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Creatine Supplementation in Sport and Medicine: Efficacy, Safety, and Therapeutic Potential in the Light of Current Scientific Evidence

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Abstract

Creatine is a naturally occurring nitrogen-containing compound synthesized primarily in the liver, kidneys, and pancreas from the amino acids glycine, arginine, and methionine. Approximately 95% of creatine is stored in skeletal muscles in the form of free creatine and phosphocreatine, which plays a key role in ATP resynthesis during high-intensity exercise (1,2). Creatine supplementation, particularly in the form of creatine monohydrate, is currently one of the most extensively studied ergogenic strategies used in sports. Research has demonstrated that increasing intramuscular creatine concentration may lead to improved anaerobic performance, enhanced muscle strength, increased lean body mass, and improved training adaptations (2,3).

The aim of this paper is to present the current state of knowledge regarding the effectiveness, safety, and applications of creatine supplementation in sports and health. The article discusses the mechanisms of creatine action, the effects of supplementation on physical performance and recovery, as well as potential clinical applications beyond sports. Particular attention is given to current dosing recommendations and the safety of long-term supplementation.

Available scientific evidence indicates that creatine supplementation may effectively enhance the capacity to perform short-duration, high-intensity exercise, support post-exercise recovery, and improve the outcomes of resistance training. Potential benefits related to neuroprotection, prevention of sarcopenia, and support of rehabilitation have also been demonstrated.

Current position statements from scientific organizations, including the International Society of Sports Nutrition (ISSN), emphasize that creatine monohydrate is safe for both short-term and long-term supplementation in healthy individuals when used according to recommended guidelines.

The significance of creatine currently extends beyond sports medicine. An increasing number of studies are investigating its effects on the health of older adults, cognitive function, neurodegenerative diseases, and glucose metabolism, suggesting a broad therapeutic potential of this compound (1).

Keywords: creatine, supplementation, physical performance, recovery, strength training, sports medicine

1. Introduction

Definition of Creatine

Creatine (methylguanidinoacetic acid) is a naturally occurring nitrogen-containing compound that plays a key role in the body's energy metabolism. It is synthesized endogenously primarily in the liver, kidneys, and pancreas from glycine, arginine, and methionine. It is then transported to tissues with high energy demands, particularly skeletal muscles and the brain (4).

Approximately 95% of creatine is stored in skeletal muscles in the form of free creatine and phosphocreatine (PCr), which participates in the rapid resynthesis of ATP during high-intensity exercise (4,5).

According to the International Society of Sports Nutrition, creatine is the most extensively researched ergogenic supplement used in sports (2).

Natural occurrence of creatine in the body

Creatine occurs naturally primarily in skeletal muscles and in animal-based food products, especially meat and fish. Its levels depend, among other factors, on diet, muscle mass, and physical activity (2) (4) (1).

Role of creatine in energy metabolism

The primary function of creatine is to maintain cellular energy homeostasis by participating in the rapid regeneration of ATP. Phosphocreatine transfers a phosphate group to ADP in a reaction catalyzed by creatine kinase, which is particularly important during short-duration, high-intensity efforts such as sprinting or strength training (5).

Thanks to the presence of phosphocreatine, rapid ATP resynthesis is possible, allowing the maintenance of high-intensity muscular work. Creatine also exhibits osmoregulatory effects, supports anabolic processes, and may influence the expression of genes associated with muscle hypertrophy (4,6).

Popularity of creatine supplementation in sports

Creatine supplementation has gained popularity among athletes since the 1990s and is currently one of the most commonly used supplements in both competitive and recreational sports. The most extensively researched form remains creatine monohydrate (1,2).

Research indicates that supplementation may increase muscular strength and power, improve the ability to perform anaerobic exercise, support recovery, and increase lean body mass as well as training adaptations (7) (1).

The greatest effectiveness is observed in disciplines requiring short-duration, high-intensity efforts, such as sprinting, strength sports, or HIIT training, although interest in creatine now extends beyond competitive sports.

Why is the topic relevant?

The topic of creatine remains relevant due to the growing number of studies analyzing its effects not only on athletic performance but also on health. Contemporary research focuses, among other areas, on cognitive function, neuroprotection, prevention of sarcopenia, women's health, aging processes, and glucose metabolism (6,8)

Particular interest concerns older adults and women in the perimenopausal period, in whom creatine may help maintain muscle strength, muscle mass, and cognitive function (7)

Despite controversies regarding safety, current scientific consensus indicates that the use of creatine monohydrate at recommended doses is safe in healthy individuals (1).

Increasing interest in creatine supplementation

In recent years, there has been a growing interest in creatine both in sports and in the general population. Initially associated mainly with strength sports, it is now also used by recreationally active individuals, older adults, and clinical patients (9) (10).

The growing popularity is due to numerous studies confirming its effectiveness in increasing muscle strength, improving performance, and supporting recovery by increasing phosphocreatine stores and accelerating ATP resynthesis (11).

An additional factor is the wide availability of supplements and the confirmed safety of using recommended doses (10,12).

Use of creatine beyond athletes

Current research indicates that the use of creatine extends beyond competitive sports and includes potential health and therapeutic benefits. Particular interest is focused on its effects on cognitive function and the nervous system (10,12,13).

Studies suggest that supplementation may improve short-term memory, concentration, and information processing speed, especially in older adults, during sleep deprivation, or under increased mental stress, which is associated with improved cellular energy availability in nerve cells (11,12).

Creatine is also being studied in the context of neurodegenerative diseases such as Alzheimer’s disease, Parkinson’s disease, and ALS, where it may exhibit neuroprotective effects by reducing oxidative stress and supporting mitochondrial function (13,14).

Furthermore, studies indicate that when combined with resistance training, it may help counteract muscle mass loss and improve functional capacity in older adults (10,15).

An increasing number of publications also focus on women, suggesting benefits of supplementation during menopause and aging, including the maintenance of muscle mass, bone health, and cognitive function (9).

Potential applications are also being investigated in type 2 diabetes, depression, and chronic fatigue, although they require further research (10,15).

New directions in creatine research

Current research on creatine is mainly focused on its clinical applications, its effects on brain function, and its neuroprotective potential in neurological and psychiatric disorders (13,14).

Its role in supporting the treatment of depression and improving cognitive function during metabolic stress, sleep deprivation, or intensive mental work is also being investigated (10,12).

An important research direction remains the use of creatine in geriatrics, particularly in preventing sarcopenia and loss of functional capacity in older adults (15,16).

Increasing attention is also being given to women, taking into account hormonal and metabolic differences that may influence the effectiveness of supplementation (9).

Research also includes optimization of dosing as well as combining creatine with other nutrients and training interventions (10,16).

Contemporary literature indicates that creatine is increasingly perceived not only as a sports supplement but also as a substance with health-promoting and therapeutic potential.

2. Methodology

This paper is a review and is based on an analysis of current scientific literature on creatine supplementation, its effects on physical performance, recovery, safety, and potential clinical applications.

The literature review was conducted using scientific databases such as PubMed, Google Scholar, MDPI, and the Journal of the International Society of Sports Nutrition (JISSN). It included mainly randomized clinical trials, meta-analyses, systematic reviews, and position statements from scientific organizations in both Polish and English.

