AUCTORES
Globalize your Research

Clinical Medical Reviews and Reports

Sadique Hussain *

Open Access

Case Report

Role of Glutamine as an Ergogenic Amino Acid during Fatigue

Keshav Trivedi[1], Md Sadique Hussain[2,*], Chandan Mohapatra[2]

[1]School of Engineering and Technology, Jaipur National University, Jagatpura (302017), Jaipur, Rajasthan, India.

[2]School of Pharmaceutical Sciences, Jaipur National University, Jagatpura (302017), Jaipur, Rajasthan, India.

Corresponding Author: Sadique Hussain, School of Pharmaceutical Sciences, Jaipur National University Jagatpura (302017), Jaipur, Rajasthan, India.

Received Date: November 01, 2021; **Accepted Date:** December 16, 2021; **Published Date:** January 05, 2022

Citation: Keshav Trivedi, Md Sadique Hussain, Chandan Mohapatra (2022) Role of Glutamine as an Ergogenic Amino Acid during Fatigue, *J, Clinical Medical Reviews and Reports.* 4(2); DOI:10.31579/2690-8794/111

Abstract

Physical activity has an impact on the interior environment's balance. Contracting muscles provide force, power, and heat during exercise. As a result, physical activity is a kind of mechanical energy. The body's energy reserves will be depleted as a result of the created energy. During exercise, metabolites and heat are produced, affecting the internal environment's steady state. Depending on the type of activity, weariness and exhaustion will set in sooner or later. Glutamine is the most common free amino acid in human muscle and plasma, and it is used extensively by rapidly proliferating cells, such as leucocytes, to supply energy and ideal circumstances for nucleotide production. As a result, it is thought to be necessary for effective immunological function. Glutamate serves a variety of functions, including protein synthesis, an anabolic precursor for muscle growth, acid-base balance in the kidney, ureagenesis in the liver, hepatic and renal gluconeogenesis, oxidative fuel for the intestine and immune system cells, inter-organ nitrogen transport, a precursor for neurotransmitter synthesis, a precursor for nucleotide and nucleic acid synthesis, and precursor for glutathione production. Severe metabolic stress, such as sepsis or extensive surgery, depletes glutamine reserves in muscles. As a result, it is regarded as conditionally vital in certain circumstances. The physiological importance of glutamine is discussed in this review, as well as how glutamine supplementation can help with weariness.

Keywords: anti-fatigue, immune booster, exercise enhancer, muscle repair

Introduction

Many physiologists have been interested in exercise-induced weariness and exhaustion for far more than a century. Even though most exercise-related research focuses on the neuromuscular system, all organs are involved. Other organs, in addition to the neuromuscular system, respond to an individual's exercise ability. This exercise ability is widely recognized to be diminished during sickness. End-stage renal failure, for example, has a significant influence on exercise ability [1, 2]. Fatigue is the inability to maintain power production and strength, resulting in a reduction in physical performance. The buildup of protons in the muscle cell, depletion of energy supplies (e.g., phosphocreatine and glycogen), ammonia accumulation in the blood and tissues, oxidative stress, muscle injury, and changes in neurotransmitter production, such as an increase in serotonin and a reduction in dopamine, are the major causes of weariness. Several dietary techniques have been used to postpone the onset of weariness and increase athletic performance. The role of amino acids in the improvement of fatigue has been debated since the mid-1980s and 1990s, and indication has shown that plasma glutamine concentrations and the glutamine/glutamate plasma ratio are diminished in athletes suffering from chronic fatigue and overtraining syndrome, raising the question of glutamine supplementation's possible ergogenic effects [3, 4].

