

# CREATINE MONOHYDRATE SUPPLEMENTATION - A LITERATURE REVIEW

Researched and composed by Eamonn Flanagan, BSc., CSCS

## INTRODUCTION

Phosphocreatine plays a central role in the maintenance of power output in prolonged high intensity exercise. Depletion of muscle phosphocreatine during intense exercise is associated with the onset of muscle fatigue during such exercise (Rossiter 1996). Increasing the phosphocreatine content of muscle through creatine monohydrate supplementation has been demonstrated to increase subjects' work output during intermittent bouts of anaerobic activity (Balsom 1993, 1995, Greenhaff 1995, Rossiter 1996, Flanagan 2004).

Based on such research, creatine monohydrate has become one of the most widely used nutritional supplements in the world with an annual estimated global consumption of 2.7 million kilograms (Williams 1999). In the U.S.A. alone, annual sales of creatine monohydrate totalling over \$400 million have been reported since the year 2000 (Bird 2003).

Chevreul, a French scientist, first discovered creatine as a constituent of meat in the 1830s (Balsom 1994, Bird 2003). Early 20<sup>th</sup> century studies examined the effect of creatine supplementation or creatine "feeding". Folin and Denis (1910s) demonstrated that creatine feeding could increase muscle creatine content in cats by upwards of 70%. In the 1920s, scientists continued to quantify creatine storage and retention in the body. An experimenter named Chanutin found that a large quantity of creatine was retained in the body when fed to man (Greenhaff 1995, Bird 2003).

Creatine supplementation has been suggested as a mechanism to load the muscle with creatine and increase its total storage in both its free and phosphorylated forms (termed "creatine" and "phosphocreatine" respectively). This theoretically serves to improve the ability to produce energy during high intensity exercise bouts and/or enhance the ability to recover from intense exercise.

The following literature review will outline the role of creatine within the body, how the body's creatine pool can be manipulated through dietary creatine monohydrate supplementation and how such supplementation can benefit athletic performance. This review will also touch on safety issues regarding creatine monohydrate supplementation as well as providing practical guidelines for athletes wishing to begin creatine monohydrate supplementation.

## MUSCLE CONTRACTION, CREATINE AND MUSCLE ENERGY METABOLISM

Muscle contraction is fuelled by free [adenosine-tri-phosphate](#) (ATP) as the immediate energy source (Brooks 2000, Williams 1999). Contraction and power production in muscle cells depends on the cyclic formation of cross bridges. In striated skeletal muscle this depends on the interaction between myosin, thick filaments, and actin, thin filaments.

There are four main steps in the cross-bridge cycle.

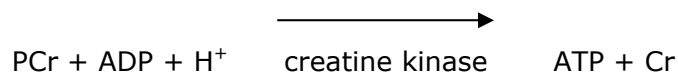
1. The attachment of myosin to actin
2. The movement of the myosin head producing tension in the actin filament
3. The detachment of myosin from actin
4. The energizing of myosin for reattachment to the next actin binding site

ATP plays a key role in the third and fourth step of the crossbridge cycle. In step 3, it binds with myosin to detach the filament from actin. In step 4, following the separation of actin and myosin, the ATP bound to myosin is hydrolysed. The free energy from this hydrolysis re-energises the myosin filament and the crossbridge cycle can be repeated.

For more information on muscular contraction, refer to [The Anatomy of A Muscle](#).

As free ATP stores are limited, they must be regenerated by other metabolic processes in the cells, in order to sustain high muscle power output. The second cellular source of immediate energy is phosphocreatine (PCr) (Brooks 2000). PCr provides a reserve of energy to regenerate ATP, which is consumed as the result of muscle contraction. PCr's rapid utilization buffers the momentary lag in energy production from glycolysis (Greenhaff 1995 – see table 1 below). Creatine (Cr) is essential to this process as approximately two-thirds of creatine stored in muscle is in the form of PCr (Greenhaff 1995, Williams 1999).

During times of increased energy demand, such as during high intensity exercise, PCr, in the presence of the enzyme creatine kinase, is cleaved of its phosphate. This phosphate is donated to degraded ATP, adenosinediphosphate (ADP), and ATP is regenerated.



Free ATP, augmented by the PCr energy pathway, also known as the alactic energy pathway, sustains maximal muscle contraction for approximately 5 – 15 seconds (Greenhaff 1995, Brooks 2000). And Greenhaff 1995 reports that the rate of PCr utilization peaks after only 1.28s and declines thereafter (table 1).

	<b>ATP Production</b> (mmol.s <sup>-1</sup> .kg <sup>-1</sup> dm)
--	--

Duration of Stimulation (s)	PCr	Glycolysis
0-1.3	9.0	2.0
0-2.6	7.5	4.3
0-5	5.3	4.4
0-10	4.2	4.5
10-20	2.2	4.5
20-30	0.2	2.1

Table 1.

*Rates of anaerobic ATP production from phosphocreatine and glycolysis during maximal contraction in human skeletal muscle (reproduced from Greenhaff 1995)*

The contributions of the varying metabolic pathways used over time during exercise is discussed further in ABC's article "[Energetic Transference Occurring in the Biosphere Part II](#)". To fully understand the PCr system's place in energy provision to an exercising body it is worth reviewing this article particularly noting the following discussion:

Astrand and Rodhal (1977) and Gollnick and Hermansen (1973) have reviewed the time energy continuum at various intensities. Evidence indicates that in the first 10 seconds, the phosphocreatine system is dominant; at 30 seconds, anaerobic metabolism is called upon for 80% of the energy requirements, but glycolysis is now much more prevalent. At this point, 33% of the energy is supplied by the alactic anaerobic system and 47% by glycolysis. At one minute, glycolysis is used at a slightly heightened extent, as well as aerobic metabolism, while the ATP-PC system continues to decrease. At five minutes, aerobic metabolism dominates as much as anaerobic metabolism did at 30 seconds. Now, 80% of the energy utilized is from aerobic work, and approximately 20% is from anaerobic metabolism; 3, and 17% coming from phosphocreatine and glycolysis, respectively. The longer exercise continues the more aerobic metabolism is called upon. It should be noted that these results can and do vary among individuals; however, this is generally an accurate account.

