THE EFFECTS OF VELOSITOL ON EXERCISED-INDUCED MYOKINES

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ABSTRACT

Background: Velositol is a novel nutritional compound comprised of a modified-release chromium complex and a specialized form of amylopectin. This compound has been clinically shown to double exercise-induced muscle protein synthesis when added to a whey protein supplement. One mechanism of action is believed to be via increased skeletal muscle insulin sensitivity and improved amino acid metabolism leading to increased mTor activation and muscle protein synthesis. Another potential mechanism of action may be via enhanced myokines. Myokines (e.g., musclin and fractalkine) are cytokines released by muscle during exercise that lead to muscle protein synthesis and hypertrophy. To evaluate if myokines are affected by Velositol, the following preclinical and clinical studies were conducted.

Methods and Results: In a preclinical study, 8-week old male Wistar rats weighing approximately 250 – 300g were reared at 22 ± 2ºC in a 12/12 hour light/dark cycle and randomized into exercise control, exercise + whey protein, and exercise + whey protein + Velositol treatment groups. Doses of whey protein increased from 6 – 40g equivalents. All rats completed a 10-day treadmill acclimation schedule that gradually increased in speed and duration up to 26 m/min for 15 minutes. On the day of the single-dose experiment, rats were exercised at 26 m/min for 2 hours and then administered by gavage study product or water, immediately after exercise. Study results showed that all active treatment groups significantly increased musclin serum levels compared to the exercise control group ($p<0.05$). However, all groups supplemented with Velositol + whey protein had significantly higher musclin levels compared to whey protein alone ($p<0.05$). The increases in musclin levels, seen in the Velositol + whey protein treatment group, were significantly correlated ($p<0.0001$) with increases in muscle protein synthesis ($r^2=0.921$).

In a clinical study, blood samples were collected from four subjects for pharmacokinetic analysis of myokines. These subjects participated in a double-blind, cross-over design study, where they consumed a beverage containing 6g whey protein or 6g whey protein + 2g of Velositol and then completed 8 sets of bilateral isotonic leg extension at 80% of their estimated 1-RM. Blood samples were collected over a 4-hour period and analyzed for cytokines (musclin, fractalkine, GRO, IL-10, IL-15, IL-1RA, IL-6, MCP-1, MIP-1a, MIP-1b, and VEGF). Study results showed that cytokine levels were highest in Velositol + whey protein treated subjects. Of particular interest were the increases in musclin and fractalkine, both being exercise-responsive myokines involved in muscle growth and endurance.

Conclusions: In conclusion, preclinical and clinical data support the beneficial effects of the addition of Velositol to whey protein on enhancing levels of various myokines after exercise. These data present a novel mechanism by which Velositol exerts its beneficial effects on increasing muscle protein synthesis.

BACKGROUND

The intake of nutrients that increase essential amino acid (EAA) and insulin levels during exercise are important for muscle protein synthesis (MPS) and growth (See Fig. 1.). The essential trace mineral chromium has been shown to increase insulin sensitivity and as such may enhance the molecular mechanism of MPS. The positive effects of chromium and amylopectin (Velositol®) on MPS have been demonstrated in a clinical study showing that Velositol (2g) significantly increases MPS when added to 6 g of whey protein (WP) [1].

An additional mechanism of action may be via enhancement of myokines. Myokines are muscle-fiber derived peptides produced and secreted in response to muscular contractions. Myokines may act as signaling molecules to various organs, impacting exercise-induced metabolic changes and skeletal muscle remodeling [2]. Musclin and fractalkine are two types of myokines. Disruption of musclin activity has been shown to decrease aerobic capacity, muscle oxidative capacity and mitochondrial count [2]. Fractalkine has been shown to have a role in muscle regeneration after injury and is thought to be crucial for hypertrophy [3]. Therefore, the results of these studies may provide insight into the cellular mechanisms by which Velositol increases MPS when added to whey protein. These results may be of interest to those interested in preserving or enhancing muscle mass with exercise.

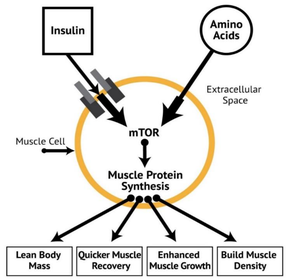

Figure 1. When insulin binds to its receptors on the cell surface, it facilitates the transportation of EAAs into muscle cells. In the presence of sufficient amino acids, the cellular protein mTOR aids in regulating muscle growth by activating the phosphorylation of translational proteins [4]. Myokines may enhance this process by modulating muscular metabolism and enabling muscle regeneration, allowing for prolonged exercise and greater muscular growth.

METHODS & MATERIALS

Study Product: Velositol® (amylopectin chromium complex)

Preclinical Study Design:

- 8-week old male Wistar rats weighing 250-300g were reared at 22 ± 2ºC in a 12/12 hour light/dark cycle.
- Rats were randomly assigned to one of nine groups (n=8 in each group):

	Treatment Group (Human Equivalent Dose)	Whey protein dose (g/kg BW)	Human protein dose equivalent (g)	Velositol dose (g/kg BW)	Human Velositol dose equivalent (g)
I	Exercise Control Group	0	0	0	0
II	(6g) whey protein	.456	6	0	0
III	(20g) whey protein	1.55	20	0	0
IV	(30g) whey protein	2.33	30	0	0
V	(40g) whey protein	3.10	40	0	0
VI	(6g) whey protein + Velositol	.465	6	.155	2
VII	(20g) whey protein + Velositol	1.55	20	.155	2
Vii	(30g) whey protein + Velositol	2.33	30	.155	2
IX	(40g) whey protein + Velositol	3.10	40	.155	2

- Rats had a 10-day treadmill acclimation that gradually increased in speed and duration.
- On the day of the experiment, rats were exercised at maximum speed for 2 hours and fed according to their assigned study product. Test products were dissolved in water and administered via oral gavage.
- Ten minutes after exercise, rats were injected with a bolus dose (250 mg/kg body weight, 25 g/L) of phenylalanine labeled with deuterium to measure fractional rates of protein synthesis (FSR) [4].
- One hour after exercise, rats were sacrificed and serum and muscle tissue samples were taken. The rate of protein synthesis was measured by GC-MS. Myokines were measured using ELISA.