Of the 20 amino acids in humans, glutamine (Gln) is the most prevalent free (non-essential) amino acid. In healthy people, no deficits are expected to exist because Gln can be produced from scratch [5] Figure 1 shows the steps in the synthesis of Gln. It also functions as a precursor of nucleotide bases and the antioxidant glutathione in acid-base control, gluconeogenesis, and as a precursor of nucleotide bases and glutathione [6, 7]. Gln levels drop dramatically in a variety of catabolic illness conditions, prompting speculation that Gln is a conditionally required dietary component rather than a non-essential amino acid [8]. During acute metabolic stress, such as sepsis or major surgery, Gln is drained from muscle reserves. As a result, it is regarded conditionally necessary under certain circumstances [9]. During a short-term fast, such as an overnight fast, Gln is the major amino acid produced from skeletal muscle. The concentration of Gln in human muscle is 20 mmol/L, compared to 0.6 mmol/L in plasma. During times of stress, such as exercise, a rise in cortisol levels in the blood causes muscle protein proteolysis and Gln release. The liver, muscle, adipose, and lung are among the tissues that may produce and release Gln into the circulation. However, skeletal muscle is the most significant, since it both synthesizes and stores Gln, which is absorbed by the colon, liver, and kidney, as well as some immune system cells. The whole human muscle releases about

8–9g of Gln each day [10]. Gln is the most common amino acid in the human body and is involved in the prevention and treatment of physiological stress and serious disease on a biological level. Gln supplementation has been linked to improvements in biological indicators of heat stress in both human and animal models, as well as a reduction in athletes' perceived weariness [11].

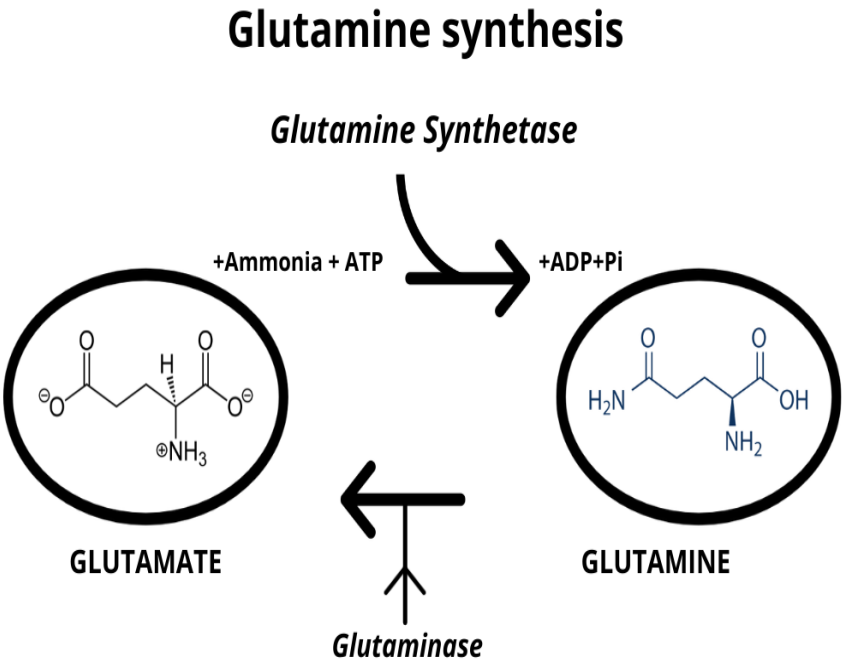

Figure 1: *Synthesis of Glutamine.*

The enzyme Gln synthetase (GS) is primarily responsible for the production of Gln, which is then hydrolyzed by glutaminase (GLS). Gln biosynthesis is catalysed by GS utilising glutamate and ammonia (NH3) as sources. One ATP is spent in this reaction. Many amino acids can supply glutamate, either exogenously (via the food) or endogenously (through the degradation of endogenous amino acids). GLS, on the other hand, is in charge of converting glutamine to glutamate and ammonium ion (NH4). GS and GLS are expressed by almost all cells in the body, and their predominant expression and activity determine whether a tissue is more likely to create or consume Gln in health and sickness [12].