## THE BIOSYNTHESIS AND DISTRIBUTION OF CREATINE

Daily demand for creatine is met through two processes, either by absorption of Cr taken in through diet or by "de novo biosynthesis" (Balsom 1994, Wyss 2000, Williams 1999). In the process of de novo biosynthesis, creatine is produced by the body itself. It is formed outside of the muscle itself and then transported to the muscle via the bloodstream.

The biosynthesis of Cr involves three amino acids: arginine, glycine and methionine. The de novo creation of Cr is thought to take place in two stages, the first taking

place in the kidney with the second occurring in the liver. Following bio-synthesis, creatine is exported from the liver and accumulated in creatine kinase containing cells (such as skeletal muscle) (Wyss 2000).

The uptake of creatine into the muscle occurs actively against a concentration gradient. Following biosynthesis or dietary intake, a higher level of creatine is in the blood compared with the muscle. Resultantly, blood borne creatine crosses the muscle cell membrane. From the blood, it appears creatine's transportation into skeletal muscle is aided by specific, creatine transporter molecules (Wyss 2000). This specific creatine transporter (CreaT) has only recently been identified in skeletal muscle and appears to be highly specific for creatine, meaning it does not facilitate other substances entry to the muscle such as protein (Williams 1999). The role and relevance of CreaT is discussed further on in this review.

Approximately 60 percent of muscle total Cr store exists in the form of phosphocreatine (Greenhaff 1995, Williams 1999). Due to its phosphorylated state, it is unable to pass through muscle membranes. This traps the Cr, keeping it exactly where we want it: within the muscle (Wyss 2000). It should also be noted here that Creatine is an osmotically active substance. This means that as creatine is drawn into the muscle cells water is drawn in with it (Wyss 2000). Without enough available water within the body, creatine will not be properly stored within the muscle.

The total creatine content (TCr) refers to the combined amount of creatine in both its free and phosphorylated forms. The TCr content of muscle cells is dependent on rates of Cr uptake, Cr trapping and rates of Cr loss via creatinine (Snow 2003). Creatine within the body is continually broken down, excreted and regenerated and its metabolic by-product is termed creatinine. Muscular Cr and PCr are converted at an almost steady rate of ~2% of total Cr content per day to creatinine (Crn) which diffuses out of the muscle cells and is excreted by the kidneys into the urine (Williams 1999, Wyss 2000).

With creatine so important during short duration high intensity exercise, increasing the body's muscles creatine pool can be highly useful as a means of increasing subjects' work capacity during bouts of anaerobic activity. But how can this increase in TCr be achieved? Supplementation methods are discussed in our next section.

## **CREATINE SUPPLEMENTATION AND MUSCLE CREATINE CONCENTRATION**

Creatine supplementation, by the oral administration of creatine in its monohydrate form has been shown to increase the muscle pool of creatine. A popular and effective method of supplementation, in the published literature, has been a 100g acute creatine loading, consisting of ~20-25g/day of creatine monohydrate, divided into 4-5 doses, administered for 5-7 days. Hultman (1996), in a comparison of differing creatine feeding protocols, investigated the effects of creatine supplementation of 20g/day in 5g doses for 6 days. Muscle TCr was elevated by ~20% after this supplementation protocol. Greenhaff (1994) demonstrated that 20g/day in 5g doses for 5 days was necessary to elevate muscle TCr concentration in 5 of 8 subjects by ~25%. In this study, muscle creatine uptake was monitored directly through muscle biopsy of the vastus lateralis. Balsom (1995), administered 20g/day in 5g doses for 6 days and increased mean TCr concentration significantly. Izquierdo (2002) also administered a feeding regime of that 20g/day in 5g doses, but for 5 days, and saw

a comparable increase in total TCr. The efficacy of this dosage, as a means of increasing TCr, was validated indirectly with monitoring of creatine and creatinine levels in subjects' urine.

On ingestion of 5g of monohydrate the plasma level of creatine has been shown to rise between five- and ten-fold after approximately 1 hour (Balsom 1994). This increase in plasma creatine content in turn increases the blood/muscle concentration gradient. Resultantly, more blood borne creatine is transported and trapped in the muscle cell. With a half-life of 1-1.5 hours, blood creatine levels remains elevated for a short time period (Havenetidis 2003). Repeating this dosage 4-5 times per day at ~4 hour intervals, therefore, keeps plasma creatine concentration constantly elevated and aids the movement of creatine from the blood into the muscle cell at a constant rate throughout the day.

While the greatest Cr uptake appears to occur within the first two to three days of supplementation with such a "loading" feeding protocol (Hultman 1996, Rossiter 1996, Flanagan 2004), administration periods shorter than 5 days have not been shown to effectively increase the muscle creatine pool. In a study by Odland (1996), subjects ingested 20g/day in 5g doses for just 3 days. Needle biopsies from the vastus lateralis revealed such a feeding strategy had no significant effect on the elevation of muscle PCr concentration.

Creatine supplementation, individualised to subjects' body mass, has been shown to significantly increase the muscular TCr pool. Rossiter (1996) and Flanagan (2004) administered creatine dosages of  $0.25\text{g}\cdot\text{kg bodymass}^{-1}$  each day divided into four doses for five days. To elaborate, 2.2 kilograms= 1 pound. Therefore, a 200 pound man (90 kg) would be administered approximately 22 grams of creatine per day in these experiments. In both studies, creatine uptake was calculated as the difference between the amount of creatine fed and the amount recovered in urine during each 24 hour period of supplementation. This protocol, in both studies, effectively raised muscle TCr.

