The Effects of Creatine Monohydrate Supplementation With and Without D-Pinitol on Resistance Training Adaptations

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Abstract

Kerksick, CM, Wilborn, CD, Campbell, WI, Harvey, TM, Marcello, BM, Roberts, MD, Parker, AG, Byars, AG, Greenwood, LD, Almada, AL, Kreider, RB, and Greenwood, M. The effects of creatine monohydrate supplementation with and without D-pinitol on resistance training adaptations. *J Strength Cond Res* 23(9): 2673–2682, 2009—Coingestion of D-pinitol with creatine (CR) has been reported to enhance creatine uptake. The purpose of this study was to evaluate whether adding D-pinitol to CR affects training adaptations, body composition, whole-body creatine retention, and/or blood safety markers when compared to CR ingestion alone after 4 weeks of resistance training. Twenty-four resistance trained males were randomly assigned in a double-blind manner to creatine + pinitol (CRP) or creatine monohydrate (CR) prior to beginning a supervised 4-week resistance training program. Subjects ingested a typical loading phase (i.e., 20 g/d^{-1} for 5 days) before ingesting 5 g/d^{-1} the remaining 23 days. Performance measures were assessed at baseline (T0), week 1 (T1), and week 4 (T2) and included 1 repetition maximum (1RM) bench press (BP), 1RM leg press (LP), isokinetic knee extension, and a 30-second Wingate anaerobic capacity test. Fasting blood and body composition using dual-energy x-ray absorptiometry (DEXA) were determined at T1 and T3. Data were analyzed by repeated measures analysis of variance (ANOVA). Creatine retention increased ($p < 0.001$) in both groups as a result of supplementation but was not different between groups ($p > 0.05$). Significant improvements in upper- and lower-body strength and body composition occurred in both groups. However, significantly greater increases in lean mass and fat-free mass occurred in the CR group when compared to CRP ($p < 0.05$). Adding D-pinitol to creatine monohydrate does not appear to facilitate further physiological adaptations while resistance training. Creatine monohydrate supplementation helps to improve strength and body composition while resistance training. Data from this study assist in determining the potential role the addition of D-pinitol to creatine may aid in facilitating training adaptations to exercise.

Key Words supplements, exercise, performance, ergogenic, retention

Introduction

Creatine supplementation has been used as an effective sports supplement for more than a decade by recreational and competitive athletes to improve athletic performance. Supplementation has been shown to increase intramuscular creatine stores anywhere from 5 to 30% (16). The typical creatine supplementation protocol is a 5-day loading dose of 20 g/d^{-1} followed by 3 to 5 g/d^{-1} for the duration of the supplementation period (16). Research has shown that concomitant ingestion of creatine with glucose (e.g., 35–95 g) or glucose + protein (e.g., 50 g each) increases the amount of creatine stored in the muscle. These findings are purported to be related to changes in circulating levels of insulin (10,11). A recent review by Kreider in 2003 reported that of the more than 300 studies that have paired creatine supplementation

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with strength training, 70% have shown an ergogenic effect (25). Research has suggested for various reasons (i.e., higher natural creatine intake, enhanced phosphagen stores, differential creatine transporter expression) that certain individuals respond more favorably to creatine supplementation (31). Thus, the existence of creatine nonresponders may account for the research demonstrating that creatine has no anabolic/ergogenic effect following adequate supplementation regimens.

In an attempt to increase the absorption and retention of creatine within skeletal muscle, an array of creatine formulations (e.g., creatine citrate, effervescent, ethyl ester, etc.) have been created in an attempt to improve the ergogenic benefit of creatine. D-pinitol (3-O-methyl-chiro-inositol) is a methylated isomer of d-*chiro*-inositol and is naturally found in the body primarily from one's diet (e.g., legumes, citrus fruits, and soy meal). D-pinitol has been found to possess insulinlike properties and presents a daily turnover rate of approximately 1 g/d^{-1} (17,18). Additionally, D-pinitol administration stimulates glucose uptake into rat myocytes and promotes glycogen synthesis (3,27). Further, Bates and colleagues found that intraperitoneal injection and oral ingestion (100 mg/kg^{-1}) of D-pinitol decrease plasma glucose by 21 and 22%, respectively, without any changes in insulin levels (3). Thus, these data suggest that D-pinitol may stimulate improvements in insulin sensitivity and subsequent insulin action (3). Equivocal evidence does exist in 2 recent studies reporting that D-pinitol may not work effectively to manage glucose and insulin kinetics in aged human participants (5,6), although these findings may relate to confounding changes in lean mass in aging populations. The potential insulinlike effects of D-pinitol have led to speculation that ingesting creatine with D-pinitol may increase creatine uptake over just creatine supplementation. If true, the enhanced availability of creatine may result in improved adaptations to exercise training.

It has recently been shown that the addition of D-pinitol ($2 \times 0.5\ g/d^{-1} \times 3$ d) to creatine monohydrate ($4 \times 5\ g/d^{-1} \times 3$ d) increases whole-body creatine retention levels that are similar to when creatine is ingested with high doses of glucose or glucose with protein (14). Regardless, no studies have been conducted to investigate the impact of adding D-pinitol to creatine on physiological adaptations associated with resistance training. Therefore, the purpose of this study was to determine if the addition of D-pinitol to creatine monohydrate would favorably improve exercise training adaptations, body composition, creatine retention, and serum and urine markers of clinical safety in comparison to supplementation with just creatine monohydrate following 4 weeks of resistance training.

Methods

Experimental Approach to the Problem

This study was conducted as a double-blind trial with all subjects being matched into clusters according to age and fat-free mass prior to beginning the resistance training program. All subjects were tested at 0 (T0), 1 (T1), and 4 (T4) weeks to determine the changes in criterion variables. Clinical safety markers were assessed to determine the safety and efficacy of each supplementation protocol. Changes in body mass, fat mass, fat-free mass, and percent body fat were measured to investigate the impact of supplementation and resistance training on body composition adaptations. Finally, maximal strength (1 repetition maximum [1RM]), endurance (repetitions to failure), peak force production using isokinetics, and anaerobic capacity (Wingate tests) were determined to investigate the ergogenic potential of supplementation. It was hypothesized a priori that supplementation with creatine monohydrate + D-pinitol (CRP) would enhance the retention of creatine (CR) and improve training adaptations in comparison to CR alone.