Athletes have an increased risk of sickness following extensive, exhausting activity, as has been widely established. Individuals who have completed a marathon, for example, have greater symptoms than athletes who engage in moderate activity or athletes who prepare for but do not compete in endurance events. Furthermore, additional evidence has been gathered indicating Gln's putative significance in the immune system. When compared to the number of infections reported by athletes following a 15-mile training session or a 10-kilometer race, infections were higher in most categories of athletes tested after an intensive training session or an endurance event. Gln in a drink reduced the frequency of infections in athletes during the week after various forms of exhausting, long-duration exercise [13] Figure 2 represents the other broader functions of glutamine.

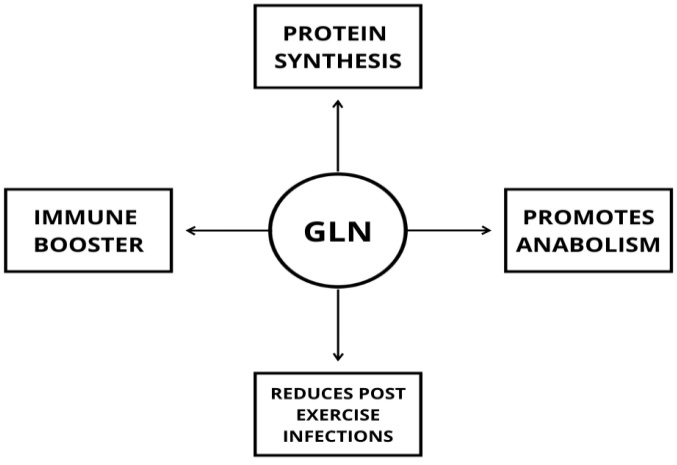

Figure 2: *General functions of glutamine.*

Glutamine as Anti-Fatigue

Gln quantities in the body are not only high but also exceedingly labile, as scientists discovered a few years ago. The concentration of Gln in the circulation and cellular pools drops rapidly after surgery, damage, systemic infection, and other serious disorders. The drop in Gln concentrations is bigger than any other amino acid, correlates to the severity of the underlying illness process in general, and is only restored late in the healing phase. The fast loss of large amounts of Gln from muscle pools in catabolic illness shows that Gln may make up a considerable portion of the labile protein pool recruited after damage [14, 15]. It's been suggested that a lack of Gln in the muscles might lead to a slower rate of lymphocyte proliferation in response to antigens, compromising immunological protection against viral infection. Intense physical activity may reduce the rate of Gln production from skeletal muscle and/or accelerate the amount of Gln absorption by other Gln-using organs or tissues, reducing Gln availability for immune system cells [16, 17]. In figure 3, it represents the mechanism of glutamine as an anti-fatigue.