The search was based on keywords such as “creatine supplementation,” “creatine monohydrate,” “physical performance,” “recovery,” and “creatine safety.” Publications included in the analysis addressed the effects of creatine on performance, muscle strength, recovery, as well as metabolic and neurological health, with particular attention paid to the recency and methodological quality of the studies.

The aim of the paper was to present the current state of knowledge regarding the efficacy, safety, and potential applications of creatine supplementation.

3. Metabolism and Mechanism of Action of Creatine

3.1. Synthesis and Storage of Creatine

Creatine is a naturally occurring nitrogen-containing compound involved in the body's energy metabolism. Approximately 95% of the total creatine pool is found in skeletal muscles, while the remaining portion is present in the brain, heart, and kidneys. Creatine can be obtained through the diet, mainly from meat and fish, or synthesized endogenously.(1,17).

Endogenous synthesis of creatine

Creatine synthesis occurs mainly in the liver, kidneys, and pancreas, involving glycine, arginine, and methionine. The process consists of two enzymatic steps leading to the formation of creatine, which is then transported to tissues with high energy demands, particularly skeletal muscles (17,18).

Guanidinoacetate is then transported to the liver, where, under the action of guanidinoacetate N-methyltransferase (GAMT), it undergoes methylation with the involvement of S-adenosylmethionine (SAM), resulting in the formation of creatine. After synthesis, creatine is released into the bloodstream and transported to tissues with high energy demands, primarily skeletal muscles (1,18).

The body synthesizes approximately 1–2 g of creatine per day, and its levels also depend on diet and physical activity. In individuals following plant-based diets, muscle creatine levels may be lower, which may increase the effectiveness of supplementation (19,20).

Transport and storage of creatine

After synthesis or absorption from the gastrointestinal tract, creatine is transported via the bloodstream to target cells through a specific creatine transporter (CreaT1, SLC6A8). This transport occurs actively and depends on the presence of sodium and chloride ions. The largest amounts of creatine are stored in skeletal muscles due to their high energy demand during physical exercise (1,18).

The total creatine content in the human body of an adult is on average approximately 120–140 g, of which about 60–70% is present in the form of phosphocreatine, while the remaining portion exists as free creatine. The amount of creatine stored in muscles depends, among other factors, on muscle mass, level of physical activity, diet, and supplementation used (17,19).

Phosphocreatine in muscles and mechanism of action

In muscles, creatine participates in maintaining energy homeostasis through the formation of phosphocreatine, which enables rapid ATP resynthesis during intense exercise (11,17).

This makes it possible to maintain high levels of muscular performance during short-duration, high-intensity efforts. Creatine supplementation increases phosphocreatine stores, which may improve strength, muscle power, and post-exercise recovery. It is also suggested to influence muscle cell hydration, protein synthesis, and the reduction of muscle damage (11,20).

By increasing phosphocreatine stores, creatine supplementation may improve the ability to perform short-term, high-intensity efforts, enhance muscle strength and power, and accelerate recovery between exercise sets. The literature also highlights that creatine may influence muscle cell hydration, stimulate muscle protein synthesis, and reduce exercise-induced muscle damage (3,10,20).

The importance of the phosphocreatine system is also observed in the brain and cardiac muscle, which explains the growing interest in creatine in neurology and clinical medicine (12,13).

3.2. Mechanism of action of creatine

Creatine plays a key role in energy metabolism, particularly in tissues with high energy demand, such as skeletal muscles, the heart, and the brain. Its primary mechanism of action involves maintaining adequate levels of ATP—the main cellular energy carrier (11,17).

ATP resynthesis

ATP is the immediate source of energy during muscle contraction; however, its stores in muscles are limited. Phosphocreatine, through a reaction catalyzed by creatine kinase (CK), enables the rapid regeneration of ATP from ADP, which allows the maintenance of high exercise intensity during sprints, strength training, or interval exercise (11,11,17,20).

Supplementation with creatine monohydrate can increase intramuscular phosphocreatine stores by up to 20–40%, improving anaerobic performance (10,20).

Effect of creatine on energy metabolism

Creatine acts as an "energy buffer," stabilizing ATP levels under conditions of increased energy demand. An important role is also played by the so-called phosphocreatine shuttle, which enables the transport of energy from mitochondria to sites of high energy consumption within the cell (1,17).(17,18).

Supplementation may reduce muscle fatigue by decreasing muscle acidosis and also support cell hydration, muscle protein synthesis, and recovery processes (11,20).

Additionally, creatine exerts an osmotic effect by increasing muscle cell hydration. An increase in cell volume may have an anabolic effect by stimulating muscle protein synthesis and reducing catabolic processes. The literature also highlights a potential influence of creatine on the expression of genes associated with muscle hypertrophy and tissue repair (3,10).

Increased exercise capacity

The best-documented effect of creatine supplementation is the improvement of exercise capacity during short-duration, high-intensity anaerobic activities, such as sprints or strength training (10,20).

Increased phosphocreatine availability enables faster ATP regeneration, which translates into greater muscle strength, improved recovery, and more favorable training adaptations (10,19,19,20)

An increasing number of studies also indicate a potential effect of creatine on cognitive function through improved neuronal energy metabolism (12,20).

Contemporary literature emphasizes that creatine's effects extend beyond muscles and include support for other tissues with high energy demands.

3.3. Forms of creatine

Many forms of creatine are available on the market, differing in chemical structure, solubility, and bioavailability. Despite the development of newer formulations, creatine monohydrate remains the best-researched and most commonly recommended form of supplementation. Current research indicates that most alternative forms do not demonstrate significantly greater efficacy than the classic monohydrate (1,3,10).

Creatine monohydrate

Creatine monohydrate (CM) is the oldest and best-researched form of creatine. Numerous studies confirm its effectiveness in increasing intramuscular phosphocreatine stores, improving muscle strength, enhancing anaerobic performance, and supporting muscle hypertrophy (10,19,20).

It is considered the "gold standard" of supplementation due to its high effectiveness, safety of use, favorable cost profile, and good tolerability by the body (1,17).

Studies indicate that supplementation can increase creatine and phosphocreatine stores in muscles by 20–40%. The most commonly used protocol includes a loading phase (around 20 g per day for 5–7 days), followed by a maintenance dose of 3–5 g per day, although using consistently lower doses without a loading phase may also be effective (10,20).

Tricreatine malate

Tricreatine malate was developed to improve creatine solubility and reduce water retention. Although its potential beneficial effect on energy metabolism was suggested due to the presence of malic acid, research has not confirmed any superior effectiveness compared to creatine monohydrate. Most ergogenic effects are attributed to the creatine itself (1,10).

Due to the limited number of studies, this form is not currently considered more effective than monohydrate (3).

Creatine hydrochloride

Creatine hydrochloride is characterized by high solubility and potentially better gastrointestinal tolerance in individuals who do not respond well to creatine monohydrate (10).

However, available studies do not demonstrate a clear advantage of this form in terms of improving muscle strength, endurance, or muscle mass gains (1).

The limited number of studies indicates the need for further evaluation of its effectiveness and the long-term safety of use (10).

Forms of creatine with the best-proven efficacy

Current scientific literature clearly indicates that creatine monohydrate is the best-researched and most effective form of creatine. Most studies on improvements in exercise performance, muscle strength, hypertrophy, and the safety of supplementation are based on this form (1,10,20).