Subjects

Twenty-four healthy resistance trained males (CRP: $n = 12$, CR: $n = 12$) between the ages of 18 and 35 years volunteered to participate in this study. Subjects were informed prior to their participation as to the experimental procedures and signed informed consent statements and medical history forms that were approved by the Institutional Review Board (IRB) for the use of Human Subjects at Baylor University. Subjects were recruited from the student population at Baylor University and from local fitness facilities (Table 1).

Procedures

Entrance Criteria. To participate in this study, subjects had to (a) sign statements indicating they had no current or past use of anabolic steroid use; (b) be experienced with resistance training (>1 year of training) and currently training >3 hours per week with a program that included both the bench press

Table 1. Baseline subject characteristics.

Variable	CR	CRP	Significance
Age (years)	22.2 ± 2.9	21.8 ± 3.2	0.79
Height (cm)	177 ± 7.2	180 ± 5.3	0.19
Weight (kg)	82.3 ± 15.8	75.6 ± 8.0	0.20
Training frequency (d/wk^{-1})	4 ± 1	4 ± 1	0.92

Creatine + D-pinitol (CRP: $n = 12$) and creatine (CR: $n = 12$) groups. Data are mean ± *SD*.

and leg press/squat exercises; (d) refrain from participating in any nonleisure endurance training for greater than 20 minutes at a time (e.g., running, cycling, swimming, etc.) for the entire study; (d) have not ingested any nutritional supplements that may affect muscle mass (e.g., creatine, HMB) or anabolic/catabolic hormone levels (e.g., androstenedione, DHEA, etc.) within 3 months prior to the start of the study and/or be relatively naïve to creatine supplementation; (e) agree to follow a predetermined workout program; (f) not have any existing medical conditions that would compromise participation in the study; and (g) avoid any regular nutritional practices that might confound the results of the study (i.e., vegetarians, caloric restriction, food allergies, etc.)

Familiarization Session. Subjects were familiarized to all experimental procedures and given detailed instruction on specific exercise technique, optimal progression of resistance, and recommended rest periods while following the training program. Following the familiarization session, the participants recorded all food intake on dietary records forms for 4 days, which included 3 weekdays and 1 weekend day. Each participant was provided detailed instructions (e.g., portion sizes, food preparation) on how to properly complete these dietary record forms. Subjects were then provided eight 3-L urine collection containers for collection of 24-hour urine samples on days 0, 1, 2, and 3 and recorded the number of times they urinated in addition to their daily fluid consumption. Twenty-four-hour baseline urine collection began at 8:00 AM the day prior to supplementation. Subjects refrigerated their urine samples during the collection period (days 0–3) prior to reporting every morning (by 9:00 AM) to turn in the previous day's urine sample. All participants were instructed to refrain from exercise for 48 hours and to observe an 8-hour fast prior to their baseline testing session.

Baseline Testing. Presupplementation assessments throughout baseline testing included (a) a 4-day dietary record; (b) a 24-hour urine sample; (c) an 8-hour fasting venous blood sample; (d) determination of body mass and body composition assessment using dual-energy x-ray absorptiometry (DEXA); and (e) performance assessments, which included 1RM strength tests on the bench press and leg press, isokinetic knee extension muscular strength, and a 30-second Wingate anaerobic capacity test.

Supplementation Protocol. On completing baseline testing, subjects were matched according to fat-free mass and age. In a double-blind manner, subjects were assigned to supplement their normal diet for 4 weeks with 1 of the 2 supplement groups including 4.5 g/d^{-1} of creatine monohydrate + 0.5 g/d^{-1} corn starch (CR) or 4.5 g/d^{-1} creatine monohydrate + 0.5 g/d^{-1} of D-pinitol (CRP). All supplements were in powder form of similar smell, consistency, and texture. In a blinded fashion all supplements were packaged in individual unlabeled foil packets by iSatori Global Technologies, LLC (Golden, Colorado, U.S.A.). During the initial 5-day loading phase, participants ingested 4 servings per day at 8:00 AM, 12:00 PM, 4:00 PM, and 8:00 PM. For the remaining 23 days, subjects ingested each daily dose at 8:00 am. Subjects were encouraged to place each entire dose on the back of the tongue prior to washing it down with water. Because of sweetness and texture of the supplement, some participants were not able to ingest their supplements in this manner and were instructed to thoroughly mix their supplement and make sure no aspect of each dose remained in the cup after ingestion. Supplements were distributed in 1-week supplies, and collecting and counting empty supplement packets was used to verify subject compliance to the supplementation protocol. Subjects were instructed to report to the research investigators at the end of each week of training to report the frequency or severity of any possible side effects and their compliance to the training and supplementation protocols.

Resistance Training Program. The training program (Table 2) consisted of 4 supervised workouts per week split into 2 upper-body and 2 lower-body workouts per week, which primarily utilized multijoint exercises that targeted the major muscle groups.

All subjects were required to perform each exercise to the point of reaching muscular failure at the last repetition of each set (2). Subjects were instructed to rest for approximately 2 minutes between sets and 3 minutes between each exercise. Training was conducted at Baylor University under the supervision of trained research assistants, documented in

TABLE 2. Resistance training program.

Weeks	Monday, Thursday*†	Tuesday, Friday*†
1–4	Bench press, 3 × 8–10	Back squat, 3 × 8–10
	Lat pull, 3 × 8–10	Leg press, 3 × 8–10
	Shoulder press, 3 × 8–10	Leg curl, 3 × 8–10
	Seated rows, 3 × 8–10	Leg extension, 3 × 8–10
	Shoulders shrugs, 3 × 8–10	Step-ups, 3 × 8–10
	Chest flies, 3 × 8–10	Heel raises, 3 × 8–10
	Biceps curl, 3 × 8–10	Abdominal crunches, 3 × 25
	Triceps press down, 3 × 8–10	

*One minute of rest between sets.
†Three minutes of rest between exercises.

training logs, and signed off to verify compliance and monitor progress.