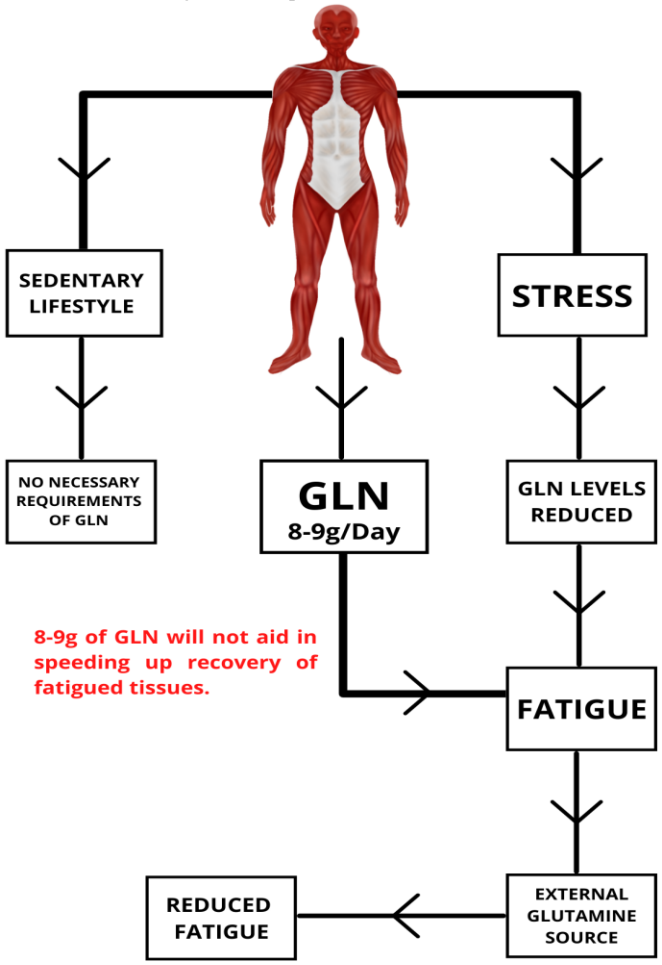

Figure 3: *Schematic diagram of the mechanism of action of glutamine as an anti-fatigue ergogenic amino acid.*

Gln has also been linked to the avoidance of ammonia buildup. Ammonia is produced during exercise as a result of amino acid oxidation and energy metabolism, implying a decrease in ATP concentration and glycogen content; consequently, Gln supplementation may reduce ammonia generation by affecting energy metabolism. Because ammonia is poisonous and impairs the activity of several flux-generating enzymes, cell permeability to ions, and the ratio of NAD+/NADH, ammonia buildup is a major cause of tiredness [18]. Finally, Gln may help to avoid dehydration, which is a potential anti-fatigue effect. A sodium-dependent mechanism transports Gln over the intestinal brush barrier, facilitating greater Gln absorption [19, 20]. Given its possible benefits, Gln appears to be a promising supplement for reducing tiredness, particularly for athletes who participate in endurance sports [21]. In Figure 4, the primary features of glutamine in postponing tiredness are shown.

