to allow for single cat housing for the duration of exposure (in order to monitor for potential adverse reactions). Cats were observed for adverse reactions (vomiting, diarrhea, decreased appetite) on a daily basis.

It was planned for each cat in the placebo group to be treated for an additional 2 weeks with Fortetropin at a dose of 4 g/day (~800 mg/kg/day), assuming that no adverse events were observed during the first phase of the study in Group 1, Group 2 and Group 3.

No adverse events were observed in any of the the cats that received 1 g/day (n=4) and 2 g/day doses (n=4) of Fortetropin. There was a single episode of diarrhea at Day 6 observed in one cat in the placebo group.

Presented at the **American College of Veterinary Internal Medicine (ACVIM) Forum, June 9-12, 2021, Poster # NM-03.**

Results

Nutritional Supplement	Daily Dose (g/day)	Adverse Events
Placebo	1 g/day (~200 mg/kg/day)	Single episode of diarrhea at Day 6 observed in one cat.
Fortetropin	1 g/day (~200 mg/kg/day)	None
Fortetropin	2 g/day (~400 mg/kg/day)	None
Fortetropin	4 g/day (~800 mg/kg/day)	Single episode of vomiting at Day 8 observed in one cat.

After the first phase of the study, the cats (n=4) that were initially in the placebo group were treated with a high dose of Fortetropin (4 g/day) for 2 weeks. On Day 8, a single episode of vomiting was observed in one cat from this treatment group (4 g/day Fortetropin). Therefore, the frequency of mild adverse events (diarrhea, vomiting) was no greater in the cats that receive a high dose of Fortetropin (4 g/day) relative to the cats that received the placebo treatment.

Discussion

A form of age-related muscle atrophy known as *sarcopenia* is a common problem for aging cats. Michel et al. [6] applied dual energy x-ray absorptiometry (DEXA) to measure the lean body mass (LBM) of cats in addition to muscle mass scoring (MMS). Their results revealed a significant decline in muscle mass score as a function of age among cats. Among cats that received the lowest MMS score (0/3), the average age of the cats was ~15 years while among cats that received the highest MMS score (3/3), the average age of the cats was ~ 8 years.

Sarcopenia is a significant risk factor for chronic kidney disease (CKD)-related mortality. Freeman et al. [7] conducted a clinical study involving 569 cats diagnosed with CKD and examined the impact of weight at the time of CKD diagnosis on survival. Cats with a weight of ~5 kg at the time of CKD diagnosis were found to have a Hazard Ratio ≈ 1. However when examining cats with a weight of ~3 kg at the time of CKD diagnosis, their Hazard Ratio ≈ 2.5. Thus, cats that were ~2 kg below their ideal weight (~5 kg) at the time of CKD diagnosis had a 2.5x greater risk of mortality relative to a cat with an ideal weight at the time of CKD diagnosis. When examining cats that were ~7 kilograms at the time of CKD diagnosis (~2 kg above their ideal weight), the Hazard Ratio < 1. Such a cat had a lower risk of mortality than a cat that was found to be at its ideal weight at the time of CKD diagnosis and is likely due to the phenomenon of the *obesity paradox*. Although obesity increases the likelihood of developing CKD, obesity appears to provide some protection to cats upon CKD diagnosis relative to cats that do not fall in this category. Freeman et al. also reported that CKD resulted in significant weight loss in cats over a 3 year duration following CKD diagnosis.

Although Fortetropin has not been shown to address muscle atrophy in cats, Fortetropin has been shown to reduce muscle atrophy in dogs recovering from TPLO surgery [3]. Human clinical studies have shown that Fortetropin supplementation increased the rate of muscle protein synthesis by ~18% relative to subjects that received the placebo. Further research will be needed to establish whether Fortetropin can address feline sarcopenia and attenuate CKD-related muscle atrophy.

Conclusions

At a dose range that corresponds to the therapeutic dose-range in dogs and people, Fortetropin is safe and well tolerated in cats.

Conflicts of Interest

Funding for this study was provided by MYOS CORP, Cedar Knolls, NJ, USA.

References

- Evans, William, et al. "Effects of Fortetropin on the Rate of Muscle Protein Synthesis in Older Men and Women: A Randomized, Double-Blinded, Placebo-Controlled Study." *The Journals of Gerontology: Series A* 76.1 (2021): 108-114.
- Sharp, Matthew H., et al. "The effects of fortetropin supplementation on body composition, strength, and power in humans and mechanism of action in a rodent model." *Journal of the American College of Nutrition* 35.8 (2016): 679-691.
- White, Dana A., et al. "Fortetropin inhibits disuse muscle atrophy in dogs after tibial plateau leveling osteotomy." *Plos one* 15.4 (2020): e0231306.
- Harkin, Kenneth R., et al. "Fortetropin leads to improvements in the quality of life and mobility in geriatric dogs based on reductions in Liverpool Osteoarthritis in Dogs (LOAD) scores." *Manuscript submitted*.
- Freeman, L. M. "Cachexia and sarcopenia: emerging syndromes of importance in dogs and cats." *Journal of Veterinary Internal Medicine* 26.1 (2012): 3-17.
- Michel, Kathryn E., et al. "Correlation of a feline muscle mass score with body composition determined by dual-energy X-ray absorptiometry." *British Journal of Nutrition* 106.S1 (2011): S57-S59.
- Freeman, L.M., Lachaud, M.P., Matthews, S., Rhodes, L. and Zollers, B., 2016. Evaluation of weight loss over time in cats with chronic kidney disease. *Journal of veterinary internal medicine*, 30(5), pp.1661-1666.