Beta-Alanine

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summary

Beta-alanine is a non-essential amino acid with the chemical formula $CfH\ddagger NO$,, classified as a beta amino acid due to its amino group attached to the beta carbon atom. It plays a critical role in the synthesis of carnosine, a dipeptide that functions as a major intracellular buffer in skeletal muscle during high-intensity exercise, thus helping to regulate pH and delay fatigue. This makes beta-alanine particularly significant for athletes and individuals engaged in strenuous physical activities, as it enhances muscle performance and overall exercise capacity by mitigating the effects of acidosis during intense workouts. [1][2][3][4].

The compound is naturally synthesized in the human body through the degradation of uracil and as a byproduct of carnosine metabolism, though dietary sources predominantly include animal proteins such as meat and fish. [5][6][7] With limited natural availability, beta-alanine supplementation has gained popularity among athletes seeking to improve performance in activities lasting from 1 to 10 minutes. Research has demonstrated that such supplementation can significantly increase muscle carnosine levels, leading to enhanced endurance and strength, while recommended dosages typically range from 3.2 to 6.4 grams per day. [6][8][9].

Despite its benefits, beta-alanine supplementation is not without potential side effects, the most notable being paresthesia, a harmless tingling sensation that can occur at higher doses. Concerns also exist regarding its interactions with certain medications, necessitating caution among individuals with specific health conditions or those taking medications.[10][11][12]. Furthermore, the regulatory environment surrounding dietary supplements highlights the importance of informed choices, as the FDA does not require manufacturers to prove safety or efficacy prior to market entry.[11].

Overall, beta-alanine remains a widely studied and utilized supplement within the athletic community, credited for its significant role in enhancing performance during high-intensity activities, while also contributing to improved overall wellness and recovery.[6][13][10][14].

Chemical Structure

²Alanine, with the chemical formula C3H7NO2, is classified as a beta amino acid due to the presence of an amino group attached to the beta carbon atom[1][2]. Its molecular weight is approximately 89.0932 g/mol[15][16]. The compound has

a standard IUPAC InChIKey of UCMIRNVEIXFBKS-UHFFFAOYSA-N and a CAS Registry Number of 107-95-9[15][17][2].

In terms of physical appearance, ²Alanine typically presents as white bipyramidal crystals and is characterized by being odorless[18][16]. The density of ²Alanine is recorded at 1.437 g/cm³ at 19 °C[18]. The chemical structure can also be represented using various notational systems, including the SMILES notation, which is given as [H]OC(=O)C([H])([H])C([H])N([H])N([H])[H][1].

The compound plays a significant role in various biological functions, including muscle performance enhancement and the buffering of acid in muscles during high-intensity exercise[3].

Synthesis and Sources

Synthesis of Beta-Alanine

Beta-alanine is synthesized in the human body through the degradation of uracil, a pyrimidine base found in RNA, as well as dihydroorotic acid[5]. It is also produced as a byproduct of carnosine metabolism, which involves the synthesis of carnosine from ²alanine and L-histidine through the action of the enzyme carnosine synthase (EC 6.3.2.11) in the presence of ATP[19][20]. The reaction can be reversed, indicating a dynamic balance between carnosine and its constituent amino acids. The plasma concentration of ²alanine is typically less than 2 M, while its uptake into muscle tissue is contingent upon its availability, making it a rate-limiting substrate for carnosine synthesis[4][6].

Dietary Sources of Beta-Alanine

Beta-alanine is found in various dietary sources, particularly in animal proteins. The primary food sources rich in beta-alanine include meats such as beef, pork, poultry, and fish[7][8]. These foods provide a direct source of beta-alanine, which can contribute to its availability for muscle synthesis. Additionally, carnosine-rich foods, such as beef and chicken, indirectly supply ²alanine since carnosine itself is a dipeptide composed of ²alanine and L-histidine[6][21].

Supplementation

Due to the limited dietary sources and the body's relatively low endogenous synthesis, ²alanine supplementation has gained popularity, particularly among athletes. Research has shown that supplementation with ²alanine can significantly increase muscle carnosine levels, leading to improved performance in high-intensity exercise-[6][9]. Recommended doses for effective supplementation typically range from 3.2 to 6.4 grams per day, which have been demonstrated to enhance muscle buffering capacity, delay fatigue, and potentially improve cognitive function during athletic performance[22][23].

Mechanism of Action

Beta-alanine functions primarily as a precursor to carnosine, a dipeptide that plays a critical role in regulating intracellular pH in skeletal muscle. Carnosine is synthesized in the muscle from ²alanine and L-histidine through the action of carnosine synthase, with the availability of ²alanine being the rate-limiting factor in this process[20][9]. The presence of carnosine is particularly important during high-intensity exercise, where it acts as a major intracellular buffer against acidosis by accepting hydrogen ions (H+) produced during anaerobic glycolysis[4][8].