This individualised feeding mechanism is largely similar to the 100g acute creatine loadings already detailed (Greenhaff 1994, Hultman 1996, Izquierdo 2002). For a standard 75kg (165 lb) male, the feeding pattern equals 18.75g in 4 doses for 5 days. However, the standardization to body mass allows for an increased supplementation for larger individuals or a reduced amount of supplementation for particularly small individuals and may be a logical improvement on the "one size fits all" administrations evidenced by Greenhaff (1994) and Izquierdo (2002), among others. At the very least, this would be a useful supplementation protocol to follow for particularly large or particularly small individuals.

Hultman (1996), demonstrated that continuous low dose creatine supplementation (3g/day, in one serving over 28 days) can, in the long term be as effective at increasing muscle TCr as the 100g acute creatine loading method. Burke (2000) in a double blind study utilising a large subject base (n=41) detailed the ergogenic effects following a continuous low dose supplementation protocol of 7.7g/day for 21 days. Subjects performed more total work until fatigue, experienced significantly greater improvements in peak force and peak power and maintained elevated mean peak power for a longer period of time when exposed to low dose creatine supplementation in tandem with training as opposed to training alone.

Hultman (1996) rightly comments however that while the low-dose method will, over time, elevate TCr comparably to the acute method, the 100g acute method is a more rapid mechanism to increase the muscle TCr store than continuous low dose supplementation protocols and should be favoured.

It is important to note that there is considerable variability in the increase of muscle creatine content following supplementation. Some individuals are "non-responders" and experience little or no increase in muscle creatine content following usually effective loading protocols. Greenhaff (1994) found a dosage sufficient to elevate muscle TCr concentration in 5 of 8 subjects by ~25% had little effect on muscle TCr concentration in 3 non-responding subjects (see subjects 5, 6 and 8 in figure 1 below). Others individuals can be "high-responders" and creatine monohydrate supplementation can illicit a >30% increase in muscle TCr content (Rawson 2003). It is not entirely clear why there is such large inter-subject variability in muscle creatine content changes following supplementation. The strongest determinant of how much creatine is taken up into muscle appears to be the initial creatine content in that muscle (Greenhaff 1994, Rawson 2003). Published evidence demonstrates subjects with lower resting muscle creatine contents have the largest magnitude of increase following supplementation, while subjects with higher creatine contents will experience little or no increase (Greenhaff 1994, Rawson 2003, Casey 2000). Greenhaff (1995) comments that individuals with below average basal TCr contents ( $120 \text{ mmol.kg dry weight}^{-1}$ ) can expect creatine supplementation to induce a >25% increase in the muscle creatine pool.

Human muscle also appears to have an upper limit to muscle creatine content (thought to be approximately  $160 \text{ mmol.kg dry weight}^{-1}$ ) which supplementation cannot exceed (Balsom 1994, 1995, Greenhaff 1995, Hultman 1996). Some evidence suggests that this upper limit can be exceeded under certain conditions. Harris (1992), while examining the effect of exercise on muscle creatine uptake, reported a TCr content of  $> 180 \text{ mmol.kg dry weight}^{-1}$  in one subject post-supplementation (cited by Wyss 2000). Additional evidence supporting such potentially high muscle TCr contents is lacking and in the context of the present study  $160 \text{ mmol.kg dry weight}^{-1}$  is considered a more reliable value of muscle creatine content's upper limit. With this in mind, athletes should not exceed recommended supplementation dosages. Increasing supplementation dosages will not further increase the muscle creatine pool beyond this proposed upper limit, however it will increase the demand on the kidneys in attempting to excrete this additional creatine as creatinine in the urine.

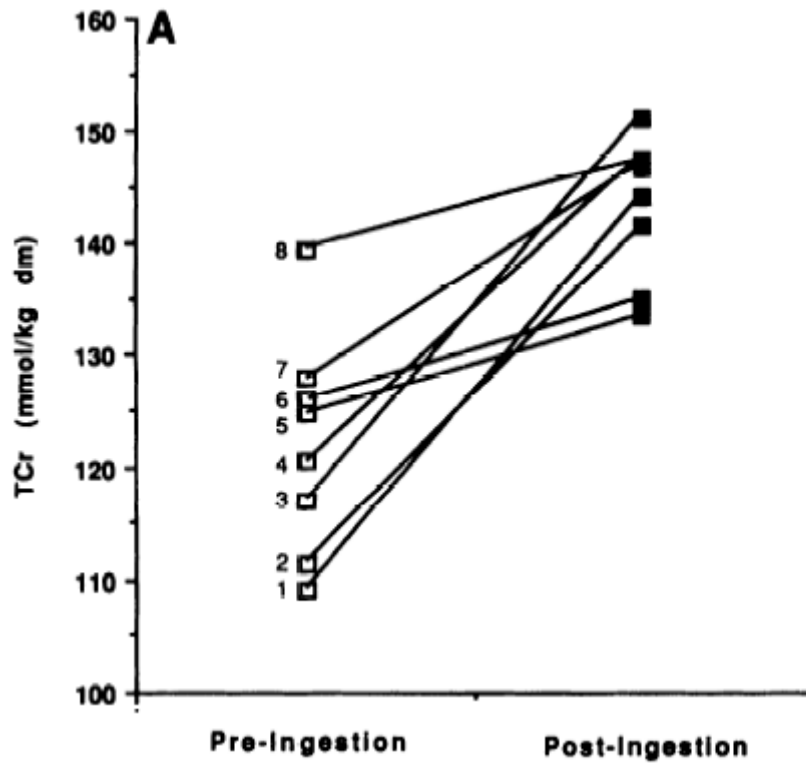


Figure 1.

*Mixed muscle total creatine concentration (TCr) in individual subjects before and after supplementation. Subjects were numbered 1 through 8 according to their initial muscle total creatine concentration. (reproduced from, and all credit to the research of Greenhaff 1994)*

Figure 2 below illustrates subjects with low baseline muscle PCr concentrations had ~50% increase in PCr levels following supplementation. Conversely, supplementation incurred only a ~10% increase in PCr concentration in those with large baseline values.