International organizations such as the International Society of Sports Nutrition (ISSN) recognize creatine monohydrate as the most effective and best-documented ergogenic form of supplementation (1,10).

Despite the development of the supplement market, current research does not confirm that other forms of creatine are more effective than the classic monohydrate.

4. Effects of creatine supplementation on physical performance

4.1. Strength training

Creatine supplementation is one of the best-documented strategies supporting training adaptations in resistance training. Studies indicate that regular use, particularly creatine monohydrate, promotes increases in muscle strength, gains in fat-free mass, and improved capacity to perform high-intensity exercise. These effects are mainly due to increased phosphocreatine stores in muscles and faster ATP resynthesis (10,19,20).

Effect of creatine on muscle strength

One of the best-documented effects of creatine supplementation is an increase in muscle strength, observed in both beginners and trained individuals (19,20).

This mechanism is related to increased ATP availability during high-intensity exercise, which enables a greater number of repetitions to be performed and allows the use of heavier training loads (11,17).

Meta-analyses indicate that supplementation combined with resistance training may increase maximal strength by an average of 5–15%, particularly in exercises involving large muscle groups (10,20).

Creatine may also support post-exercise recovery and reduce muscle damage and inflammation, which helps maintain a higher training volume (3,10).

Effect of creatine on muscle mass

Creatine supplementation supports increases in fat-free body mass and muscle hypertrophy. The initial increase in body weight is mainly related to greater muscle cell hydration, whereas long-term effects result from enhanced anabolic processes and the ability to perform more intense training (19,20).

Creatine may stimulate muscle protein synthesis and reduce catabolic processes (3,17).

Studies indicate that long-term supplementation combined with resistance training leads to greater muscle mass gains compared to training alone, and may influence the activation of satellite cells and the expression of growth factors such as IGF-1, which support muscle recovery and hypertrophy (10,18–20).

It is worth emphasizing that the increase in body weight observed in the first days of supplementation is mainly due to water retention within the muscles, whereas the long-term increase in muscle mass is associated with actual muscle fiber hypertrophy (17,19).

Effect of creatine on anaerobic power

Creatine shows particularly strong ergogenic effects in short-duration, high-intensity efforts that rely mainly on anaerobic metabolism, such as sprints, jumps, weightlifting, and high-intensity interval training (11,20).

Increasing phosphocreatine stores enables faster ATP resynthesis during intense exercise and between sets, which allows for a longer maintenance of high power output and faster recovery of exercise capacity (11,17).

Creatine supplementation may increase maximal anaerobic power, improve repeated sprint ability, and enhance the effectiveness of interval training, which is particularly important in strength- and speed-based sports (10,20).

The literature also emphasizes that creatine may delay the onset of muscle fatigue by stabilizing ATP levels and reducing the accumulation of metabolites associated with anaerobic exercise (11,17).

The International Society of Sports Nutrition (ISSN) recognizes creatine as one of the most effective ergogenic supplements for supporting the development of muscle strength, muscle mass, and anaerobic performance (1,10).

4.2. Endurance sports

The effects of creatine supplementation on performance in endurance sports are less clear than in strength training and anaerobic efforts. Creatine is most effective in short-duration, high-intensity exercise; therefore, its impact in disciplines primarily based on aerobic metabolism remains limited and depends on the specific characteristics of the activity (10,20).

Nevertheless, studies indicate that it may provide benefits in disciplines requiring intermittent changes in intensity, finishing sprints, or strength-based components (1,17).

Effect of creatine on VO_2max

VO_2max is one of the key indicators of aerobic fitness, reflecting the body's ability to take up and utilize oxygen during exercise (20).

Existing studies indicate that creatine supplementation does not typically lead to a significant increase in VO_2max, as its mechanism of action is primarily based on increasing phosphocreatine stores and improving ATP resynthesis during short-duration efforts, rather than directly affecting cardiorespiratory fitness (10,11).

However, studies suggest that creatine may indirectly support endurance performance by improving the ability to perform high-intensity training efforts and finishing sprints, which can enhance training quality and promote exercise adaptations (1,20).

It is also suggested that it may have a potential effect on muscle glycogen replenishment, especially when combined with carbohydrate intake, which may be relevant during frequent training sessions or multi-day competitions (21,22).

Some studies also suggest a beneficial effect of creatine on exercise tolerance under hypoxic conditions and a potential reduction in central fatigue; however, the findings remain inconclusive and require further investigation (12,13).

Limitations of creatine's effects in endurance sports

Despite its well-documented benefits in strength and anaerobic activities, the effectiveness of creatine in endurance sports remains limited. This is because the phosphocreatine system plays a key role primarily during short-duration, high-intensity efforts, whereas aerobic metabolism predominates during prolonged exercise (11,17).

One potential limitation of creatine supplementation in endurance athletes is the increase in body weight, primarily due to intracellular water retention, which may negatively affect exercise economy in disciplines such as long-distance running, cycling, and triathlon (10,19).

Furthermore, most studies indicate that creatine has little effect on key markers of aerobic performance, such as VO_2max and lactate threshold, particularly in well-trained endurance athletes (10,20).

However, the literature highlights the potential benefits of supplementation in disciplines with a mixed energy-demand profile, where aerobic exercise is accompanied by short periods of intense anaerobic effort, including team sports, rowing, and middle-distance running (1,20).

Increasing attention has also been given to the effects of creatine on recovery, the reduction of muscle damage, and the enhancement of training adaptations. However, current evidence indicates that in traditional endurance sports, creatine is not considered a first-line supplement, and its ergogenic effects are less pronounced than those observed in resistance training and anaerobic exercise (3,10).

4.3. Team and Intermittent Sports

Team and intermittent sports are characterized by repeated, short-duration bouts of high-intensity exercise interspersed with periods of partial recovery. Under these conditions, the phosphocreatine system plays a crucial role; therefore, creatine supplementation is considered an effective ergogenic strategy for athletes participating in disciplines such as soccer, basketball, rugby, combat sports, and high-intensity interval training (HIIT). Of particular importance is the ability to repeatedly perform sprints, jumps, and rapid changes of direction (1,10,11,20).

Effects of Creatine on Sprint Performance

Creatine supplementation increases intramuscular phosphocreatine stores, enabling faster ATP resynthesis during high-intensity exercise and between successive bouts of activity. This enhanced energy availability can contribute to improved sprint performance, particularly during repeated sprint efforts (11,17).

Studies indicate that creatine supplementation may improve both single-sprint and repeated-sprint performance, enhance explosive power, increase jump height, and support the ability to maintain high exercise intensity during team-sport activities (1,10,20).

These benefits result from improved muscular energy homeostasis and increased ATP availability. Additionally, creatine supplementation may support neuromuscular function and enhance motor unit recruitment (17,18).

By accelerating the recovery of energy stores, creatine supplementation enables athletes to perform more intensive training sessions, thereby promoting the development of speed and strength capacities (10,19).

Recovery Between Exercise Bouts

One of the most important effects of creatine supplementation is the enhancement of recovery between successive bouts of high-intensity exercise. Increased intramuscular creatine stores facilitate faster phosphocreatine resynthesis, improving tolerance to repeated efforts and reducing performance declines during subsequent bouts of activity (1,11,17,20).