Clinical Study Design:

- Four subjects (ages 21-45) received either 6 g whey protein + placebo (control) or 6 g whey protein + 2 g Velositol (active).
- To measure FSR, muscle biopsies were taken from the vastus lateralis muscle at 2, 4, and 8 hours. After the hour 4 muscle biopsy, subjects consumed a single dose of their assigned product and completed 8 sets of isotonic leg extension resistance exercise at ~80% of their estimated 1-repetition maximum. A final biopsy was obtained 4 hours later. After 5-7 days washout, subjects crossed over treatments.
- Blood samples were collected at baseline and after isotope infusion for a 4-hour time period to analyze for cytokines, amino acids, insulin, and glucose levels.

RESULTS: PRECLINICAL MUSCLIN LEVELS

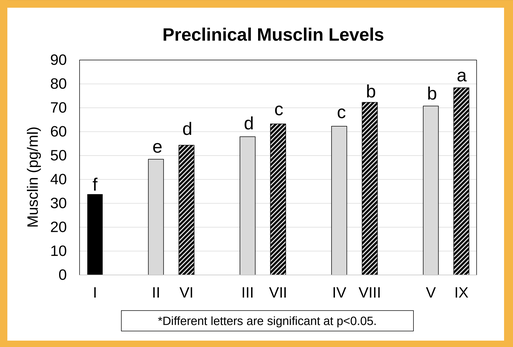

Figure 2. Musclin levels were higher in all WP groups (grey bars) compared to the exercise control group ($p<0.05$). Musclin levels were also higher in each WP+Velositol group (striped bars) compared to WP alone equivalent groups ($p<0.05$), suggesting that Velositol augments WP's effect on exercise-induced musclin levels.

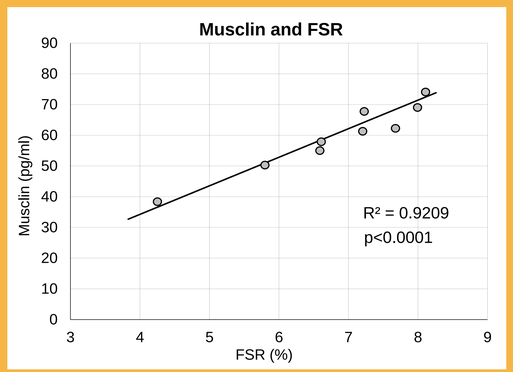

Figure 3. Increases in MPS (measured as FSR) and musclin levels seen in the active treatment group were highly correlated with each other ($r^2=0.921$, $p<0.0001$), suggesting that Velositol's ability to increase FSR may be due to the increase in the release of the muscle myokine, musclin.

RESULTS: CLINICAL MUSCLIN AND FRACTALKINE LEVELS

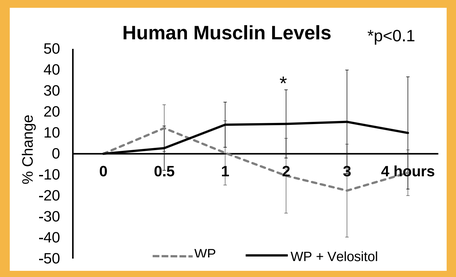

Figure 4. The graph shows percent change in musclin levels post-dose over a 4-hour period for both the control and active group. Musclin levels were higher in the Velositol group than in the control group, particularly at the 2 hour timepoint ($p<0.1$).

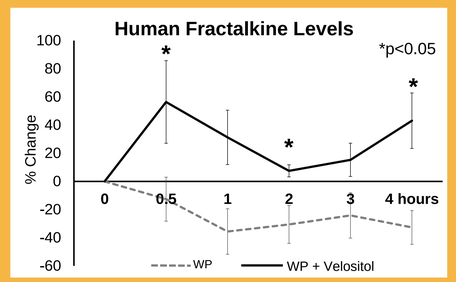

Figure 5. The graph shows percent change in fractalkine levels post-dose over a 4-hour period for both the control and active group. At several timepoints there was a significant difference between groups ($p<0.05$).

DISCUSSION & CONCLUSIONS

- ✓ Velositol has been shown in a clinical study to double the amount of MPS with a 6g dose of whey protein when compared to 6g of whey protein alone.
- ✓ It is possible that Velositol enhances MPS through the production of muscle myokines, which are peptides produced and released by muscle cells in response to muscular contractions.
- ✓ This preclinical study showed that the addition of Velositol to 6-40g equivalents of whey protein enhanced musclin levels compared to whey protein doses alone and these results were highly correlated with the increases seen in MPS.
- ✓ In a clinical study, the addition of Velositol to 6g of whey protein increased musclin and fractalkine levels compared to 6g of whey protein alone.
- ✓ In conclusion, because myokines are involved in improving muscle growth and endurance, the results of these studies represent a mechanism by which Velositol enhances muscle protein synthesis.

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