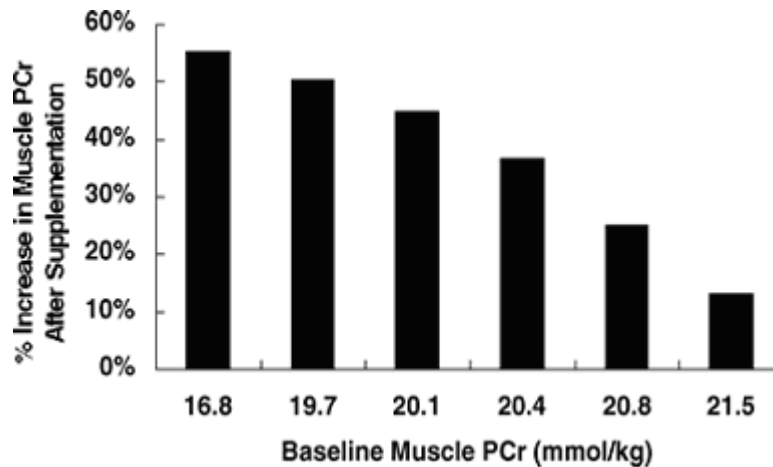


Figure 2.

*Baseline levels of muscle phosphocreatine influence the magnitude of the increase in muscle phosphocreatine following creatine supplementation (reproduced from, and credit to the research of Rawson 2003)*

Other factors can influence the magnitude of creatine uptake however. For example, as we previously mentioned creatine is an osmotically active substance, requiring water influx for it to be drawn into and stored within the muscle. An individual's hydration status would therefore influence the amount of creatine taken up by the muscle. A number of important other factors can also have effects on uptake and these are discussed in the following section.

## **FACTORS INFLUENCING CREATINE UPTAKE IN SKELETAL MUSCLE**

### **CARBOHYDRATE INGESTION**

Green (1996a), examined the effect of simple carbohydrate (CHO) ingestion during creatine supplementation. Volunteers undergoing a loading protocol of 5g\*4/day for five days, were assigned to two groups, a control group and a CHO group who consumed 500ml of an 18% carbohydrate solution 30 minutes after each creatine monohydrate dosage.

The CHO group exhibited a significantly greater muscle concentration of free Cr and PCr and resultantly a significantly greater TCr concentration than the control group (which itself did show a significant increase in Cr, PCr and TCr concentrations in comparison to pre-supplementation values). The authors postulate that the significant augmentation of muscle Cr uptake when creatine is ingested with CHO probably occurs as a result of the stimulatory effect of insulin on muscle Cr transport.

Steenge (1998), examined the effect of directly infusing insulin at varying rates with ingestion of creatine monohydrate. The findings validate the assumption that the augmentation of creatine uptake with co-ingestion of CHO is likely due to an insulin-mediated increase in muscle creatine transport. Steenge's results demonstrated that

ingestion of 100g of CHO is necessary to stimulate a sufficiently large insulin response to stimulate muscle Cr transport. Importantly however, there is currently a dearth of research pertaining to insulin's direct effect on the role of CreaT (the specific creatine transporter molecule). Such work would be necessary to firmly establish the specific role of CHO ingestion and the insulin response, regarding creatine transport and enhanced intra-muscular creatine accumulation.

An ingestion of such levels of excess dietary CHO, as administered by Green (1996a), however appears excessive and Green's protocol equates to an intake of ~92.5g for every 5g of creatine monohydrate ingested and would amount to a daily carbohydrate excess of 370g, amounting to a potential energy surplus of approximately 1500 kcals for each day of a loading phase. Such a caloric surplus could prove problematic for any athletes adhering to a strict nutritional plan especially those involved in aesthetic sports such as bodybuilding and weight categorised sports such as wrestling and Olympic weightlifting. This problem could be further increased considering creatine supplementation is already associated with weight gain associated with an increase in water retention.

Furthermore, research has shown that while supplementing with creatine and CHO together may increase TCr compared with Cr alone, the performance effect induced by this extra CHO intake is not significantly greater than the Cr alone method.

Theodorou (2005) examined the effects of acute creatine loading with or without carbohydrate on repeated bouts of maximal swimming. Each swimmer ingested five 5 g doses of creatine for 4 days, with the Cr + CHO group also ingesting 100 g of simple CHO 30 minutes after each dose of creatine. Performance was measured twice at "baseline" (prior to creatine feeding) and then again within 48 hours after the creatine feeding intervention. All subjects swam faster after either creatine loading regimen however, there was no difference in the extent of improvement of performance between groups. These findings suggest that no performance advantage was gained from the addition of carbohydrate to a creatine-loading regimen in the swimmers.

## **EXERCISE**

It has been suggested that combining creatine supplementation with exercise can further increase skeletal muscle Cr uptake. When combined with exercise training, Cr supplementation has been demonstrated to enhance exercise performance more so than exercise training alone or Cr supplementation alone (Brannon 1997). Such an exercise-induced effect, was also reported by Harris (1992, cited by Williams 1999).

Interestingly however, exercise may provide a comparable benefit for increasing muscle TCr to using a creatine-carbohydrate supplementation strategy. Green (1996b) reported that creatine retention in the muscle was similar when exercise, prior to ingestion, was introduced, compared to creatine ingestion with simple carbohydrates.

## **CAFFEINE**

Caffeine is an ergogenic aid in its own right. The ingestion of caffeine has been proposed as a limiter to the performance enhancing effect of supplementation. Vandenberghe (1996), utilised a cross-over experimental design involving 9

participants. Participants were randomly assigned to three, 6-day, treatments; placebo, creatine supplementation and creatine plus caffeine supplementation.