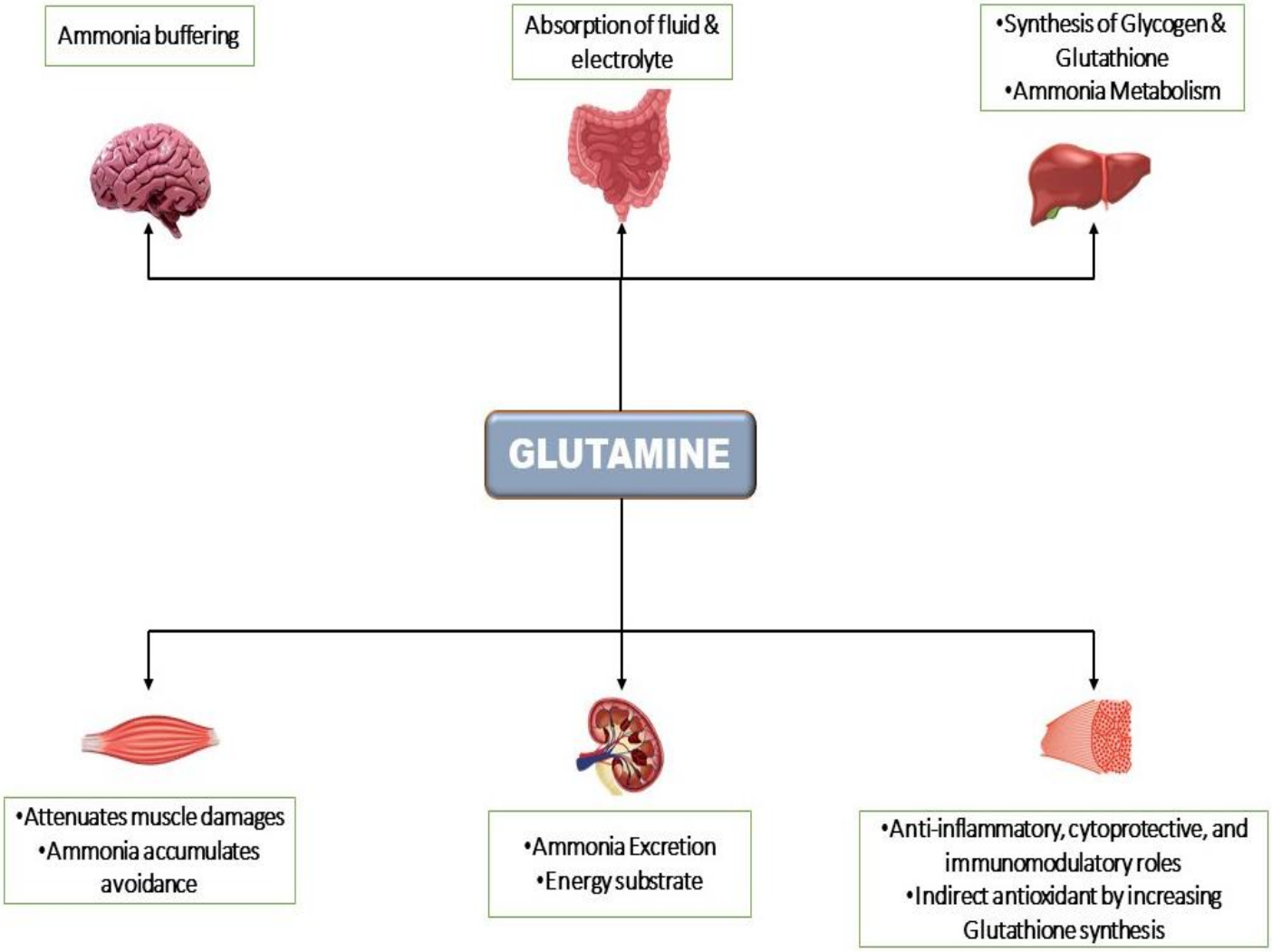

Figure 4: *Anti-fatigue properties of Glutamine.*

Glutamine Supplements and Muscle Anabolic Processes

In a fasting condition, muscle protein is broken down. A recent study suggests that resistance training lowers protein catabolism, but an anabolic (muscle growth) response needs the consumption of necessary amino acids (dietary protein) during the recovery period following exercise. This improves the rate of tissue protein synthesis without influencing the rate of protein breakdown by increasing amino acid absorption into the muscle. Taking supplements of specific non-essential amino acids at this time is unlikely to give any further benefit if the consumed protein contains the 8 necessary amino acids [22].

Serial No.	Changes in the muscle fibers
1	Pi (inorganic phosphate) accumulates in the sarcoplasm, resulting in a reduction in contractile force owing to the suppression of cross-bridge contacts.
2	H+ ion accumulation in the sarcoplasm, which results in a reduction in contractile force owing to suppression of cross-bridge interactions. Furthermore, an increase in H+ ions in the sarcoplasmic reticulum may induce a decrease in calcium re-uptake. This might be the major reason for the increased relaxing period following fatiguing contractions.
3	Mg2+ ions accumulate in the sarcoplasm. The release of Ca2+ from the sarcoplasmic reticulum is inhibited by Mg2+.
4	Pi buildup inhibits the sarcoplasmic reticulum's release of Ca2+. Precipitation of calcium phosphate inside the sarcoplasmic reticulum lumen and phosphorylation of the Ca2+ release channels both impede Ca2+ release.
5	Glycogen reserves are depleting, and blood glucose levels are dropping (in severe situations). Even a brief drop in blood glucose can have a significant impact on CNS processes. Increased muscular fatigue is caused by the depletion of glycogen reserves in an unknown way.