Role in Muscle Acidosis

During intense physical activity, the accumulation of H+ ions results in a decrease in muscle pH, contributing to fatigue and limiting performance. Research has shown that carnosine can buffer H+ and slow the decline in muscle pH, thereby mitigating the effects of acidosis[4][9]. Specifically, carnosine contributes approximately 15% to the total buffering capacity of muscle, highlighting its significance in maintaining optimal pH levels during exercise[4]. Additionally, the binding of carnosine to H+ enhances calcium (Ca2+) unloading at the sarcomere, promoting increased cross-bridge formation and force production[13][8].

Energy Systems and Exercise Performance

In high-intensity sports lasting approximately 1-10 minutes, energy production relies heavily on anaerobic systems, such as phosphocreatine degradation and anaerobic glycolysis, as aerobic metabolism cannot meet the immediate energy demands[4]. As such, carnosine's buffering capacity is vital in facilitating sustained performance during these high-energy efforts. Studies have indicated that ²alanine supplementation increases muscle carnosine levels, which can enhance performance in short-duration, high-intensity exercises ranging from 6 to 60 seconds[8][23][24]. While ²alanine may not directly improve maximal strength or VO2 max, it significantly aids aspects of endurance performance like anaerobic threshold and time to exhaustion, ultimately delaying the onset of fatigue[9][24].

Benefits of Supplementation

Performance Enhancement

Beta-alanine supplementation has been shown to significantly improve athletic performance, particularly in high-intensity exercises lasting from 4 to 10 minutes. Research indicates that beta-alanine can enhance repeated sprint performance and increase the volume of work completed during strength training sessions, as evidenced by the increased number of sets performed by subjects taking beta-alanine compared to those on a placebo[8][25]. Additionally, it may also lead to substantial

gains in strength, as evidenced by improvements in one-repetition maximum (1RM) lifts[8].

Delayed Fatigue

One of the primary benefits of beta-alanine is its ability to delay fatigue during high-intensity activities. Beta-alanine increases muscle carnosine levels, which helps buffer the accumulation of lactic acid during intense exercise, thereby reducing acidity in the muscles and postponing the onset of fatigue[10][26]. This buffering capacity is particularly beneficial for athletes engaged in sports that require sustained high-intensity efforts lasting between 6 to 60 seconds[8][27].

Aerobic Endurance

Beta-alanine supplementation has also been linked to improvements in aerobic endurance during activities exceeding four minutes in duration[13]. Athletes utilizing beta-alanine may experience enhanced endurance, which contributes to improved performance across various sports disciplines.

Overall Wellness

In addition to its performance benefits, beta-alanine is associated with improved overall wellness. It is suggested that regular supplementation can lead to increased endurance ability and decreased feelings of fatigue, promoting better recovery and exercise performance[10][14][6].

Combination with Other Supplements

When used in conjunction with other performance-enhancing supplements, such as branched-chain amino acids (BCAAs) and electrolytes, beta-alanine can further optimize athletic output. This combination may lead to increased VO2 max, enhanced anaerobic thresholds, and reduced exercise-related fatigue by targeting different mechanisms of fatigue and performance enhancement [28][29].

Dosage and Administration

Beta-alanine supplementation has been extensively studied, with clinical evidence suggesting effective daily doses ranging from 2 to 5 grams, with an optimal dosage of approximately 3.2 grams[30][4]. To achieve the best ergogenic effects, a chronic loading dose of 4 to 6 grams per day, divided into smaller doses of 2 grams or less, is recommended[31][32]. This approach helps in minimizing the risk of paresthesia, a common side effect associated with beta-alanine supplementation, which can be managed by taking 0.8 to 1.6 grams every 3 to 4 hours[33].

Timing of Supplementation

The timing of beta-alanine intake can also influence its effectiveness. It is generally advised to take beta-alanine 30 to 45 minutes before exercising, allowing sufficient time for the supplement to be absorbed into the bloodstream and exert its effects during high-intensity workouts[32]. However, consistent intake over an extended period (at least 4 weeks) is crucial, as the benefits of beta-alanine become more pronounced after achieving saturation levels in the body, estimated to be around 179 grams[34].

Dosing Strategies

Different dosing strategies have been proposed to tailor beta-alanine supplementation according to body weight. For instance, one method suggests administering 50% of the total dose as a fixed dose (FD) and the remaining 50% as a weight-relative dose (WRD), using a 70 kg individual as a reference point[35]. This means a targeted 1,400 mg dose would translate to 700 mg for a 70 kg person, with proportional adjustments for those weighing less or more. Furthermore, some studies indicate that beta-alanine doses are most effective when taken multiple times throughout the day, rather than as a single bolus, to maintain optimal plasma levels and performance enhancement[23][36].

Side Effects and Precautions

Beta-alanine is generally considered safe for healthy individuals; however, there are several side effects and precautions to be aware of before using this supplement.