Both the creatine supplementation and the creatine plus caffeine supplementation treatments elicited a significant increase in muscle PCr concentrations. However the performance effect was seen with the creatine only treatment but not with creatine plus caffeine supplementation.

We have demonstrated that creatine monohydrate supplementation can effectively raise total muscle creatine content and we have mentioned that this increase in TCr can induce a performance effect. But what specifically is the nature of this performance effect? This will be discuss in our next section.

## **CREATINE SUPPLEMENTATION'S ERGOGENIC EFFECT**

Creatine supplementation has been most effectively demonstrated to enhance work in short duration (<30 seconds), intermittent, high intensity exercise.

A repeated trial experimental design of 5 bouts of 30 voluntary extensions on an isokinetic dynamometer with 60-seconds rest following the administration of 20g/day in 5g doses for 5 days indicated significantly greater muscle peak torque following Cr supplementation in comparison to a placebo-fed control group. Supplementation increased peak torque during the final 10 contractions of bout 1, throughout the whole of bouts 2,3 and 4 and during contractions 11-30 of bout 5 (Greenhaff 1993).

Balsom (1993) found that during 10 intermittent bouts of sprint cycling creatine supplementation ensured performance would be better sustained during the end of each sprinting bout. The tightly controlled study utilized two matched groups of 8 volunteers randomly assigned to a placebo group and a creatine group. The creatine group were administered 25g/day in five equal doses for six days. Subjects attempted to maintain a pedal velocity of 140 rpm against a pre-determined resistive load for repeated 6-second high intensity exercise bouts. The main findings of the study analysed pedalling performance over two key intervals, 2-4s and 4-6s of each sprinting bout. Before the intervention period, there was no significant difference in the mean pedal speed between the creatine and placebo groups during trials for either of the intervals, 2-4s or 4-6s. After the intervention period there was a trend over the last number of bouts of the 2-4s interval for the creatine group to maintain a higher pedalling frequency. Significant difference between pedalling frequency was seen during the 4-6s interval. Figure 3 displays that this ergogenic effect of creatine monohydrate supplementation appears to occur after the fourth exercise bout.

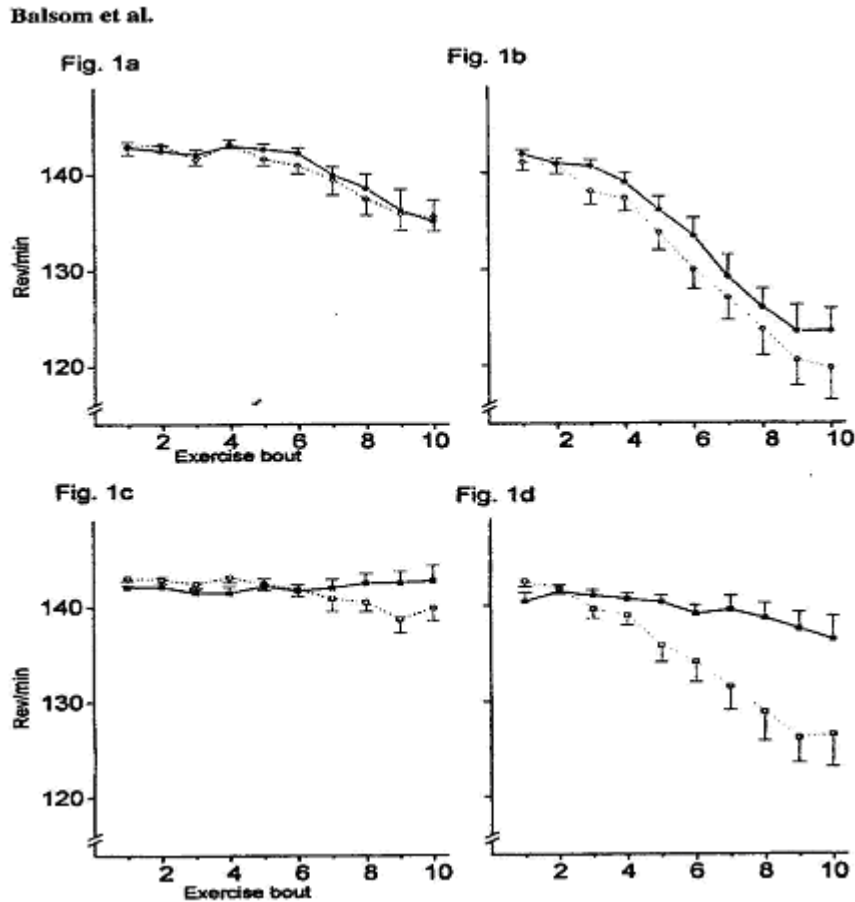


Figure 3.

Performance data before (a & b: creatine ●: n=8 and placebo ○: n=8) and after (c & d: creatine ■: n=8 and placebo □: n=8) the administration period. Mean rev/min over the 10 exercise bouts for the interval 2-4s are presented in 1a and 1c, and for the interval 4-6s in 1b and 1d (reproduced from, and credit to the research of Balsom 1993)

Havenetidis (2003), examined the administration of varying creatine supplementation regimes on sprint cycling performance utilizing three repeated 30 second sprints. A low dose creatine loading (10g/day, 5g doses, 4 days) elicited no significant ergogenic effect. Larger acute creatine loadings of 100g (25g/day, 5g doses, 4 days) and 140g (35g/day, 5g doses, 4 days) both produced an ~11% increase in mean power output over the three repeated sprints. The data appears again to validate 100g acute creatine loading's capacity to increase the TCr of skeletal muscle and invoke a performance response in repeated maximal intensity exercise. In relation to methods of creatine supplementation, it also suggests greater quantities of acute ingestion (140g) do not provide an increased performance benefit.

Seven days of creatine supplementation (25g/day, 5g doses) enhanced muscular performance during repeated sets of bench press and jump squat exercise in resistance trained subjects. Subjects performed 5 sets of bench press exercise with a

resistive load equivalent to their 10 repetition maximum and squat jump exercise with a resistive load equivalent to 30% of their 1 repetition maximum to failure with 2 minute rest intervals between sets (Volek 1997).