6	Reduced action potential conduction velocity along the sarcolemma, most likely as a result of exercise-related metabolic changes in and around muscle fibers. The decrease in conduction velocity is mirrored in the EMG (change in frequency content), but no immediate effect on muscle force output is recognized.
7	Potassium ions (K+) outflow from muscle fibers is increased. Because of the depression of excitation-contraction coupling, an increase in potassium in the t-tubule lumen may result in a block of the tubular action potential and hence reduced force.
8	Neuromuscular synaptic transmission can be impeded; however, this appears to be a disease-related component (myasthenia gravis).

Table 1: *Overview of exercise-related changes that can occur in the muscle fibers [23, 24].*

There's some evidence that Gln supplementation can help promote glycogen synthesis in the first few hours following a workout: Ingesting 8g of Gln along with 61g of glucose polymer after a glycogen-depleting bout of exercise resulted in a 25% increase in whole-body glucose disposal in the 2 hours following the exercise, compared to glucose polymer alone. However, a further study including appropriate carbohydrate eating after exercise is needed to back up this conclusion and provide it practical application [25]. The amount of carbohydrate consumed is insufficient; more than 100g is required to reach the maximal rate of muscle glycogen synthesis throughout a 2-hour post-exercise interval. As a result, a post-workout meal that is primarily carbohydrate (100g) with some protein (20g) appears to be the optimal strategy for promoting both glycogen and protein synthesis in muscle. The plasma content of growth hormone was boosted 4-fold 90 minutes after oral administration of 2g Gln, according to one research. However, because 1 hour of moderate to high-intensity activity can result in a 20-fold rise in plasma growth hormone concentration, Gln supplements are not recommended for athletes who exercise [26, 27]. Plasma Gln concentrations are unaffected by eccentric exercise-induced muscle injury. There is no empirical evidence that oral Gln supplementation improves muscle regeneration following exercise-induced injury, and there is no evidence that Gln consumption reduces muscular soreness when compared to placebo [28, 29].

Glutamine Intakes in the Athletic Population

Gln intake through dietary protein is typically 3–6 g/d (assuming a daily protein consumption of 0.8–1.6 g/kg bm for a 70-kg person). L-glutamine pills or capsules (250, 500, and 1000 mg) or powder are now available as supplements. Protein supplements, such as whey protein and protein hydrolysates, are other dietary sources of Gln for athletes. Although Gln is regarded to be quite safe and well accepted by most individuals, it is not indicated for persons with renal issues. In healthy athletes, no adverse effects to short-term Gln supplementation of 20–30 g within a few hours have been documented [30, 31].

Although there is little research on Gln supplement in the athletic population in terms of strength and performance, it seems logical to conclude that it may be useful for those who engage in prolonged and rigorous exercise training. The amount of glutamine in muscle decreases in proportion to the amount of stress. Furthermore, during and after intense training, plasma glutamine levels drop. Furthermore, under stressful conditions, the quantity of glutamine produced by skeletal muscle is larger than the amount detected in the intracellular pool and incorporated into proteins. Glutamate, on the other hand, may promote skeletal muscle hydration, increasing cellular volume. Increased cell volume might be an anabolic signal for muscle cells, resulting in increased muscular strength [32-34].

Conclusion

It is now well understood that Gln is used extensively by a vast variety of bodily tissues and cells and that it is required for their proper function. Kidney, gut, liver, certain neurons in the CNS, immune system cells, and pancreatic β-cells are among these tissues and cells. Because quick workout, nutrient intake, disease, and traumatic injury all affect plasma Gln levels, researchers should be aware of these influences and consider it if they plan to use plasma Gln measurement as part of a series of tests to oversee athletes for indications of impending overtraining. The usage of Gln as a dietary supplement by athletes has ergogenic effects. Athletes that participate in strength-power exercises, which need a substantial amount of skeletal muscle mass, would benefit from the Gln. In all athletes, glutamine may help to mitigate the immune system's impacts of overtraining.

Conflict of Interest

None.

Funding

None.