Follow-Up Testing Sessions. Subjects reported back to the lab after 1 week (T1) and 4 weeks (T2) of training and supplementation for follow-up assessments. Subjects reported to the lab after avoiding strenuous exercise for 48 hours and fasting for 8 hours prior to T0 and T2. Subjects generally reported to the lab between 8:00 AM and 10:00 AM during T0, and all follow-up tests were completed at similar times to help control for any changes in diurnal variations in hormone levels. Prior to each follow-up testing session, subjects were instructed to provide a completed 4-day diet log to monitor any changes in dietary intake throughout the study. All dietary logs and training logs were turned in and subjects underwent follow-up testing that was identical to the baseline testing session with the exception of blood sampling and body composition assessment during the 1-week follow-up (T1). Specifically, subjects donated an 8-hour fasting venous blood sample and had body mass, total body water, and body composition determined. Subjects then completed performance assessments, which consisted of 1RM leg press, 1RM bench press, an isokinetic strength protocol, and a 30-second Wingate anaerobic capacity test.

Analytical and Testing Procedures. All dietary records were analyzed by a registered dietician using the ESHA Food Processor (Version 8.3) software (ESHA Research; Salem, Oregon, U.S.A.). Unavailable foods were entered into the database from manufacturer labels. The 4-day average of caloric intake, carbohydrate intake, protein intake and fat intake was computed for later statistical analysis.

During the urine collection period, participants returned each refrigerated 24-hour urine sample on a daily basis. On collection, investigators measured the total volume of urine returned and then vortexed each 3-L container by completely inverting each container 10 consecutive times. A standard urinalysis panel was then completed using a Roche Chem-Strip (Roche Diagnostics Corporation, Indianapolis, Indiana, U.S.A.) following the manufacturer's procedures. Urine samples were also analyzed for creatine and creatinine using a Dade Dimension clinical chemistry analyzer (Dade Behring Inc., Deerfield, Illinois, U.S.A.). The test–retest reliability of measuring these parameters ranged from 2 to 3%.

On blood collection days, subjects donated approximately 25 mL of blood via venipuncture of a forearm vein using standard procedures. Two 10-mL serum separation vacutainers were inserted for blood collection using multiple sample phlebotomy techniques. Serum was centrifuged at 5,000 revolutions per minute using a standard benchtop centrifuge for 15 minutes, transferred into 3 microcentrifuge tubes, and frozen at −80°C for subsequent analysis. Remaining serum was refrigerated and sent to a diagnostic laboratory (Quest Diagnostics Labs, Dallas, Texas, U.S.A.) for duplicate analysis of a complete 31-panel clinical chemistry profile including various markers of muscle/protein metabolism (e.g., aspartate aminotransferase, alanine aminotransferase, creatine kinase, urea nitrogen, creatinine, and total protein) and kidney/liver function. Test–test reliability of performing these assays ranged from 2 to 6% for individual assays with an average variation of ±3%.

Subjects' body weights were obtained during T0, T1, and T2 using a digital strain gauge electronic scale (Sunbeam Products Inc, Bridgeview, Illinois, U.S.A.) with a precision of ±0.02 kg. Whole-body (excluding cranium) composition was estimated at T0 and T2 following previously reported procedures (20,22) by certified investigators using a Hologic QDR-4500W DEXA and the Hologic software version 11.0C (Hologic, Waltham, Massachusetts, U.S.A.). Subjects were positioned on the DEXA table using standardized methods for each test. An analysis of the subject's fat mass, soft tissue (muscle) mass, and bone mass was provided and used to determine body composition changes throughout the duration of the study. DEXA has been found to be a highly reliable method of determining soft-tissue body composition and percent body fat for whole body and all respective regions determined (8,19,20,22,26). Test–retest reliability studies performed on male athletes with this DEXA machine yielded mean deviation for total bone mineral content and total fat free/soft tissue mass of 0.31% with a mean intraclass correlation of 0.985 (1).

After body composition analysis, participants then had their 1RM determined at T0, T1, and T2 while using a standard leg press/hip sled (Nebula Fitness, Inc., Model # 6000a; Versailles, Ohio, U.S.A.) and bench press (Nebula Fitness, Inc., Model # 1005). Prior to testing, standardized warm-up and progression of all 1RM attempts was conducted following the NSCA protocol for 1RM determination (2). Exercise technique and body position were standardized according to commonly accepted exercise technique guidelines (13). Determination of 1RM again followed NSCA guidelines and on 1RM determination, subjects rested for 10 minutes prior to completing an isokinetic muscular strength protocol. During all testing sessions, subjects were equally advised using standardized lifting criteria (2) and encouraged by the testers, who were all certified strength and conditioning specialists by the NSCA. Test–test reliability of performing these strength tests in our lab on resistance-trained subjects have yielded low mean coefficients of variation and high reliability for the bench press (1.9%, intraclass $r = 0.94$) and hip sled/leg press (0.7%, intraclass $r = 0.91$) (24).

Before the isokinetic leg extension was conducted, subjects warmed up on a stationary bicycle (Monark Cycle Ergometer; Sweden) for 2 to 3 minutes at a work rate of 150 kg/m/min^{-1}. All participants were strapped into the chair and settings were recorded to standardize position and minimize additional torque production except through the knee extensors and flexors. Participants were instructed to cross their arms in front of their torso and were given 5 practice repetitions prior to the actual test set. Each exercise set

Table 3. Dietary intake for the supplementation groups.