Studies also suggest that creatine supplementation may attenuate muscle damage and inflammation following intense exercise by reducing the levels of biomarkers such as creatine kinase (CK) and lactate dehydrogenase (LDH) (3,10).

Furthermore, creatine may support muscle glycogen resynthesis, particularly when combined with adequate carbohydrate intake, thereby accelerating recovery and enhancing readiness for subsequent exercise (20,23).

An increasing body of evidence also suggests that creatine may help reduce central fatigue and support cognitive function during prolonged intermittent exercise, thereby contributing to the maintenance of concentration and rapid decision-making in the later stages of competition (13,24).

Current evidence therefore indicates that creatine supplementation may serve as an effective ergogenic aid in team and intermittent sports, particularly by enhancing sprint performance, supporting the maintenance of high-intensity exercise, and accelerating recovery between successive bouts of activity.

5. Creatine and Recovery

5.1. Muscle Recovery

Recovery following physical exercise is a crucial component of training adaptation. A growing body of research suggests that creatine may support recovery processes not only by enhancing exercise performance but also by reducing muscle damage, alleviating delayed-onset muscle soreness (DOMS), and accelerating the restoration of muscle glycogen stores (3,10,20).

Effects of Creatine on Muscle Damage

Intense physical exercise, particularly resistance training and eccentric exercise, leads to microdamage of muscle fibers. Although this process is a natural component of training adaptation, it may prolong the recovery period and temporarily impair performance (11,17).

Studies suggest that creatine supplementation may attenuate the extent of muscle damage by improving cellular energy homeostasis, stabilizing cell membranes, and reducing oxidative stress (10).

It has been demonstrated that individuals supplementing with creatine following intense exercise often exhibit lower levels of muscle damage biomarkers, such as creatine kinase (CK), lactate dehydrogenase (LDH), and myoglobin (3,25).

Creatine may also help attenuate inflammation and support a faster recovery of muscle function following exercise (10,26).

Additionally, increased hydration of muscle cells may support the structural integrity of muscles and enhance post-exercise recovery and repair processes (3,17).

Creatine and DOMS (Delayed Onset Muscle Soreness)

DOMS, or delayed onset muscle soreness, typically occurs 24–72 hours after intense physical exercise, especially when it involves a significant eccentric component. It is characterized by muscle pain, stiffness, and a temporary reduction in physical performance and functional capacity (11,27).

Increasing evidence suggests that creatine supplementation may reduce the severity of DOMS and accelerate the recovery of muscle function following exercise. This effect is thought to be mediated by a reduction in muscle fiber microdamage, attenuation of the inflammatory response, and improvements in muscle energy metabolism (3,26).

Studies have shown that individuals supplementing with creatine reported less muscle soreness and recovered muscle function more rapidly following intense exercise, particularly after resistance training and high-intensity interval workouts (10,25).

It should be emphasized, however, that the research findings remain partially inconclusive. Some studies have not demonstrated a significant effect of creatine on the subjective perception of muscle soreness, suggesting that the effectiveness of supplementation may depend on the type of exercise, the level of training, and the supplementation protocol used (10,20).

Creatine and Muscle Glycogen Replenishment

Muscle glycogen is the primary source of energy during moderate- and high-intensity exercise; therefore, its rapid replenishment after training or competition is crucial for recovery and maintaining exercise performance (17,23).

Studies indicate that Creatine supplementation may support muscle glycogen resynthesis, particularly when combined with carbohydrate intake. This mechanism may be associated with increased glucose transport into muscle cells and improved activity of GLUT-4 transporters (20,23).

It has been demonstrated that individuals supplementing with Creatine after exercise achieved greater muscle glycogen accumulation than non-supplementing individuals, which may be particularly important in sports requiring frequent training sessions or multi-day competition (10,23).

Creatine may also indirectly support recovery by improving intracellular hydration and increasing muscle cell volume, which promotes anabolic and repair processes (3,17).

The current state of knowledge indicates that Creatine may constitute a valuable support for recovery processes, particularly in reducing muscle damage, improving recovery between exercise sessions, and restoring muscle energy stores.

5.2. Anti-Inflammatory and Antioxidant Effects

Contemporary research suggests that Creatine may exhibit not only ergogenic properties but also anti-inflammatory and antioxidant effects. These mechanisms may support post-exercise recovery, protect muscle cells, and have potential applications in the prevention and treatment of selected disorders (3,10,13).

Creatine and Oxidative Stress

Oxidative stress arises from an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them. Intense physical exercise may increase the production of free radicals, leading to damage to cell membranes, proteins, and DNA (17,26).

Studies suggest that Creatine may reduce the effects of oxidative stress by improving cellular energy metabolism, stabilizing mitochondrial function, and potentially exerting direct antioxidant activity (10,13).

It has been demonstrated that Creatine supplementation may reduce lipid peroxidation and lower the levels of oxidative stress markers following intense exercise (3,26).

An important role is also attributed to the influence of Creatine on mitochondrial function and the maintenance of energy homeostasis, which may help limit excessive ROS production (13,14).

Some studies also indicate an increase in the activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) in individuals supplementing with Creatine (10,26).

The potential antioxidant effects of Creatine are currently being investigated not only in sports but also in the context of neurodegenerative diseases, aging, and disorders associated with mitochondrial dysfunction (13,14).

Creatine and Inflammatory Markers

Intense physical exercise may activate the body's inflammatory response, which is a natural component of recovery and training adaptation. However, excessive inflammation may prolong recovery time and impair muscle function (10,11).

An increasing number of studies suggest that Creatine supplementation may attenuate the inflammatory response following physical exercise. Some publications have reported reduced concentrations of inflammatory markers after intense training sessions or sports competitions (3,26).

The most commonly analyzed markers included C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α) (10,26).

Studies conducted in endurance athletes suggest that Creatine may attenuate the increase in pro-inflammatory cytokines following exercise, likely through reducing cellular damage, improving energy homeostasis, and decreasing oxidative stress (3,26).

It should be emphasized, however, that the research findings are not entirely consistent—some publications have not demonstrated significant changes in inflammatory markers, which may result from differences in supplementation protocols, the type of exercise performed, or the participants' level of training (10,20).

The potential use of Creatine in disorders associated with chronic inflammation, including neurodegenerative, muscular, and metabolic diseases, is also being increasingly investigated. Through its effects on energy metabolism, mitochondrial function, and the reduction of oxidative stress, creatine may exert protective effects on various tissues throughout the body (13,14).

Current evidence therefore suggests that Creatine may serve not only an ergogenic function but also support the body's protection against the effects of an excessive inflammatory response.

6. Safety of Creatine Supplementation

6.1. Side Effects

Creatine is one of the most extensively studied dietary supplements used in sports and medicine. Current research, as well as position statements from organizations involved in sports nutrition, indicate that creatine monohydrate supplementation is safe for healthy individuals when used at recommended doses (1,9,10).

Despite its strong safety profile, Creatine supplementation may be associated with mild adverse effects, most commonly water retention and transient gastrointestinal discomfort (10,20).

Water Retention

The most commonly observed side effect of Creatine supplementation is increased water retention within muscle cells, resulting from the osmotic properties of creatine (17,19).