In a randomly assigned, double blind investigation, 5 days of creatine supplementation (20g/day, 5g doses) lead to significant improvements in lower body maximal repetitive upper and lower body high power exercise bouts in well trained male handball players. (Izqueirido 2001).

In the high intensity intermittent activity of rowing, creatine supplementation standardized to body mass, induced a 1% time improvement in 1000m rowing time for the experimental creatine fed group in comparison to a placebo administered control group. Major performance enhancement of the experimental group occurred during the 600-800m and 800-1000m sections. These sections of the testing protocol were performed significantly faster in comparison to the control group.

Balsom (1995) examined the ergogenic effect of creatine supplementation with a testing protocol of repeated sprints on a stationary exercise bike. Five 6-second sprints were performed with 30 second rest intervals. The final 6-second sprint was followed by a 40 second rest interval before the completion of 10-second sprint. In the 10-second exercise period, subjects maintained a significantly higher power output following creatine supplementation.

The study also examined the effect of creatine supplementation on height achieved in counter-movement and squat jump exercises. Jump performance was not enhanced, suggesting an increase in the TCr content of muscle through supplementation does not increase peak power output when the subject is not fatigued.

Peak power output is highly dependent on the velocity of muscle contraction which is determined by the rate of crossbridge cycling. Myosin ATPase is classified as a rate limiting enzyme. Its activity limits the rate of crossbridge cycling and resultantly the velocity of muscular contraction. This is evidenced by the myosin in fast contracting type II muscle fibres having a higher myosin ATPase activity than myosin in slow twitch type I fibers. Essentially, the peak rate of cross bridge cycling is dependent on factors outside the PCr pool. Factors such as PCr availability or rate of PCr resynthesis do not directly affect the maximal rate of cross-bridge cycling in non-fatigued muscle. An enhanced muscle TCr pool, achieved through creatine supplementation, would not be expected to increase the maximal contraction velocity of muscle nor the peak power production of a muscle in a non-fatigued state. But what does this all mean for an athlete? Supplementing with creatine will not suddenly, directly increase your bench press or deadlift maximum. It will however allow you to perform more work in a given training session, which in time will assist you with increasing your maximum lifts.

So, creatine monohydrate supplementation has been continuously shown in the published literature to increase work capacity during high intensity exercise. But exactly how does it cause this ergogenic effect? This will be discussed in the next session.

## **CREATINE'S MECHANISM OF ACTION**

Muscle fatigue can be caused by a failure of the energetic processes (such as the PCr energy pathway) to generate ATP at an adequate rate. Williams (Hultman 1991) reports that during brief, near-maximal exercise of durations approximating 30 seconds, the anaerobic utilization of muscle PCr and glycogen fuel muscle contraction. Evidence suggests that fatigue during this type of exercise is related to the inability of type II fibres to maintain the very high rate of ATP resynthesis required to maintain high muscle power output. When type II PCr stores are rapidly depleted, glycogenolysis is unable to compensate for the fall in energy production. Resultantly power generation decreases due to insufficient energy supplies.

Several mechanisms through which creatine supplementation can augment high intensity exercise performance have been proposed.

An increased initial availability of PCr is one such mechanism proposed which may help sustain muscle power output and delay the onset of fatigue. Williams (1999), citing Sahlin (1998), states that it could be expected that the maximal rate of PCr breakdown would decrease when PCr content in muscle decreases. This would explain why, during high intensity exercise, power can be diminishing although PCr stores are not completely depleted. Theoretically, Cr supplementation could increase TCr, aiding in the generation of intra-muscular PCr and subsequent ATP formation. This would prolong the duration of high intensity physical activity (Balsom 1994).

Also proposed as an explanation of performance enhancement is the increase in PCr resynthesis between exercise bouts, which Cr supplementation can induce. Greenhaff (1995) states that free Cr is recognized as having a central role in the control of PCr resynthesis. "PCr resynthesis during recovery period from high intensity exercise appears to be a determining factor in restoration of energy for a subsequent high intensity exercise task" (Bogdanis 1995, cited by Williams 1999, pp.35-36). Relating importantly to this point is the contention that regardless of the amount of Cr taken up by the muscles during a supplementation period, the ratio of PCr to Cr in the muscle appears to be unaffected (Green 1996a, Green 1996b). As Cr supplementation therefore also increases the free Cr muscle pool, this can lead to an increase in the rate of PCr resynthesis during intermittent high intensity exercise bouts.

Following high intensity exercise approximately half of the pre-exercise muscle PCr content is restored within within one minute of recovery but it can take 5-6 minutes for complete restoration of the PCr pool (Balsom 1994). Greenhaff (1994) reported that creatine supplementation led to an increased rate of PCr resynthesis after 1 minute recovery durations in comparison to placebo control groups. This higher rate of resynthesis lead to higher muscle PCr concentrations after 1 minute of recovery in the creatine supplementation group. Yquel (2002), observed higher rates of PCr resynthesis after 16 and 32 second recovery intervals following exercise bouts of maximal plantar flexion. This higher rate of resynthesis led to a higher phosphocreatine availability for succeeding exercise bouts.

A third mechanism suggested to explain exercise performance enhancement is creatine supplementation's buffering effect on muscle acidity. [Glycolysis](#) causes lactic acid production. Lactic acid dissociates a hydrogen ion (H<sup>+</sup>) and it is the accumulation of these H<sup>+</sup> which cause cellular pH to decrease (Brooks 2000, ASC 2000). This increase in acidity, can inhibit the enzyme phosphofructokinase (PFK), slowing glycolysis, it can displace calcium (Ca<sup>2+</sup>) from troponin interfering with muscle

contraction and can stimulate pain receptors (Brooks 2000). The net effect can be a cessation of high intensity exercise. ATP resynthesis from ADP + PCr consumes a hydrogen ion, due to this process the utilization of PCr will therefore aid in buffering H<sup>+</sup> accumulation. The benefit of this increased buffering capacity would be that Cr supplementation may allow working muscle to accumulate more lactic acid before reaching a fatigue inducing muscle pH (Balsom 1995, Rossiter 1996). This implies that creatine supplementation may have a possible benefit for aerobic exercisers as well as anaerobic athletes.