Intake Variable	Group*	Week 0	Week 1	Week 4	Significance	
Energy (kcal/kg^{-1}/d^{-1})	CRP	32.8 ± 7.7	35.9 ± 14.8	32.7 ± 9.9	Group	0.90
	CR	33.7 ± 11.3	36.0 ± 17.4	33.2 ± 12.0	Time	0.54
					G × T	0.98
Carbohydrate (g/kg^{-1}/d^{-1})	CRP	3.8 ± 1.3	3.8 ± 1.6	3.7 ± 1.6	Group	0.96
	CR	3.7 ± 1.4	4.0 ± 1.7	3.6 ± 1.8	Time	0.66
					G × T	0.82
Protein (g/kg^{-1}/d^{-1})	CRP	1.7 ± 0.5	1.8 ± 0.8	1.7 ± 0.5	Group	0.92
	CR	1.7 ± 0.7	1.9 ± 1.1	1.7 ± 0.5	Time	0.47
					G × T	0.99
Fat (g/kg^{-1}/d^{-1})	CRP	1.2 ± 0.3	1.5 ± 0.8	1.3 ± 0.4	Group	0.91
	CR	1.3 ± 0.7	1.4 ± 0.9	1.3 ± 0.6	Time	0.47
					G × T	0.85

*Creatine + D-pinitol (CRP: $n = 12$) and creatine (CR: $n = 12$) groups. Data are means + *SD*.

began from a reference angle of 90 degrees of knee flexion position and continued through a complete 80-degree range of motion. For the isokinetic exercise bout, participants completed a standard concentric–concentric knee extension/knee flexion protocol on a Biodex System 3 (Biodex Medical Systems, Shirley, New York, U.S.A.) at 60 degrees/second^{-1}, 180 degrees/second^{-1}, and 300 degrees/second^{-1}. Peak torque and average torque for each direction of movement was recorded from each test. Test to test reliability of performing isokinetic testing in our laboratory has yielded intraclass correlations of $r = 0.82$ and $r = 0.70$ for relative peak torque and total work.

Wingate anaerobic capacity tests were performed on a computerized Lode BV Excalibur Sport (Groningen, The Netherlands) cycle ergometer that was equipped with toe clips at a manufacturer-recommended and population-specific torque factor 0.7 N/m/kg^{-1}. Seat position, seat height, handlebar height, and handlebar position were determined during familiarization sessions and repeated for both testing sessions. Subjects were instructed to begin sprinting 5 seconds prior to beginning of data collection to ensure optimal force and power production at the beginning of the test and to remain sprinting for the entire duration of the test. All visual feedback was removed during testing and all subjects were instructed to remain in the saddle for the entire duration of the test while researchers provided verbal encouragement. The ergometer was interfaced to a PC computer using Wingate for Windows software Version 1 by

Table 4. Urine output variables for the creatine + D-pinitol (CRP) and creatine (CR) groups.

Variable	Group*	Day 0	Day 1	Day 2	Day 3	Significance	
Total urine volume (L)	CRP	2.3 ± 1.4	2.3 ± 1.2	2.0 ± 1.1	2.2 ± 0.8	Group	0.75
	CR	2.3 ± 1.1	2.5 ± 1.4	2.4 ± 1.1	2.2 ± 1.0	Time	0.43
						G × T	0.63
Urine-specific gravity	CRP	1.015 ± 0.002	1.015 ± 0.003	1.014 ± 0.006	1.012 ± 0.002	Group	0.12
	CR	1.015 ± 0.004	1.015 ± 0.005	1.016 ± 0.003	1.016 ± 0.004	Time	0.56
						G × T	0.06
Urine pH	CRP	6.33 ± 0.78	6.08 ± 0.51	6.08 ± 0.99	6.33 ± 0.65	Group	0.06
	CR	5.83 ± 0.72	6.25 ± 0.87	5.75 ± 0.62	5.75 ± 0.62	Time	0.69
						G × T	0.29
Urine creatine (g)	CRP	0.68 ± 1.4	5.04 ± 3.76	8.84 ± 5.52	10.56 ± 5.49	Group	0.77
	CR	0.26 ± 0.14	5.08 ± 4.57	9.68 ± 4.85	11.72 ± 7.00	Time	<0.001
						G × T	0.89
Urine creatinine (mmol/L)	CRP	10.7 ± 3.4	9.2 ± 4.2	11.0 ± 4.8	9.0 ± 3.3	Group	0.52
	CR	12.1 ± 6.7	9.6 ± 4.8	9.8 ± 3.3	12.0 ± 4.7	Time	0.29
						G × T	0.24

*Creatine + D-pinitol (CRP: $n = 12$) and creatine (CR: $n = 12$) groups. Data are means ± *SD*.

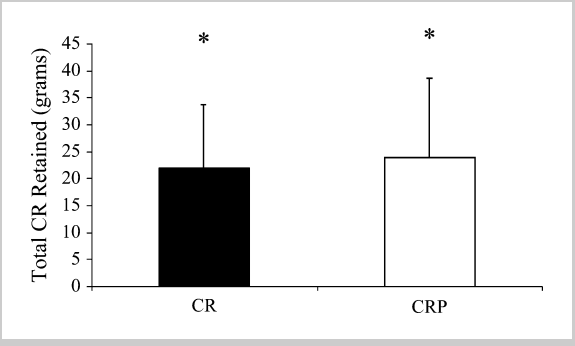

Figure 1. Three-day cumulative creatine retention for the supplementation groups. Creatine + D-pinitol (CRP: $n = 12$) and creatine (CR: $n = 12$) groups. *Day 4 > day 0 value; no between-group differences. Data are mean ± *SE*.

Lode BV (Groningen, The Netherlands). The Excalibur Sport has a range of 0 to 2,000 watts with typical variation of measurement less than 2% with the sampling frequency of data at 5 times/s^{-1}. Test–test variability in performing repeated Wingate tests in our lab has yielded an intraclass correlation of $r = 0.98$ for mean power.

Statistical Analyses

A priori power analysis revealed power values of 0.16, 0.78, and 1.03 for small (0.25), moderate (0.75), and large (1.25) effect sizes, respectively, for the n-size used in this study. Separate univariate 2-way (group × testing session) analysis of variance (ANOVA) with repeated measures was conducted respectively for each criterion variable and dietary intake variables (i.e., caloric intake, carbohydrate, protein, and fat). Data were considered significantly different when the probability of error was 0.05 or less. Post hoc procedures were conducted when significant interaction effects were found using Tukey post hoc procedures. Delta scores (post–pre values) were calculated on selected variables and analyzed by 1-way ANOVA for further interpretation of these data. Data are presented as means ± standard deviation.