This effect is usually manifested by a rapid increase in body weight of approximately 1–3 kg during the initial phase of supplementation and is primarily associated with increased muscle hydration rather than an increase in body fat (19,20).

Increased cellular hydration may support anabolic and recovery processes by improving metabolic conditions and stimulating muscle protein synthesis (3,17).

In some sports disciplines, particularly endurance and weight-class sports, the additional body mass may, however, represent a factor that limits exercise performance or affects an athlete's weight classification (10,20).

Contrary to common beliefs, current research does not confirm an increased risk of dehydration, muscle cramps, or electrolyte disturbances during Creatine supplementation. Some publications even suggest that improved cellular hydration may support exercise tolerance in high-temperature environments (1,10).

Gastrointestinal Complaints

The second most commonly reported group of adverse effects associated with Creatine supplementation includes gastrointestinal complaints, such as a feeling of fullness, bloating, abdominal pain, nausea, and diarrhea (10,20).

These symptoms occur most frequently when high doses of Creatine are used, particularly during the loading phase involving approximately 20 g per day. Consuming large single doses may increase the amount of unabsorbed creatine in the gastrointestinal tract, causing an osmotic effect and intestinal irritation (17,20).

To reduce the risk of gastrointestinal complaints, it is recommended to divide the daily dose into smaller portions, take Creatine with meals, maintain adequate hydration, and use lower doses without a loading phase (1,10).

Some alternative forms, such as creatine hydrochloride (HCl), are marketed as being better tolerated; however, there is currently insufficient evidence confirming their superiority over creatine monohydrate (1,10).

Contemporary literature emphasizes that most adverse effects associated with Creatine supplementation are mild and transient in nature, and that properly used creatine remains a supplement with a strong safety profile in both athletes and recreationally active individuals (1,24).

6.2. The Effects of Creatine Supplementation on the Kidneys and Liver

Creatine, particularly in the form of creatine monohydrate, is among the most extensively studied supplements used in sports and recreational settings. Despite frequent concerns regarding its effects on the kidneys and liver, current scientific evidence does not confirm that creatine use at recommended doses causes damage to these organs in healthy individuals. The position stand of the International Society of Sports Nutrition indicates that both short- and long-term creatine supplementation are safe and well tolerated (1)

Effects of Creatine on the Kidneys

Most controversies concern the effects of Creatine on kidney function, mainly due to the increase in creatinine concentration—a marker commonly used to assess renal function. However, a slight increase in creatinine levels in individuals supplementing with creatine does not necessarily indicate impaired kidney filtration, but may instead result from the natural metabolism of creatine (28).

Meta-analyses and clinical studies have not demonstrated a significant effect of Creatine supplementation on the glomerular filtration rate (GFR) or any nephrotoxic effects in healthy physically active individuals (29,30).

It is emphasized, however, that individuals with chronic kidney disease, reduced eGFR, or those using nephrotoxic medications should consult a physician before starting Creatine supplementation. Reported cases of impaired kidney function have most commonly involved individuals with additional risk factors, dehydration, or the concurrent use of multiple supplements.

Effects of Creatine on the Liver

Scientific studies also do not confirm hepatotoxic effects of Creatine when used according to recommendations. Although creatine synthesis partially occurs in the liver, no significant changes indicative of liver damage have been demonstrated in healthy individuals supplementing with creatine (1).

In a 2025 meta-analysis including numerous clinical studies, the authors also did not demonstrate any significant negative effects of Creatine on liver function parameters (28).

In some studies, slight changes in liver markers such as AST and ALT were observed; however, these changes may have resulted from intense physical exercise, a high-protein diet, dehydration, or the concurrent use of other supplements rather than from the direct effects of Creatine itself. Current evidence indicates that creatine monohydrate, when used according to recommendations, remains a supplement with a strong safety profile for healthy individuals (31).

6.3. Long-Term Safety of Creatine Supplementation

Creatine is one of the most extensively studied dietary supplements used in sports and physical activity. Current scientific evidence indicates that long-term supplementation with creatine monohydrate in healthy individuals is safe and does not cause significant adverse effects (1).

Long-term observations of athletes using Creatine also do not confirm the occurrence of serious health consequences. In a study conducted by Richard B. Kreider and colleagues, the effects of prolonged creatine supplementation in strength-trained athletes were analyzed. No negative effects on kidney function, liver function, or hematological and biochemical parameters were demonstrated (32).

In studies involving National Football League players supplementing with Creatine over extended periods, no increased risk of dehydration, muscle cramps, muscle injuries, or gastrointestinal problems was observed. These findings challenge the common myth suggesting that chronic creatine use may lead to disturbances in water and electrolyte balance (17).

The long-term safety of Creatine has also been investigated in older adults. Studies have shown that several months of creatine supplementation, particularly when combined with resistance training, was well tolerated and did not result in impaired organ function. Moreover, some participants demonstrated improvements in muscle strength, functional performance, and body composition (33).

To date, studies have also not demonstrated any negative effects of Creatine on the cardiovascular system, blood pressure, lipid profile, or glucose metabolism in healthy individuals (1).

It should be emphasized that most safety data concern creatine monohydrate, which remains the best-studied and most recommended form of Creatine supplementation. Individuals with chronic kidney disease, liver disease, or other serious medical conditions should consult a physician before using creatine supplementation. Nevertheless, current evidence clearly indicates that, in healthy individuals, long-term use of creatine monohydrate is not associated with an increased health risk and remains one of the best-documented and safest supplementation strategies in sports nutrition.

7. Applications of Creatine Beyond Sports

7.1. Older Adults – Sarcopenia and Muscle Strength

In recent years, growing interest has emerged regarding the use of Creatine beyond sports, particularly in the prevention and support of treatment for age-related changes. One of the major health problems affecting older adults is sarcopenia, defined as the progressive loss of muscle mass and strength, which increases the risk of falls, loss of independence, and reduced quality of life (16) (15).

Creatine may help counteract sarcopenia by increasing phosphocreatine stores in muscles and improving ATP regeneration, which enables more effective resistance training and supports the maintenance of muscle strength and mass. Studies indicate that creatine supplementation combined with resistance training leads to greater increases in muscle strength and lean body mass in individuals over 50 years of age compared with resistance training alone (1,24).

Improvements in both lower- and upper-limb strength have been demonstrated, which may translate into better functional performance and a reduced risk of falls in older adults (33).

Creatine may also support the maintenance of muscle mass by improving cellular hydration, enhancing training capacity, and stimulating anabolic processes (9).

Some studies also suggest beneficial effects of Creatine on cognitive function in older adults, including improvements in working memory, concentration, and reductions in mental fatigue, although this area requires further research (34).

The greatest effectiveness of Creatine supplementation is observed when it is combined with regular resistance training, whereas supplementation alone may produce limited effects. The most commonly used doses are approximately 3–5 g of creatine monohydrate per day.

Current studies indicate that Creatine is well tolerated by healthy older adults and does not demonstrate significant negative effects on kidney or liver function when used according to recommendations (1).

Current evidence suggests that Creatine may provide effective support in the prevention and treatment of sarcopenia by improving muscle strength, body composition, and functional performance in older adults.