## **HEALTH RELATED CONCERNS/SAFETY**

The most-documented adverse effect of creatine supplementation is an increase in body mass caused by increased water retention within the muscle. As previously mentioned, creatine is an osmotically active substance; thus increasing intracellular creatine concentration may induce water into the cell (Wyss 2000). This increase in body mass can range from 1 to 3 kg following a 100g acute creatine loading (Greenhaff 1994, Balsom 1995, Rossiter 1996, Yquel 2002).

Anecdotally, creatine supplementation has been associated with an increased occurrence of heat illness, muscle cramping and a detrimental effect on renal function. However, these reports have only been anecdotal and in the examination of the literature presented in this review, no studies reported negative effects of creatine supplementation (aside from increases in body mass).

In fact recently, creatine supplementation's effect on Cramping and Injury Incidence has been examined in Collegiate Football Players. Thirty-eight of 72 athletes participating in the 1999 Division IA collegiate football season from the same university volunteered to take creatine in a research study in the Journal of Athletic Training. The subjects utilized an acute loading period standardized to body mass for 5 days followed by a maintenance loading dose each day thereafter. Subjects trained, practiced, or played in environmental conditions ranging from 15 to 37 degrees Celsius and 46.0% to 91.0% relative humidity. Injuries treated by the team's athletic training staff were recorded and categorized as cramping, heat illness or dehydration, muscle tightness, muscle strains, non-contact joint injuries, contact injuries, and illness. The number of missed practices due to injury and illness was also recorded. The research found that the incidence of cramping or injury in these creatine using Division IA football players was significantly lower or proportional when compared with their non-creatine supplementing counterparts.

Kreider 2003 reported the effects of creatine monohydrate supplementation over a 21-month period on plasma markers of health and on urinary measures of renal function in a large sample size (n=98). Following the monitoring period subjects were classed into four categories, those who did not supplement with creatine, those who did so for 0-6 months, 6-12 months and 12-21 months. There were no differences in the blood and urine variables between groups with the exception of sodium, chloride and hematocrit levels which still remained within normal ranges. The authors deemed these changes to be of no physiological or health related significance. The study indicates that creatine supplementation for durations of up to 21 months does not acutely affect markers of health status and renal function in healthy athletes.

It appears then, that creatine supplementation, either through acute high-dose feeding for 5-7 days or through continuous low-dose feeding for 21-28 days has no proven serious health implications.

## CONCLUSION

Creatine monohydrate is among the most popular and widely used supplements in the realm of sports and exercise. Phosphocreatine provides a reserve of energy to regenerate ATP, which is consumed as the result of muscle contraction. This energy pathway is predominant during high intensity exercise such as that endured in the gym, by bodybuilders. Appropriate oral supplementation with creatine monohydrate has been shown to increase the muscle pool of creatine in both its free creatine and phosphocreatine forms. Such supplementation enhances work in short duration, intermittent, high intensity exercise. For bodybuilders this allows a greater volume and intensity of work during weight training.

Please refer to article 2 for practical applications by clicking [Here](#).

## REFERENCES

Balsom, P., Ekholm, B., Söderland, K., (1993), Creatine Supplementation and Dynamic High Intensity Exercise, *Scand. J. Medicine and Science in Sports*, Vol. 3, pp. 143-149

Balsom, P., Söderland, K., Ekholm, B., (1994), Creatine in Humans with Special Reference to Creatine Supplementation, *Sports Medicine*, Vol. 18, pp. 268-280

Balsom, P., Sjödín, B., (1995), Skeletal Muscle Metabolism During Short Duration High Intensity Exercise: Influence of Creatine Supplementation, *Acta Physiologica Scandinavica*, Vol. 154, pp. 303-310

Bird, S.P., (2003), Creatine Supplementation and Exercise Performance: A Brief Review, *J. Sports Science and Medicine*, Vol. 2, pp. 123-132

Brannon, T.A., Adams, G.R., Conniff, C.L., Baldwin, K.M., (1997), Effects of Creatine Loading and Training on Running Performance and Biochemical Properties of Rat Skeletal Muscle, *Med. Sci. Sports and Exercise*, Vol. 29, pp. 489-495

Brooks, G.A., Fahey, T.D., White, T.P., Baldwin, K.M., (1999), *Exercise Physiology: Human Bioenergetics and its Applications*, Mayfield Publishing, California

Burke, D.G., Silver, S., Holt, L.E., Smith-Palmer, T., Culligan, C.J., Chilibeck, P.D., (2000), The Effects of Continuous Low Dose Creatine Supplementation on Force, Power and Total Work, *Int. J. Sport Nutrition and Exercise Metabolism*, Vol. 10, pp. 235-244

Casey, A., Greenhaff, P.L., (2000), Does Dietary Creatine Supplementation Play a Role in Skeletal Muscle Metabolism and Performance?, *Am. J. Clinical Nutrition*, Vol. 72 (Supplement), pp. 607S-617S

E.P. Flanagan, P.M. Jakeman, Foley, M., Rossiter, T., 2004, Oral Creatine Supplementation and Short-Term Dynamic Power Production in Healthy Young Men, Presented to the Royal Academy of Medicine in Ireland, Conference of Human Sciences, Trinity College Dublin, 2004.