Results

Nutritional Data

All nutritional data are represented relative to body weight in kilograms (Table 3). No significant differences among groups for total calories, carbohydrate, protein, or fat intake were found throughout the study ($p > 0.05$).

Medical Monitoring

No significant clinical side effects, related or unrelated to the study, were reported to the research nurse by any subject throughout the entire course of the study. All subjects tolerated both the training and supplementation protocols without any problems.

Training Volume

Total training volume (sets × reps × load) was calculated for all subjects. No significant differences were found between

Table 5. Body composition values for the creatine + D-pinitol (CRP) and creatine (CR) groups.

Variable	Group*	Week 0	Week 4	Significance	
DEXA total scanned mass (kg)	CRP	69.7 ± 7.5	70.5 ± 7.5	Group	0.19
	CR	75.8 ± 15.2	77.7 ± 15.5	Time	<0.001
				G × T	0.08
DEXA lean mass (kg)	CRP	58.6 ± 6.9	59.5 ± 7.0†	Group	0.36
	CR	61.1 ± 9.0	63.2 ± 9.1†	Time	<0.001
				G × T	0.03
DEXA fat mass (kg)	CRP	8.7 ± 2.6	8.7 ± 2.8	Group	0.12
	CR	12.3 ± 6.9	12.0 ± 6.9	Time	0.30
				G × T	0.29
DEXA bone mineral content (kg)	CRP	2.34 ± 0.2	2.33 ± 0.2	Group	0.56
	CR	2.43 ± 0.4	2.41 ± 0.4	Time	0.19
				G × T	0.85
DEXA fat-free mass (kg)	CRP	61.0 ± 7.1	61.8 ± 7.2†	Group	0.36
	CR	63.5 ± 9.3	65.6 ± 9.4†	Time	<0.001
				G × T	0.03
DEXA % body fat (%)	CRP	12.5 ± 3.7	12.4 ± 3.8	Group	0.21
	CR	15.4 ± 6.0	14.5 ± 5.6	Time	0.32
				G × T	0.09

*Creatine + D-pinitol (CRP: $n = 12$) and creatine (CR: $n = 12$) groups. Data are means + *SD*.
†CR > CRP ($p < 0.05$).

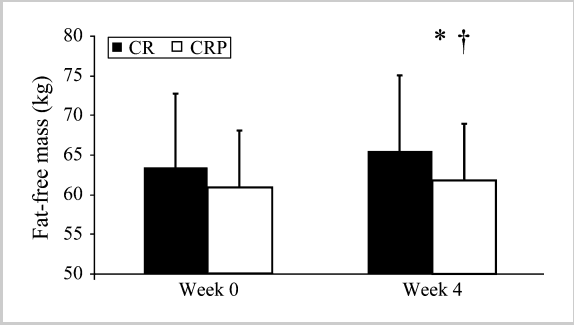

Figure 2. Delta value change in dual-energy x-ray absorptiometry (DEXA) lean mass (kg) after 4 weeks of supplementation and resistance training. Creatine + D-pinitol (CRP: $n = 12$) and creatine (CR: $n = 12$) groups. Data are mean ± *SE*. *Significant greater than baseline. †CR > CRP.

any of the groups for both upper-body (CRP: 171,634 ± 31,287 kg, CR: 185,918 ± 53,453 kg; $p = 0.44$) and lower-body (CRP: 226,415 ± 88,052 kg, CR: 269,985 ± 61,748 kg; $p = 0.17$) total training volume.

Urinalysis

All measures of urinalysis are presented in Table 4. No significant changes were noted for any urinalysis measures except for urine creatine. Urine creatine values displayed significant increases over time for both groups ($p < 0.01$), although there were no differences between groups throughout the study. Further, retention of creatine significantly increased in both groups ($p < 0.001$), although there were no differences between groups throughout the study. Total retention of creatine in both groups over the 3-day loading period demonstrated similar patterns (CR: 21.9 ± 11.9 g/d^{-1}; CRP: 23.8 ± 14.9 g/d^{-1}; $p < 0.001$) with no differences existing between groups (Figure 1). Urine-specific gravity did tend to increase more in the CR group when compared to the CRP ($p = 0.06$).

Body Composition

Table 5 presents body composition and bone density values for both groups. A significant main effect for time was observed for DEXA total scanned mass ($p < 0.001$), DEXA lean mass ($p < 0.001$), and DEXA fat-free mass ($p < 0.001$). A significant interaction and subsequent post hoc analysis of the DEXA lean mass ($p = 0.03$) and DEXA fat-free mass ($p = 0.03$) data revealed that the CR group demonstrated significantly greater increases after 4 weeks of supplementation and training when compared to CRP (Figure 2).

Strength and Performance Measures

Table 6 presents the strength and performance measures assessed throughout the study. Significant main effect increases were found in BP 1RM and LP 1RM, indicating that both groups accrued positive training adaptations.

Table 6. Maximal strength (1RM/kg^{-1}), Wingate anaerobic capacity, and relative isokinetic values for the creatine + D-pinitol (CRP) and creatine (CR) groups normalized to body mass.