7.2. Neurological Diseases – Neuroprotection and Potential Clinical Applications

In recent years, growing interest has emerged regarding the use of Creatine in neurology and neuroprotection. Due to its key role in cellular energy metabolism, creatine may support the functioning not only of muscles but also of the central nervous system, whose cells are characterized by high energy demands. Disturbances in energy metabolism and mitochondrial function are important components of many neurological disorders.

The mechanism of action of Creatine in the nervous system is primarily associated with the role of phosphocreatine in ATP regeneration, stabilization of mitochondrial function, reduction of oxidative stress, and potential anti-inflammatory and anti-apoptotic effects. Consequently, creatine may exhibit neuroprotective properties and reduce neuronal damage caused by energy deficiency (10).

One of the most extensively studied areas is Parkinson's disease, in which mitochondrial dysfunction and increased oxidative stress are commonly observed. Experimental studies suggested a potential protective effect of Creatine on dopaminergic neurons; however, larger clinical trials have not conclusively confirmed the effectiveness of creatine supplementation in slowing disease progression (35) (36).

Similar results have been observed in Huntington's disease and Amyotrophic Lateral Sclerosis, where, despite promising preclinical findings, no clear clinical benefits have been demonstrated (37,38).

The effects of Creatine on depression, cognitive function, and brain injuries are also being increasingly investigated. Some studies suggest improvements in mood, memory, and concentration, as well as potential protective effects following traumatic brain injuries and hypoxia through enhanced neuronal energy metabolism (34).

Despite promising findings from experimental studies, Creatine is not currently considered a standard treatment for neurological disorders. Current evidence rather suggests a supportive than a therapeutic role, and further studies are necessary to determine its effectiveness, optimal dosage, and long-term safety in neurological patients.

7.3. Metabolic Health – Diabetes, Obesity, and Insulin Resistance

In recent years, an increasing number of studies have focused on the potential effects of Creatine on metabolic health. Although this supplement is primarily associated with sports and improvements in physical performance, current evidence suggests that creatine may also influence glucose metabolism, insulin sensitivity, and body composition. For this reason, its potential supportive use in Type 2 Diabetes, obesity, and insulin resistance is being investigated.

One of the most important mechanisms of action of Creatine in the context of metabolic health is its effect on glucose transport and utilization by skeletal muscles. Creatine may increase the expression of the GLUT-4 transporter, which is responsible for transporting glucose into muscle cells. As a result, glucose uptake may improve, along with tissue sensitivity to insulin (39–41).

Studies indicate that particularly beneficial effects are observed when Creatine supplementation is combined with regular physical exercise. Physical activity itself improves insulin sensitivity, and creatine may further enhance this effect by increasing the muscles' capacity to store glucose (1).

Creatine and Diabetes

Most studies concerning metabolic health have been conducted in individuals with Type 2 Diabetes. This disease is characterized by chronic hyperglycemia resulting from insulin resistance and impaired insulin secretion. In a study conducted by Bruno Gualano and colleagues, creatine supplementation combined with physical training improved glycemic control in patients with type 2 diabetes. Among the observed effects were reductions in glycated hemoglobin (HbA1c) levels and improvements in glucose tolerance (42).

The authors suggested that the improvement in glucose metabolism may have resulted from increased translocation of GLUT-4 transporters to the muscle cell membrane. This mechanism may enhance glucose uptake by muscles independently of insulin action (39–41).

Scientific reviews emphasize, however, that Creatine should not be considered a standalone treatment for Type 2 Diabetes. It may, however, serve as a supportive component of therapy, particularly in physically active individuals (10).

Creatine and Insulin Resistance

Insulin resistance is a condition characterized by reduced tissue sensitivity to insulin and is one of the main factors contributing to the development of Type 2 Diabetes and metabolic syndrome. Studies suggest that Creatine may support improvements in glucose–insulin metabolism by increasing the metabolic activity of muscles and enhancing glycogen storage capacity.

Experimental studies have demonstrated that creatine supplementation may increase the number of GLUT-4 transporters in muscles and improve the body’s response to insulin (17).

Additionally, Creatine may indirectly improve insulin sensitivity by enhancing the capacity for physical exercise. Individuals using creatine often achieve greater training volume and improved recovery, which may contribute to better metabolic parameters.

Creatine and Obesity

Obesity is a chronic metabolic disease associated with excessive accumulation of body fat and an increased risk of Type 2 Diabetes, cardiovascular diseases, and metabolic disorders. Although Creatine is not a weight-loss supplement, it may indirectly support body weight reduction and improvements in body composition.

Creatine supplementation may enhance training capacity and facilitate the maintenance or increase of muscle mass during fat loss. Greater muscle mass is associated with higher energy expenditure, which may support body weight control (9).

Some studies also indicate that Creatine may help limit the loss of lean body mass during calorie-restricted diets, which is particularly important in individuals with obesity and in older adults (16,24).

It is worth emphasizing that Creatine may cause a temporary increase in body weight resulting from increased muscle hydration. However, this is not associated with an increase in body fat. This phenomenon is often mistakenly interpreted as “weight gain from creatine.”

Potential Metabolic Mechanisms of Creatine Action

The potential beneficial effects of Creatine on metabolic health may result from several mechanisms:

- increased expression of GLUT-4 transporters,
- improved muscle glycogen storage,
- enhanced exercise capacity and physical activity,
- improved mitochondrial function,
- increased lean body mass,
- indirect improvement in insulin sensitivity.

Despite promising research findings, further long-term clinical studies are necessary to precisely determine the role of creatine in the treatment of metabolic disorders.

Current scientific evidence suggests that Creatine may positively influence glucose metabolism, insulin sensitivity, and body composition. The best-documented benefits concern improved glycemic control and support of physical training in individuals with Type 2 Diabetes and insulin resistance. However, creatine is not a standalone treatment for metabolic diseases, but rather may serve as a supportive element of a healthy lifestyle and therapy supervised by a healthcare professional.

8. Current Supplementation Recomendations

8.1. Dosing Protocols – Loading Phase and Maintenance Doses

Currently, creatine monohydrate is the best-studied and most commonly recommended form of Creatine used in both competitive sports and recreational physical activity. Current dosing recommendations are based on numerous clinical studies evaluating the effectiveness and safety of various supplementation protocols. The most commonly used strategies include a loading phase followed by maintenance-dose supplementation.

The position stand of the International Society of Sports Nutrition indicates that the most effective method of rapidly increasing muscle creatine stores is the use of a loading phase consisting of approximately 20 g of creatine per day for 5–7 days. This dose is usually divided into four servings of approximately 5 g taken throughout the day (1).

The loading phase allows for the rapid saturation of muscles with Creatine and increases phosphocreatine concentrations within muscle cells. As a result, the effects of supplementation—such as improvements in muscle strength, exercise capacity, and recovery—may appear more quickly compared with using lower doses from the beginning of supplementation (43).

After completing the loading phase, it is recommended to transition to maintenance doses, typically consisting of 3–5 g of Creatine per day. This amount helps maintain elevated creatine stores in the muscles over the long term (1).

An alternative approach is to omit the loading phase and use a consistent dose of approximately 3–5 g of Creatine per day from the beginning. Studies show that this supplementation model also effectively increases creatine concentrations in the muscles; however, the process of full muscle saturation takes longer—usually around 3–4 weeks (41).