Green, A.L., Hultman, E., MacDonald, I.A., Sewell, D.A., Greenhaff, P.L., (1996a), Carbohydrate Ingestion Augments Skeletal Muscle Creatine Accumulation during Creatine Supplementation in Humans, *Am. J. Physiology*, Vol. 271, pp. 821-826

Green, A.L., Simpson, E.J., Littlewood, J.J., MacDonald, I.A., Greenhaff, P.L., (1996b), Carbohydrate Ingestion Augments Creatine Retention during Creatine Feeding in Humans, *Acta Physiologica Scandinavica*, Vol. 158, pp. 195-202

Greenhaff, P.L., Bodin, K., Harris, R.C., (1993), (abstract), The Influence of Oral Creatine Supplementation on Muscle Phosphocreatine Resynthesis Following Intense Contraction in Man, *J. Physiology (London)*, pp. 467-475

Greenhaff, P.L., Bodin, K., Söderland, K., Hultman, E., (1994), Effect of oral Creatine Supplementation on Skeletal Muscle Phosphocreatine Resynthesis, *Am. J. Physiology*, Vol. 266, pp.725-730

Greenhaff, P.L., (1995), Creatine and its Application as an Ergogenic Aid, *Int. J. Sport Nutrition*, Vol. 5, pp.100-110

Harris, R.C., Söderland, K., Hultman, E., (1992), Elevation of Creatine in Resting and Exercised Muscle of Normal Subjects by Creatine Supplementation, *Clinical Science*, Vol. 83, pp. 367-374

Havenetidis, K., Matsouka, O., Cooke, C.B., Theodorou, A., (2003), the Use of Varying Creatine Regimes on Sprint Cycling, *J. Sports Science and Medicine*, Vol. 2, pp. 88-97

Hultman, E., Söderland, K., Timmons, J.A., Cederblad, G., Greenhaff, P.L., (1996), Muscle Creatine Loading in Men, *J. Applied Physiology*, Vol. 81, pp. 232-237

Izquierdo, M., Ibanez, J., Gonzalez-Badillo, J.J., Gorostiaga, E.M., (2001), Effects of Creatine Supplementation on Muscle Power, Endurance and Sprint Performance, *Medicine and Science in Sports and Exercise*, Vol. 34, pp. 332-343

Kreider, R.B., Melton, C., Rasmussen, C.J., Greenwood, M., Lancaster, S., Cantler, E.C., Milnor, P., Almada, A.L., (2003), (abstract), Long-term Creatine Supplementation Does Not Significantly Affect Clinical Markers of Health in Athletes, *Molecular and Cellular Biochemistry*, Vol. 244, pp. 95-104

Murphy, R.M., Tunstall, R.J., Mehan, K.A., Cameron-Smith, D., McKenna, M.J., Spriet, L.L., Hargreaves, M., Snow, R., (2003), Human Skeletal Muscle Transporter mRNA Protein Expression in Healthy, Young Males and Females, *Molecular and Cellular Biochemistry*, Vol. 244, pp. 151-157

Odland, M.L., MacDougall, D.J., Tarnopolsky, M.A., Elorriaga, A., Borgmann, A., (1996), Effect of Creatine Supplementation on Muscle PCr and Short-Term Maximum Power Output, *Medicine and Science in Sports and Exercise*, Vol. 29, pp. 216-219

Rawson, E.S., Clarkson, P.M., (2003), Scientifically Debatable: Is Creatine Worth its Weight?, *Gatorade Sports Science Institute – Sports Science Exchange*, Vol. 16, pp. 1-8

Rossiter, H.B., Cannell, E.R., Jakeman, P.M., (1996), the Effect of Oral Creatine Supplementation on the 1000-m Performance of Competitive Rowers, *J. Sports Sciences*, Vol. 14, pp. 175-179

Snow, R.J., Murphy, R.M., (2003), Factors Influencing Creatine Loading into Human Skeletal Muscle, *Exercise and Sport Sciences Reviews*, ACSM, Vol. 31, pp.154-158

Steenge, G.R., Lambourne, J., Casey, A. I., Macdonald, A., Greenhaff, P. L., (1998), Stimulatory Effect of Insulin on Creatine Accumulation in Human Skeletal Muscle, *Am. J. Physiology*, Vol. 275, pp. 974-97.

Theodorou, A.S., K. Havenetidis, C.L. Zanker, J.P. O'Hara, R.F.G.J. King, C. Hood, G. Paradisis, and C.B. Cooke, 2005, Effects of acute creatine loading with or without carbohydrate on repeated bouts of maximal swimming in high-performance swimmers. *Journal of Strength and Conditioning Research*. pp. 265–269.

Vandenbergh, K., Gillis, N., van Leemputte, M., van Hecke, P., Vanstapel, F., Hespel, P., (1996), Caffeine Counteracts the Ergogenic Action of Muscle Creatine Loading, *J. Applied Physiology*, Vol. 83, pp. 2055-2063

Volek, J.S., Kraemer, W.J., Bush, J.A., (1997), Creatine Supplementation Enhances Muscular Performance during High Intensity Resistance Exercise, *J.Am. Dietetic Association*, Vol. 97, pp. 765-770

Williams, M.H., Kreider, R.B., Branch J.D., (1999), *Creatine: The Power Supplement*, Human Kinetics, Champaign, Illinois

Wiroth. J.B., Bermon, S., Andrei, S., Dalloz, E., Hēbuterne, X., Dolisis, C., (2001), Effects of Oral Creatine Supplementation on Maximal Pedalling Performance in Older Adults, *Eur. J. Applied Physiology*, Vol. 84, pp. 533-539

Wyss, M., Kaddurah-Daouk, R., (2000), Creatine and Creatinine Metabolism, *Physiological Reviews*, Vol. 80 , pp. 1107-1213

Yquel, R.J., Arsac, L.M., Thiaudiere, E., Canioni, P., Manier, G., (2002), Effect of Creatine Supplementation on Phosphocreatine Resynthesis, Inorganic Phosphate Accumulation and pH during Intermittant Maximal Exercise, *J. Sports Sciences*, Vol. 20, pp. 427-437