Variable	Group*	Day 0 (T0)	Day 7 (T1)	Day 28 (T2)	Significance	
Relative leg press 1RM (kg/kg^{-1})	CRP	3.75 ± 0.8	3.95 ± 0.7	3.98 ± 0.8	Group	0.14
	CR	4.21 ± 0.7	4.36 ± 0.9	4.49 ± 0.7	Time	0.002
					G × T	0.74
Relative bench press 1RM (kg/kg^{-1})	CRP	1.26 ± 0.2	1.26 ± 0.2	1.33 ± 0.17	Group	0.84
	CR	1.25 ± 0.2	1.28 ± 0.2	1.28 ± 0.23	Time	0.003
					G × T	0.13
Wingate peak power(watts/kg^{-1})	CRP	17.4 ± 2.4	17.8 ± 2.5	17.9 ± 2.7	Group	0.88
	CR	17.3 ± 3.0	17.9 ± 2.8	17.4 ± 2.6	Time	0.27
					G × T	0.65
Total work (joules/kg^{-1})	CRP	276 ± 24	280 ± 23	278 ± 22	Group	0.92
	CR	276 ± 26	276 ± 25	279 ± 27	Time	0.56
					G × T	0.58
Peak torque @ 60 degrees/s^{-1} extension (N/m/kg^{-1})	CRP	2.67 ± 0.4	2.55 ± 0.4	2.62 ± 0.5	Group	0.62
	CR	2.51 ± 0.5	2.55 ± 0.5	2.51 ± 0.5	Time	0.79
					G × T	0.45
Peak torque @ 180 degrees/s^{-1} extension (N/m/kg^{-1})	CRP	1.99 ± 0.3	1.98 ± 0.3	2.05 ± 0.4	Group	0.93
	CR	1.93 ± 0.4	2.06 ± 0.4	2.00 ± 0.4	Time	0.38
					G × T	0.25
Peak torque @ 300 degrees/s^{-1} extension (N/m/kg^{-1})	CRP	1.68 ± 0.1	1.68 ± 0.3	1.78 ± 0.3	Group	0.65
	CR	1.56 ± 0.3	1.71 ± 0.4	1.71 ± 0.4	Time	0.02
					G × T	0.26

*Creatine + D-pinitol (CRP: $n = 12$) and creatine (CR: $n = 12$) groups. Data are means + *SD*.

Table 7. Selected markers of protein metabolism and muscle/liver enzymes for the creatine monohydrate + D-pinitol (CRP) and creatine (CR) groups.

Variable	Group*	Week 0 (T0)	Week 4 (T2)	Significance	
Creatine kinase (U/L)	CRP	189 ± 95	240 ± 169	Group	0.29
	CR	325 ± 301	242 ± 146	Time	0.73
				G × T	0.17
Lactate dehydrogenase (U/L)	CRP	143 ± 26	146 ± 23	Group	0.76
	CR	143 ± 26	153 ± 41	Time	0.32
				G × T	0.60
Aspartate aminotransferase (U/L)	CRP	24.9 ± 10.1	26.6 ± 15.9	Group	0.73
	CR	25.2 ± 6.0	23.6 ± 6.5	Time	0.96
				G × T	0.23
Alanine aminotransferase (U/L)	CRP	19.8 ±5.9	19.5 ± 7.0	Group	0.46
	CR	22.4 ± 10.0	21.3 ± 7.0	Time	0.53
				G × T	0.71
Total protein (g/L)	CRP	75.3 ± 5.0	73.9 ± 4.3	Group	0.40
	CR	76.7 ± 4.3	75.3 ± 4.1	Time	0.09
				G × T	0.93
GGT (U/L)	CRP	15.6 ± 3.1	15.8 ± 4.6	Group	0.39
	CR	16.8 ± 3.1	17.0 ± 3.5	Time	0.68
				G × T	0.98
Creatinine (μmol/L)	CRP	105.2 ± 14.1	118.5 ± 10.6	Group	0.73
	CR	102.5 ± 8.84	118.5 ± 15.9	Time	<0.001
				G × T	0.64
BUN (mmol/L)	CRP	5.9 ± 1.2	6.0 ± 1.5	Group	0.61
	CR	6.1 ± 1.2	6.4 ± 1.5	Time	0.47
				G × T	0.84
BUN/creatinine ratio	CRP	14.3 ± 3.7	12.6 ± 3.5	Group	0.54
	CR	14.8 ± 2.9	13.8 ± 4.3	Time	0.08
				G × T	0.65
Uric acid (μmol/L)	CRP	345 ± 59	339 ± 71	Group	0.12
	CR	315.2 ± 89	280 ± 59	Time	0.07
				G × T	0.12

*Creatine + D-pinitol (CRP: $n = 12$) and creatine (CR: $n = 12$) groups. Data are means + *SD*.

Serum Measures of Clinical Safety

Table 7 presents selected markers of catabolism (e.g., creatinine, blood urea nitrogen, total protein, and uric acid) and muscle/liver enzymes (e.g., alanine aminotransferase, aspartate aminotransferase, creatine kinase, lactate dehydrogenase. and gamma-glutamyl transferase). Significant main effects ($p < 0.05$) were observed for serum creatinine; however, the reported values were within clinically accepted normative values (7).

Discussion

The purpose of this study was to examine the effects of creatine supplementation with and without the addition of D-pinitol on changes in exercise performance, body composition, and clinical safety following 4 weeks of resistance training. A primary weakness of the present study was the 4-week duration of the resistance training program. Studies have suggested that any physiological adaptations presented were early-phase adaptations to the supplementation and training programs and may or may not have been entirely physiological adaptations (29). To minimize this confounding effect, participants for this study were screened to ensure they were already completing resistance training using both their upper and lower bodies. Training history records of our participants indicated a training history of 4 days per week for an average of 9 months. An additional criticism of the present research design may have been the exclusion of a control group. This decision was made a priori because scores of published original investigations and reviews have clearly illustrated the ergogenic characteristics of creatine supplementation (13,21,23,24). Nonetheless, significant main effects for strength and body composition to improve were found, suggesting positive adaptations to the resistance training program and creatine supplementation. A significantly greater increase in lean and fat-free mass were found in the CR group when compared to the CRP group ($p = 0.03$; Figure 2). Furthermore, retention of creatine was substantially improved in both creatine supplementation groups with no between-group changes. Additionally, both

supplementation protocols were well tolerated and did not result in any significant changes of clinical safety markers.

Retention of creatine significantly increased in CR (44.3 ± 15.1%; $p < 0.001$) and CRP (49.8 ± 20.8%; $p < 0.001$) groups, although there was no significant difference between groups. This finding contrasts previous findings by Greenwood et al. (14), who reported significantly greater levels of creatine retention with CRP using a similar dosing protocol. Although differences in analytical techniques to assess urinary creatine levels may explain some of this discrepancy, our findings challenges the previous notion that adding D-pinitol to CR does in fact promote further increases in creatine retention.