References

1. Kaur G, Hussain MS, Mohit, Kataria T. (2021) A review of acute or chronic renal failure, common kidney diseases, and herbal plants used for management. *International Journal of Botany Studies*. 6(1):50–6.
2. Gandevia SC. (2001) Spinal and supraspinal factors in human muscle fatigue. *Physiological reviews.* 81(4):1725–89.
3. Castell LM. (2003) Glutamine supplementation in vitro and in vivo, in exercise and in immunodepression. *Sports medicine.* 33(5):323–45.
4. Hiscock N, Pedersen BK. (2002) Exercise-induced immunodepression– plasma glutamine is not the link. 93(3):813–22.
5. van Zanten ARH, Dhaliwal R, Garrel D, Heyland DK. (2015) Enteral glutamine supplementation in critically ill patients: a systematic review and meta-analysis. *Critical care*. 19(1).
6. Gleeson M. (2008) Dosing and efficacy of glutamine supplementation in human exercise and sport training. *The Journal of nutrition.* 138(10).
7. Bowtell JL, Bruce M. (2002) Glutamine: an anaplerotic precursor. *Nutrition.* 18(3):222–4.
8. Smith RJ, Wilmore DW. (1990) Glutamine nutrition and requirements. *JPEN Journal of parenteral and enteral nutrition*. 14(4 Suppl).
9. Kim H. (2011) Glutamine as an immunonutrient. *Yonsei medical journal.* 52(6):892–7.
10. Coqueiro AY, Rogero MM, Tirapegui J. (2019) Glutamine as an Anti-Fatigue Amino Acid in Sports Nutrition. *Nutrients*. 11(4).
11. Moore M, Moriarty TA, Connolly G, Mermier C, Amorim F, Miller K, et al. (2019) Oral Glutamine Supplement Reduces Subjective Fatigue Ratings during Repeated Bouts of Firefighting Simulations. Safety. 5(2):38.
12. Cruzat V, Rogero MM, Keane KN, Curi R, Newsholme P. (2018) Glutamine: Metabolism and Immune Function, Supplementation and Clinical Translation. *Nutrients.* 10(11).
13. Castell LM, Newsholme EA. (1997) The effects of oral glutamine supplementation on athletes after prolonged, exhaustive exercise. *Nutrition.* 13(7–8):738–42.