In practice, this means that the loading phase may accelerate the appearance of ergogenic effects; however, it is not necessary to achieve the benefits of Creatine supplementation. For this reason, some individuals choose to omit it, particularly if they wish to reduce the risk of temporary gastrointestinal discomfort or sudden body weight gain resulting from increased muscle hydration.

Some recommendations also suggest individualizing the dosage according to body weight. In scientific studies, doses of approximately 0.3 g/kg of body weight per day during the loading phase and around 0.03 g/kg of body weight per day during the maintenance phase have frequently been used (1).

An important consideration is also the timing of Creatine intake. Current research does not clearly indicate that a specific timing of supplementation plays a crucial role in the effectiveness of creatine. However, some studies suggest that taking creatine close to the training session—either before or after exercise—may slightly enhance the effectiveness of supplementation (44).

The absorption of Creatine may be further enhanced by the simultaneous intake of carbohydrates or protein, as insulin increases the transport of creatine into muscle cells (1).

Current recommendations also emphasize the importance of adequate hydration during Creatine supplementation. This is because creatine increases the hydration of muscle cells by promoting water retention within the muscles. However, this does not mean that creatine causes dehydration—studies have not confirmed such an effect in healthy individuals (17).

It is worth noting that most scientific studies and recommendations concern creatine monohydrate. Other forms of Creatine, such as creatine malate, creatine ethyl ester, or creatine hydrochloride (HCl), have not yet demonstrated superior effectiveness or safety compared with creatine monohydrate (1).

Current recommendations indicate that the most effective and best-studied protocol for Creatine supplementation involves a loading phase of approximately 20 g per day for 5–7 days, followed by a maintenance dose of 3–5 g per day. Alternatively, a consistent intake of 3–5 g per day without a loading phase may also be used, which likewise leads to muscle creatine saturation, although over a longer period of time.

8.2. Timing of Supplementation – Before or After Training and the Importance of Timing

One of the most frequently discussed issues regarding Creatine supplementation is the optimal timing of intake. In sports practice, creatine is commonly taken before training, after training, or at any time of the day. Current scientific evidence indicates, however, that overall consistency of supplementation is more important than the exact timing of ingestion. Nevertheless, some studies suggest that taking creatine close to the training session may produce slightly better effects.

Creatine primarily works by increasing phosphocreatine stores in the muscles, allowing for faster ATP resynthesis during high-intensity exercise. This mechanism mainly depends on the gradual saturation of muscles with creatine; therefore, unlike caffeine or stimulant substances, creatine does not exert an immediate acute effect. This means that a single dose of creatine taken directly before exercise does not instantly improve performance. The key factor is regular supplementation leading to the maintenance of elevated creatine levels in the muscles (1).

Despite this, some studies suggest that Creatine supplementation immediately after training may be slightly more beneficial than taking it before exercise. In a study conducted by Jose Antonio and Victoria Ciccone, the effects of creatine supplementation administered before versus after resistance training were compared. The authors demonstrated greater improvements in body composition and muscle strength in the group taking creatine after training (44).

The potential benefits of post-workout Creatine supplementation may result from increased blood flow through the muscles and greater insulin sensitivity following exercise. After training, muscles take up nutrients more efficiently, which may facilitate the transport of creatine into muscle cells.

There are also studies suggesting that consuming Creatine together with carbohydrates or protein may increase its retention in muscles. This mechanism is associated with the action of insulin, which enhances the transport of creatine into muscle cells (1,45).

In practice, this means that it may be beneficial to take Creatine after training together with a meal containing protein and carbohydrates. However, this is not a necessary condition for achieving the benefits of supplementation.

On non-training days, the timing of creatine intake likely has little significance. The most important factor remains consistent daily supplementation in order to maintain elevated creatine levels in the muscles (1).

Some studies have also analyzed the effects of so-called nutrient timing, meaning the precise planning of nutrient intake around training sessions. Current findings suggest that the timing of Creatine intake may have a modest optimizing effect; however, its influence appears to be considerably smaller than the total supplement dose, consistency of use, and appropriate training (46).

It is also worth noting that some studies have not demonstrated significant differences between taking Creatine before versus after training. For this reason, current recommendations do not clearly indicate a single best time for supplementation (47).

An important practical aspect is also gastrointestinal tolerance. In some individuals, taking larger doses of Creatine immediately before training may cause gastrointestinal discomfort. In such cases, taking creatine after training or together with a meal may be more beneficial.

Recent scientific evidence indicates that the most important factor determining the effectiveness of Creatine is regular supplementation leading to muscle saturation with creatine. Some studies suggest that taking creatine after training may slightly enhance the effectiveness of supplementation, particularly when the supplement is consumed together with carbohydrates and protein. However, these differences are not substantial enough for the timing of creatine intake to be considered more important than an appropriate dose and consistent supplementation.

8.3. Combining Creatine with Other Supplements – Protein, Caffeine, and Beta-Alanine

Creatine is often used simultaneously with other dietary supplements that support exercise performance, recovery, and muscle mass development. The most commonly analyzed combinations include protein, caffeine, and beta-alanine. Current scientific evidence suggests that appropriately combining creatine with other supplements may enhance some ergogenic effects, although effectiveness depends on the type of supplement, dosing strategy, and type of physical activity.

Creatine and Protein

One of the most popular supplementation combinations is the simultaneous use of Creatine and protein supplements. Protein provides amino acids necessary for muscle protein synthesis, whereas creatine enhances exercise capacity and supports ATP regeneration. As a result, both supplements may act synergistically in increasing muscle mass and strength.

Studies indicate that creatine supplementation combined with adequate protein intake and resistance training may lead to greater increases in lean body mass compared with resistance training alone (19).

Additionally, consuming Creatine together with protein and carbohydrates may enhance the transport of creatine into muscles. This mechanism is associated with insulin secretion, which increases creatine uptake by muscle cells (1,45).

In sports practice, Creatine is often taken together with a protein supplement after training. This approach may support post-exercise recovery and anabolic processes occurring in the muscles.

Creatine and Caffeine

The relationship between Creatine and caffeine remains one of the most controversial topics in sports supplementation. Caffeine is a potent ergogenic aid that improves concentration, alertness, and exercise performance, particularly during endurance and interval exercise. However, hypotheses have emerged suggesting that caffeine may weaken the effects of creatine.

One earlier study demonstrated that the simultaneous use of high doses of caffeine may partially counteract the beneficial effects of Creatine on muscular performance. The authors suggested that this could result from the opposing effects of both substances on muscle relaxation time (48).

Later studies, however, did not conclusively confirm a negative interaction between Creatine and caffeine. It is currently believed that moderate caffeine intake likely does not significantly reduce the effectiveness of creatine in most individuals (49).

It is worth noting, however, that the simultaneous use of large amounts of caffeine and Creatine may increase the risk of gastrointestinal discomfort in some individuals. Additionally, caffeine may negatively affect sleep quality, which can indirectly impair recovery.

Despite some controversy, Creatine and caffeine are often used together in pre-workout supplements. Current evidence suggests that both supplements may work in parallel by influencing different mechanisms involved in performance enhancement.

Creatine and Beta-Alanine

Beta-Alanine is an amino acid that serves as a precursor to carnosine—a compound that functions as a buffer for hydrogen ions in muscles. Beta-alanine supplementation may delay the onset of fatigue during high-intensity exercise lasting approximately 1–4 minutes.