Total scanned mass, lean mass, and fat-free mass increased in both groups after 4 weeks of following the supplementation and resistance training protocols. Significant interactive findings for lean and fat-free mass were found with the CR group reporting greater changes for lean mass (CR: 2.1 ± 0.1 kg vs. CRP: 0.9 ± 0.1 kg; $p = 0.03$) and fat-free mass (CR: 2.1 ± 0.1 kg vs. CRP: 0.9 ± 0.1 kg; $p = 0.03$; Figure 2). Dietary intake levels were similar among groups, negating this factor as a means to explain this change (Table 4). These results are consistent with previous published reports that show greater increases in lean tissue mass following creatine supplementation while resistance training (24,28), although these findings do not explain why the addition of D-pinitol may have negated some of the changes in lean mass. Many investigators have researched the impact of adding various forms of creatine (e.g., ethyl ester, solubilized, etc.) in conjunction with other nutrients, although this is the first study to investigate the impact of adding D-pinitol to creatine on physiological adaptations (e.g., strength and body composition) while following a resistance training program. Considering the previous data that suggested D-pinitol enhanced creatine retention (14), we hypothesized the addition of D-pinitol would increase creatine retention and subsequently promote the accretion of lean mass and enhance training adaptations. Thus, it appears that the 4-week duration of our study may not have been an adequate duration or the inclusion of D-pinitol may have acted in a negative fashion over this time period to limit gains in lean tissue accretion with exercise training, although mechanisms supporting this contention remain unknown. Considering D-pinitol's purported role in mimicking insulin action or acting as an insulin-sensitizing agent (3), this finding is counterintuitive to our initial hypothesis. Nonetheless, future mechanistic approaches should include examining its effects (whether synergistic or dysregulatory) on the insulin-signaling pathway involving the downstream activation of the Akt-mTOR-p70S6 kinases (9,15) to further elucidate the downstream impact of D-pinitol's insulin signaling.

As previously reported, relative bench press 1RM and leg press 1RM increased significantly ($p < 0.05$) in both groups across time (23). Kelly et al. reported an increase in bench press 3RM and an increased number of repetitions of the bench press over multiple sets in 18 powerlifters following a 26-day creatine supplementation protocol (20 $g/d^{-1} \times 4$ day; 5 $g/d^{-1} \times 22$ day) that was similar to the supplementation protocol in the current study (21). Another study that followed 42 collegiate football players during a 5-week creatine supplementation protocol (10–20 g/d^{-1} with and without pyruvate) showed improved gains in the 1RM bench press, combined 1RM squat and bench press, vertical jump power output, and peak rate of force development (30). Although CRP did not elicit greater training adaptations compared to CR, continuing this supplementation regimen for an additional 4 to 8 or more weeks may or may not be advantageous in further promoting positive training adaptations–a finding that is consistent in other scientific reports using longer supplementation periods (4). However, these results remain to be determined.

In conjunction with other previous studies (12,13), no clinically or statistically significant changes occurred relative to renal or hepatic function and markers of protein metabolism. Furthermore, the addition of D-pinitol to the creatine regimen was well tolerated and does not appear to invoke any negative health consequence from its use in healthy, resistance-training males, which is consistent with the available literature (5,6,14).

Results from the present study suggest that the combination of resistance training and creatine supplementation increases strength and improves body composition. The further addition of D-pinitol, however, did not provide any further benefit and may have actually negated changes in body composition. The ingestion of CR, however, did promote increases in lean mass in comparison to CRP (Figure 2). Significant but equal increases in all groups in relative strength and body composition parameters demonstrated positive adaptations to the resistance training program and creatine ingestion. Additionally, both supplementation regimens were well tolerated and appear to be clinically safe. Careful consideration of these findings should be made because the short duration of investigation may have not allowed for an adequate amount of time for physiological adaptations to the resistance training program (29).

Practical Applications

Improving power production and explosive potential is a primary attribute for many sporting events. Creatine monohydrate supplementation is a popular dietary strategy used by athletes and coaches to improve these attributes. Careful interpretation of our data should be considered because of the short term (4 weeks) of our resistance training program. Data from this study suggest that supplementation was safe and well tolerated while promoting improvements in lean tissue, although the addition of D-pinitol did not provide any additional effect over creatine alone. Coingestion of creatine with large amounts of sugar increases the caloric load associated with supplementation and may be detrimental for athletes particularly concerned with changes in their body

weight (e.g., wrestlers, dancers, swimmers, gymnasts, strength trainers, etc.). The findings from this study, however, do not support the inclusion of D-pinitol to creatine as a means to increase lean body mass and performance when compared to supplementing with just creatine monohydrate. Future research in clinical and aging populations may prove efficacious; however, these data currently are lacking.