14. Hakimi M, Mohamadi MA, Ghaderi Z. (2012) The effects of glutamine supplementation on performance and hormonal responses in non-athlete male students during eight-week resistance training. *Journal of Human Sport and Exercise.* 7(4):770–82.
15. Durkalec-Michalski K, Kusy K, Główka N, Zieliński J. (2021) The effect of multi-ingredient intra- versus extra-cellular buffering supplementation combined with branched-chain amino acids and creatine on exercise-induced ammonia blood concentration and aerobic capacity in taekwondo athletes. *Journal of the International Society of Sports Nutrition.* 18(1):1–14.
16. Jongkees BJ, Immink MA, Colzato LS. (2021) Influences of glutamine administration on response selection and sequence learning: a randomized-controlled trial OPEN.
17. Bruce M, Constantin-Teodosiu D, Greenhaff PL, Boobis LH, Williams C, Bowtell JL. (2001) Glutamine supplementation promotes anaplerosis but not oxidative energy delivery in human skeletal muscle. *American journal of physiology Endocrinology and metabolism*. 280(4).
18. Bassini-Cameron A, Monteiro A, Gomes A, Werneck-de-Castro JPS, Cameron L. (2008) Glutamine protects against increases in blood ammonia in football players in an exercise intensity-dependent way. *British journal of sports medicine*. 42(4):260–6.
19. Hoffman JR, Williams DR, Emerson NS, Hoffman MW, Wells AJ, McVeigh DM, et al. (2012) L-alanyl-L-glutamine ingestion maintains performance during a competitive basketball game. *Journal of the International Society of Sports Nutrition*. 9:4.
20. Resende NM, Neto AM de M, Bachini F, Castro LEV de, Bassini A, Cameron LC. (2011) Metabolic changes during a field experiment in a world-class windsurfing athlete: a trial with multivariate analyses. OMICS: *A Journal of Integrative Biology*. 15(10):695–705.
21. Howarth KR, Phillips SM, MacDonald MJ, Richards D, Moreau NA, Gibala MJ. (2010) Effect of glycogen availability on human skeletal muscle protein turnover during exercise and recovery. *Journal of applied physiology*. 109(2):431–8.
22. Häberle J, Shahbeck N, Ibrahim K, Schmitt B, Scheer I, Ogorman R, et al. (2012) Glutamine supplementation in a child with inherited GS deficiency improves the clinical status and partially corrects the peripheral and central amino acid imbalance. *Orphanet Journal of Rare Diseases.* 7(1):1–10.
23. Wan JJ, Qin Z, Wang PY, Sun Y, Liu X. (2017) Muscle fatigue: general understanding and treatment. *Experimental & Molecular Medicine* 49:10. 2017;49(10):e384–e384.
24. Ament W, Verkerke G. (2009) Exercise and fatigue. *Sports medicine.* 39(5):389–422.
25. Bowtell JL, Gelly K, Jackman ML, Patel A, Simeoni M, Rennie MJ. (1999) Effect of oral glutamine on whole body carbohydrate storage during recovery from exhaustive exercise. *Journal of applied physiology.* 86(6):1770–7.
26. Brooks GA, Gaesser GA. (1980) End points of lactate and glucose metabolism after exhausting exercise. Journal of applied physiology: respiratory, *environmental and exercise physiology.* 49(6):1057–69.
27. Rennie MJ, Bowtell JL, Bruce M, Khogali SEO. (2001) Interaction between glutamine availability and metabolism of glycogen, tricarboxylic acid cycle intermediates and glutathione. *The Journal of nutrition*. 131(9 Suppl).
28. van Hall G, Saris WHM, van de Schoor PAI, Wagenmakers AJM. (2000) The effect of free glutamine and peptide ingestion on the rate of muscle glycogen resynthesis in man. International *journal of sports medicine*. 21(1):25–30.
29. Wilkinson SB, Kim PL, Armstrong D, Phillips SM. (2006) Addition of glutamine to essential amino acids and carbohydrate does not enhance anabolism in young human males following exercise. Applied physiology, nutrition, and metabolism = Physiologie appliquee, nutrition et metabolisme. 31(5):518–29.
30. Koo GH, Woo J, Shin KO, Kang S. (2014) Effects of Supplementation with BCAA and L-glutamine on Blood Fatigue Factors and Cytokines in Juvenile Athletes Submitted to Maximal Intensity Rowing Performance. *Journal of Physical Therapy Science*. 26(8):1241–6.
31. Chen YM, Li H, Chiu YS, Huang CC, Chen WC. (2020) Supplementation of L-Arginine, L-Glutamine, Vitamin C, Vitamin E, Folic Acid, and Green Tea Extract Enhances Serum Nitric Oxide Content and Antifatigue Activity in Mice. Evidence-based Complementary and Alternative Medicine. 2020.
32. Petróczi A, Naughton DP, Pearce G, Bailey R, Bloodworth A, McNamee M. (2008) Nutritional supplement use by elite young UK athletes: fallacies of advice regarding efficacy. *Journal of the International Society of Sports Nutrition.* 5:22.
33. Froiland K, Koszewski W, Hingst J, Kopecky L. (2004) Nutritional supplement use among college athletes and their sources of information. *International journal of sport nutrition and exercise metabolism.* 14(1):104–20.
34. Zhang Y, Bishop PA. (2020) Can L-glutamine augmented heat shock protein 70 expression prevent exercise-induced exertional heat stroke and sudden cardiac death? *CNS Neuroscience & Therapeutics.* 26(1):148.

DOI: 10.31579/2690-8794/111