Common Side Effects

The most frequently reported side effect of beta-alanine supplementation is paresthesia, which manifests as a tingling sensation on the skin, particularly in the face, hands, and extremities. This harmless sensation is typically dose-dependent and can occur after taking doses greater than 800 mg, lasting from 30 to 60 minutes before subsiding. [11][12][26] While paresthesia is generally not a health concern, some users may find it uncomfortable. To mitigate this effect, it is recommended to split the daily dosage into smaller amounts taken at intervals throughout the day. [37] In addition to paresthesia, some users may experience gastrointestinal issues such as nausea, stomach cramps, or diarrhea, especially when consuming high doses. [38][12] These side effects are rare and can often be avoided by adhering to recommended dosages.

Interactions and Precautions

It is crucial for individuals to consult a healthcare professional before starting beta-alanine supplementation, particularly if they have underlying health conditions or are taking medications. There is potential for beta-alanine to interact with certain heart medications and drugs used for erectile dysfunction, highlighting the importance of medical guidance.[11][38] Moreover, the safety of beta-alanine for children,

pregnant women, and breastfeeding mothers has not been established, warranting additional caution for these populations.[11]

Regulatory Considerations

While the U.S. Food and Drug Administration (FDA) regulates dietary supplements, it treats them more like food products than medications, which means manufacturers are not required to prove the safety or efficacy of their products before they reach the market. This regulatory environment underscores the importance of being cautious and well-informed about the supplements one chooses to use.[11]

Research and Evidence

Overview of ²Alanine Supplementation

Research on ²alanine (BA) supplementation has demonstrated its effectiveness in enhancing exercise performance, particularly in resistance training. Studies have shown that BA can lead to an increase in the number of repetitions performed during exercises like the leg press when using a load equivalent to 65% of an individual's one-repetition maximum (1RM) [8]. Additionally, the combination of BA and creatine has been linked to improved performance in 1RM squat tests [8].

Dosing Strategies and Performance Outcomes

Despite the promising findings, the current evidence suggests that standard dosing methods for BA supplementation may not adequately address the diverse physiological responses among athletes. A systematic review indicated that neither fixed doses (FD) nor weight-related dosing (WRD) produced consistent results, as individual responses varied significantly based on anthropometric characteristics [35]. This variation emphasizes the need for more tailored dosing strategies to optimize performance and minimize side effects. For instance, insufficient intake can lead to minimal increases in carnosine levels, which are crucial for performance enhancement, while excessive doses may result in adverse effects such as paraesthesia [35].

Future Research Directions

Future investigations should focus on refining dosing strategies and expanding the duration of supplementation periods to assess the potential for more substantial improvements in performance metrics. It is also suggested that studies explore the synergistic effects of BA with other supplements, such as sodium bicarbonate and caffeine, during strength training programs [8]. This will help establish more precise recommendations for athletes based on their unique physiological profiles and training needs [24].

Comparative Analysis with Other Supplements

Overview of Beta-Alanine and Other Performance Supplements

Beta-alanine is a non-essential amino acid that is commonly used to enhance athletic performance, particularly in high-intensity, sustained exercise events. It primarily functions by increasing muscle carnosine levels, which helps buffer lactic acid and reduce muscle fatigue during prolonged physical activity[26][4]. In comparison, creatine, another popular supplement, enhances high-intensity performance by increasing the availability of adenosine triphosphate (ATP), crucial for maximal effort activities like sprinting or heavy lifting[12][26].

Effects on Performance

Research indicates that beta-alanine can improve performance, particularly in activities lasting from 1 to 10 minutes, with reported improvements in high-intensity functional training and resistance exercises[24][8][4]. Studies have shown that beta-alanine supplementation can lead to a 2-3% increase in performance during sustained efforts, while the combination of beta-alanine and creatine has been found to further amplify strength and endurance benefits[8][26][4]. Specifically, the joint supplementation has shown effectiveness in increasing the number of repetitions in resistance training and improving one-repetition maximum (1RM) lifts[8].

Dosing Strategies

Beta-alanine is typically recommended in doses of 4-6 grams per day, taken consistently to maintain elevated muscle carnosine levels, whereas creatine is often consumed in a daily loading phase followed by maintenance doses[12][26]. Combining beta-alanine with other supplements, such as sodium bicarbonate, may enhance its efficacy, particularly for athletes focused on endurance and resistance training[6][26].

Potential Side Effects and Considerations

While both beta-alanine and creatine are generally safe, they may present some mild side effects. Beta-alanine is associated with paresthesia, a tingling sensation in the skin, particularly at higher doses[6][26]. In contrast, creatine may lead to gastrointestinal discomfort if not properly dosed[12]. Moreover, individual responses to these supplements can vary, with some research indicating that well-trained athletes might experience smaller performance gains compared to untrained individuals due to a biological performance ceiling effect[4].

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