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References

1. Almada, A and Kreider, RB. Comparison of the reliability of repeated whole body DEXA scans to repeated spine and hip scans. *J Bone Miner Res* 14: S369, 1999.
2. Baechle, TR and Earle, RW. *Essentials of Strength Training and Conditioning*. Champaign, IL: Human Kinetics, 2005
3. Bates, SH, Jones, RB, and Bailey, CJ. Insulin-like effect of pinitol. *Br J Pharmacol* 130: 1944–1948, 2000.
4. Buford, TW, Kreider, RB, Stout, JR, Greenwood, M, Campbell, B, Spano, M, Ziegenfuss, T, Lopez, H, Landis, J, and Antonio, J. International society of sports nutrition position stand: Creatine supplementation and exercise. *J Int Soc Sports Nutr* 4: 6, 2007.
5. Campbell, WW, Haub, MD, Fluckey, JD, Ostlund Jr, RE, Thyfaulty, JP, Morse-Carrithers, H, Hulver, MW, and Birge, ZK. Pinitol supplementation does not affect insulin-mediated glucose metabolism and muscle insulin receptor content and phosphorylation in older humans. *J Nutr* 134: 2998–3003, 2004.
6. Davis, A, Christiansen, M, Horowitz, JF, Klein, S, Hellerstein, MK, and Ostlund Jr, RE. Effect of pinitol treatment on insulin action in subjects with insulin resistance. *Diabetes Care* 23: 1000–1005, 2000.
7. Deska Pagana, K and Pagana, TJ. *Mosby's Manual of Diagnostic and Laboratory Tests*. St. Louis, MO: Mosby, Inc., 2002.
8. Fuller, NJ, Jeff, SA, Laskey, MA, Coward, WA, and Elia, M. Four-component model for the assessment of body composition in humans: Comparison with alternative methods, and evaluation of the density and hydration of fat-free mass. *Clin Sci (Lond)* 82: 687–693, 1992.
9. Glass, DJ. Signalling pathways that mediate skeletal muscle hypertrophy and atrophy. *Nat Cell Biol* 5: 87–90, 2003.
10. Green, AL, Hultmnan, E, MacDonald, IA, Sewell, DA, and Greenhaff, PL. Carbohydrate ingestion augments skeletal muscle creatine accumulation during creatine supplementation in humans. *Am J Physiol* 271: E821–E826, 1996.
11. Green, AL, Simpson, EJ, Littlewood, JJ, MacDonald, IA, and Greenhaff, PL. Carbohydrate ingestion augments creatine retention during creatine feeding in humans. *Acta Physiol Scand* 158: 195–202, 1996.
12. Greenwood, M, Kreider, RB, Greenwood, L, and Byars, A. Cramping and injury incidence in collegiate football players are reduced by creatine supplementation. *J Athl Train* 38: 216–219, 2003.
13. Greenwood, M, Kreider, RB, Melton, C, Rasmussen, C, Lancaster, S, Cantler, E, Milnor, P, and Almada, A. Creatine supplementation during college football training does not increase the incidence of cramping or injury. *Mol Cell Biochem* 244: 83–88, 2003.
14. Greenwood, M, Kreider, RB, Rasmussen, C, Almada, A, and Earnest, CP. D-pinitol augments whole body creatine retention in man. *JEP Online* 4: 41–47, 2001.
15. Guttridge, DC. Signaling pathways weigh in on decisions to make or break skeletal muscle. *Curr Opin Clin Nutr Metab Care* 7: 443–450, 2004.
16. Harris, RC, Soderlund, K, and Hultman, E. Elevation of creatine in resting and exercised muscle of normal subjects by creatine supplementation. *Clin Sci (Lond)* 83: 367–374, 1992.
17. Haughland, RB and Chang, DT. Insulin effect on creatine transport in skeletal muscle (38464). *Proc Soc Exp Biol Med* 148: 1–4, 1975.
18. Holman, GD and Kasuga, M. From receptor to transporter: Insulin signaling to glucose transport. *Diabetologia* 40: 991–1003, 1997.
19. Horber, FF, Thomi, F, Casez, JP, Fonteille, J, and Jaeger, P. Impact of hydration status on body composition as measured by dual energy x-ray absorptiometry in normal volunteers and patients on hemodialysis. *Br J Radiol* 65: 895–900, 1992.
20. Kellie, EE. Measurement of bone density with dual-energy x-ray absorptiometry (DEXA). *JAMA* 267: 286–294, 1992.
21. Kelly, VG and Jenkins, DG. Effect of oral creatine supplementation on near maximal strength and repeated sets of high-intensity bench press exercise. *J Strength Cond Res* 12: 109–115, 1998.
22. Klesges, RC, Ward, KD, Shelton, ML, Applegate, WB, Cantler, ED, Palmieri, GM, Harmon, K, and Davis, J. Changes in bone mineral content in male athletes. Mechanisms of action and intervention effects. *JAMA* 276: 226–230, 1996.
23. Kreider, RB. Effects of creatine supplementation on performance and training adaptations. *Mol Cell Biochem* 244: 89–94, 2003.
24. Kreider, RB, Ferreira, M, Wilson, M, Grindstaff, P, Plisk, S, Reindardy, J, Cantler, E, and Almada, A. Effects of creatine supplementation on body composition, strength and sprint performance. *Med Sci Sports Exerc* 30: 73–82, 1998.
25. Kreider, RB, Melton, C, Rasmussen, C, Greenwood, M, Lancaster, S, Cantler, E, Milnor, P, and Almada, A. Long-term creatine supplementation does not significantly affect clinical markers of health in athletes. *Mol Cell Biochem* 244: 95–104, 2003.
26. Mazess, RB, Barden, HS, Bisek, JP, and Hanson, J. Dual-energy x-ray absorptiometry for total-body and regional bone-mineral and soft-tissue composition. *Am J Clin Nutr* 51: 1106–1112, 1990.
27. Narayanan, CR, Joshi, DD, Mudjummer, AM, and Dhenke, VV. Pinitol: A new anti-diabetic compound from the leaves of bougainvillea spectabilis. *Curr Sci* 56: 139–141, 1987.
28. Peters, BM, Lantz, CD, and Mayhew, JL. Effect of oral creatine monohydrate and creatine phosphate supplementation on maximal strength indices, body composition and blood pressure. *J Strength Cond Res* 13: 3–9, 1999.
29. Staron, RS, Karapondo, DL, Kraemer, WJ, Fry, AC, Gordon, SE, Falkel, JE, Hagerman, FC, and Hikida, RS. Skeletal muscle adaptations during early phase of heavy-resistance training in men and women. *J Appl Physiol* 76: 1247–1255, 1994.
30. Stone, MH, Sanborn, K, Smith, LL, O'Bryant, HS, Hoke, T, Utter, AC, Johnson, RL, Boros, R, Hruby, J, Pierce, KC, Stone, ME, and Garner, B. Effects of in-season (5 weeks) creatine and pyruvate supplementation on anaerobic performance and body composition in American football players. *Int J Sport Nutr* 9: 146–165, 1999.
31. Syrotiuk, DG and Bell, GJ. Acute creatine monohydrate supplementation: A descriptive physiological profile of responders vs. Nonresponders. *J Strength Cond Res* 18: 610–617, 2004.