Creatine and Beta-Alanine act through different mechanisms; therefore, combining them may potentially produce a synergistic effect. Creatine increases ATP availability and improves the capacity for short-duration explosive efforts, whereas beta-alanine reduces muscle acidosis during intense exercise.

Researchers suggest that simultaneous supplementation with Creatine and Beta-Alanine may improve exercise performance and increase lean body mass more effectively than using either supplement alone (50).

Some studies have observed improvements in strength, power output, and exercise capacity during interval and resistance training (51).

The greatest benefits from combining Creatine and Beta-Alanine may be achieved by individuals involved in strength sports, speed-based sports, and activities requiring repeated high-intensity efforts.

Practical Significance of Combining Supplements

Current scientific evidence indicates that Creatine can be effectively combined with other supplements that support performance and training adaptations. The best-documented benefits concern the combination of creatine with adequate protein intake and resistance training.

In the case of caffeine, research findings are less conclusive; however, moderate caffeine intake likely does not significantly impair the effects of Creatine. In contrast, combining creatine with Beta-Alanine may produce synergistic effects in improving exercise performance.

Therefore, appropriately combining Creatine with other supplements may enhance the effectiveness of supplementation and support training adaptations. Nevertheless, proper dosing, consistency of use, and tailoring supplementation to the type of physical activity and individual needs remain crucial.

9. Limitations of Current Research

Despite the very large number of publications concerning Creatine, many aspects of its effects still require further investigation. Current scientific evidence confirms the high effectiveness and safety of creatine supplementation in many areas; however, the interpretation of research findings should take existing methodological limitations into account. The most important issues include small sample sizes, differences in study design, an insufficient number of studies conducted in women, and the limited number of long-term observations in selected clinical populations.

Small Sample Sizes

One of the most common limitations of studies on Creatine is the relatively small number of participants included in research groups. Many clinical studies involve only several or several dozen participants, which limits the ability to generalize the findings to the broader population. Small sample sizes also increase the risk of statistical errors and make it more difficult to detect subtle effects of supplementation.

This problem particularly concerns studies conducted in specific populations, such as older adults, patients with neurological disorders, and women. In some studies, the positive effects of supplementation may have been overestimated or underestimated precisely because of the limited number of participants (10).

Additionally, some studies include only young and physically active individuals, which limits the ability to generalize the findings to the general population or to individuals with medical conditions.

Methodological Differences

Another important issue in interpreting research on Creatine is the substantial methodological variability between individual studies. Research differs in terms of the type of creatine used, dosage, duration of supplementation, the presence or absence of a loading phase, type of physical activity, participants' training status, and the methods used to assess supplementation outcomes.

Some studies have used creatine monohydrate, whereas others have investigated less extensively studied forms, such as creatine ethyl ester or creatine malate. This makes direct comparison of the results more difficult (1).

Significant differences also concern the duration of supplementation. Some studies lasted only a few days or weeks, whereas others involved observations extending over many months. Short study durations may limit the ability to assess the full effects of supplementation as well as its long-term safety.

Another methodological issue is the lack of standardization of participants' training and diet. The effects of Creatine are strongly influenced by the type of physical activity, protein intake, and total caloric intake; therefore, insufficient control of these factors may affect the obtained results.

Insufficient Number of Studies in Women

Most studies concerning Creatine have been conducted in men, particularly young strength-trained athletes. Women remain clearly underrepresented in research on creatine supplementation, which constitutes one of the most important limitations of the current scientific literature (9).

Hormonal, physiological, and metabolic differences between women and men may influence the effects of Creatine. These differences involve, among others, fluid balance, energy metabolism, phosphocreatine levels, and the influence of sex hormones on muscles and recovery.

An increasing number of studies suggest that Creatine may be particularly beneficial for women during specific stages of life, such as menopause; however, the number of high-quality studies in this area remains limited (52).

There is also an insufficient number of studies involving physically active women participating in endurance sports, which makes it difficult to formulate clear recommendations regarding dosing and the effectiveness of Creatine supplementation in this group.

Lack of Long-Term Observations in Certain Populations

Although Creatine is considered a supplement with a high safety profile, there is still a lack of long-term studies involving certain population groups. This particularly concerns individuals with chronic diseases, children and adolescents, pregnant women, older adults with multiple comorbidities, and neurological patients.

Most available long-term studies have been conducted in healthy, young, physically active individuals (1).

In patients with neurological or metabolic disorders, study results are often inconclusive, and the observation periods are frequently too short to assess the actual impact of Creatine supplementation on disease progression (10).

The limited number of long-term studies also makes it difficult to assess the potential effects of many years of Creatine supplementation in the general population. Although the available evidence does not indicate significant health risks, further studies involving long-term observation of large participant groups are necessary.

Summary

Despite the large number of scientific studies concerning Creatine, important limitations still hinder a complete evaluation of its effects across all populations. The main issues arise from small sample sizes, substantial methodological differences, insufficient representation of women, and the lack of long-term observations in certain clinical groups. Current scientific evidence confirms the effectiveness and safety of creatine in healthy physically active individuals; however, further high-quality research is necessary to more precisely determine its effects in different populations and clinical settings.

10. Conclusions

Creatine is currently one of the best-researched dietary supplements used in both competitive and recreational sports. Numerous scientific studies and meta-analyses confirm its high ergogenic effectiveness, particularly in the context of high-intensity, short-duration anaerobic exercise (1).

The mechanism of action of Creatine is primarily related to increasing phosphocreatine stores in the muscles, which enables faster ATP resynthesis during intense physical exercise. As a result, creatine supplementation may lead to improvements in muscle strength, power output, exercise capacity, and post-exercise recovery. The greatest effectiveness is observed in disciplines requiring short-duration, repeated high-intensity efforts, such as strength sports, sprinting, and resistance training (32).

Current scientific evidence also indicates that Creatine may support increases in lean body mass and improve training adaptations, particularly when supplementation is combined with regular resistance training (24).

At the same time, Creatine is considered a supplement with a high safety profile. Current studies have not demonstrated significant negative effects of properly used creatine on kidney function, liver function, or the cardiovascular system in healthy individuals. The most commonly observed effect of supplementation remains a temporary increase in body weight resulting from increased muscle hydration (1,28).

Contemporary research increasingly points to potential clinical applications of Creatine beyond sports performance. Its effects are being investigated in relation to sarcopenia and muscle mass loss in older adults, neurological disorders, cognitive function, metabolic disorders, as well as Type 2 Diabetes and insulin resistance.

Current findings suggest that Creatine may exhibit neuroprotective properties and support energy metabolism not only in muscles, but also in the brain (10).

Despite the very large number of scientific publications, certain limitations still exist in research concerning Creatine. These mainly involve small sample sizes, methodological differences between studies, and the limited number of long-term observations in certain clinical populations. Further research is particularly needed in women, older adults, and patients with chronic diseases (9).

In summary, Creatine is one of the best-documented and safest supplements used in modern sports nutrition. Its effectiveness in improving exercise performance has been confirmed in numerous scientific studies, while a growing body of evidence also points to the broad potential clinical applications of creatine in medicine and preventive healthcare.

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