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KIDNEY HEALTH IN SPORT: INVESTIGATING THE INFLUENCE OF CREATINE, CITRULLINE, L-ARGININE, BETA-ALANINE AND BRANCHED CHAIN AMINO ACIDS (BCAA) ON RENAL FUNCTION

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ABSTRACT

Aims: The purpose of this review was to examine how five commonly used supplements, including creatine, citrulline, L-arginine, beta-alanine, and branched-chain amino acids (BCAAs), affect physical performance and kidney health. These compounds are widely consumed in the context of athletic training, yet their long-term safety with respect to renal function remains insufficiently defined.
Methodology: Relevant literature published between 1990 and 2024 was identified using PubMed, Scopus, and Google Scholar. The selection included studies describing the physiological effects and potential renal impact of each supplement.
State of Knowledge: Analysis of the available research suggests that creatine does not impair kidney function in healthy individuals. Citrulline is considered metabolically safe and may support renal health in specific contexts, although elevated concentrations in patients with reduced kidney function could indicate metabolic imbalance. L-arginine may be beneficial in acute clinical settings but shows potentially harmful effects when used long term, especially in older or chronically ill individuals. Beta-alanine has demonstrated safety and antioxidant properties that could protect kidney cells. In contrast, high or prolonged intake of BCAAs may contribute to insulin resistance and worsen renal outcomes in people with diabetes or hereditary kidney disorders.
Conclusions: When used appropriately by healthy individuals, these supplements are generally safe for kidney function. However, individual health status, dosage, and duration of use can significantly affect renal outcomes. BCAA supplementation, in particular, should be approached with caution in at-risk populations. More long-term studies are needed to fully assess the renal safety of these compounds in both athletic and clinical settings.

KEYWORDS

Creatine, Citrulline, L-Arginine, Beta-Alanine, BCAA, Sport, Athletes, Supplementation, Kidney

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Methodology

To prepare this review, a structured search of scientific literature was conducted in three electronic databases: PubMed, Scopus, and Google Scholar. The aim was to gather and analyze current knowledge on the effects of selected dietary supplements on physical performance and kidney function. The search focused on studies published between 1990 and 2024. During the selection process, priority was given to peer-reviewed publications, including clinical trials, systematic reviews, meta-analyses, and preclinical studies involving human and animal subjects. To identify relevant articles, combinations of keywords related to each supplement's ergogenic properties and renal implications were used. The search queries included terms such as: "supplementation", "kidney function", "renal function", "renal safety", "kidney damage", "exercise performance", "athletic performance", and "metabolism". These were applied separately for each of the five substances: creatine, citrulline, L-arginine, beta-alanine, and branched-chain amino acids (BCAAs). Studies that were not published in English or lacking sufficient methodological detail were excluded. The collected articles were then reviewed to extract key data regarding mechanisms of action, dosing regimens, observed physiological effects, and documented or hypothesized impacts on kidney function. Emphasis was placed on studies reporting indicators such as glomerular filtration rate (GFR), serum creatinine concentration, renal histopathological findings, and markers of oxidative or metabolic stress. The findings were synthesized to provide a balanced overview of both potential benefits and risks of supplementation in the context of renal health.

Creatine in Sports: Performance Enhancement, Supplementation, and Kidney Health Implications.

Creatine is one of the most popular supplements used by strength athletes. Studies have shown its positive impact on muscle strength and recovery [1]. According to findings from a 12-week trial investigating creatine supplementation combined with resistance training revealed significant improvements in bench press and squat performance compared to the placebo group. Additionally the creatine group demonstrated enhanced hypertrophy in type I, IIA and IIB muscle fibers [2]. Consistent with prior research, Pirola et al. found creatine supplementation enhances muscle mass recovery in hip fracture patients compared to a placebo group [3]. Cooke et al. reported that creatine supplementation significantly accelerates the recovery of the knee extensor muscle. Recovery potential was evaluated based on isometric and isokinetic muscle extension strength, measured during the regeneration phase following muscle damaging protocols. Blood markers of muscle damage – creatine kinase (CK) and lactate dehydrogenase (LDH) were also assessed. Plasma CK and LDK activity were significantly lower in the creatine supplementing group compared to placebo group [4]. A meta-analysis examining the effects of creatine supplementation on athletic performance in soccer players analyzed 101 publications, focusing on creatine's impact on aerobic performance, phosphagen metabolic performance, and anaerobic performance. The findings revealed no significant differences in aerobic performance or phosphagen metabolism performance compared to placebo, while demonstrating significant improvements in anaerobic performance [5]. The performance-enhancing benefits of creatine in sports originates from its physiological impact on the body. Creatine is a substrate for creatine kinase (CK), an enzyme that catalyzes the phosphorylation of creatine. The reaction involves ATP which is converted to ADP and phosphate group. The energy generated during ATP hydrolysis is used by CK to transfer phosphate group to creatine, thus forming phosphocreatine (PCr). PCr serves as an energy buffer. In times of low energy demand PCr stores high-energy phosphates and during periods of high energy demand it donates the phosphoryl group, converting ADP back to ATP. The result of these reactions is the maintenance of ATP reserves during anaerobic exercise [6]. The human body typically requires between 1 and 3 grams of creatine per day to meet baseline physiological needs. At this intake level, muscle creatine reserves reach approximately 60–80% saturation. To maximize intramuscular creatine levels for enhanced athletic performance, supplementation protocols must exceed standard dietary intake levels. A common strategy involves a loading phase of 20 grams of creatine monohydrate per day, divided into four equal doses, sustained for 5–7 days. This short-term loading regimen rapidly saturates muscle creatine stores to optimal levels. Following this initial phase, a daily maintenance dose of 3–5 grams helps sustain elevated creatine concentrations in muscle tissue [7].

Creatine is metabolized to creatinine and excreted renally [6]. Because creatinine production and excretion occur at a relatively constant rate, it serves as a reliable biomarker for estimating glomerular filtration rate (GFR) and detecting kidney dysfunction. However, this can be misleading in clinical practice for individuals routinely supplementing with creatine. Elevated dietary creatine intake increases serum creatinine levels independently of renal pathology, which may falsely suggest impaired kidney function in standard blood tests [8]. A 2019 meta-analysis concluded that creatine supplementation has no significant impact on serum creatinine levels and causes no risk of kidney damage in healthy individuals [9]. Aligning with these findings, Lugaresi et al. found no significant differences in renal parameters between creatine-supplemented and placebo groups. In their 12-week randomized, double-blind trial, participants underwent resistance training while adhering to a high-protein diet under controlled conditions [10]. Research further indicates that creatine supplementation does not compromise renal function in individuals with type 2 diabetes [11].

Citrulline: Ergogenic Potential, Supplementation, and Renal Implications

Citrulline is another well-known supplement used by athletes. Research suggests that a single dose of 4-10 g of citrulline malate, consumed one hour before the training, may increase muscle power and reduce post-exercise soreness [12]. While many studies have supported this claim, the ergogenic effect of citrulline remains inconclusive [13]. Citrulline is an important intermediate in the urea cycle. It is synthesized from L-ornithine and carbamoyl phosphate within the mitochondria. Subsequent enzymatic conversions in the cytosol result in the formation of L-arginine, which undergoes hydrolysis. That reaction regenerates L-ornithine and completes the cycle. In result a toxic ammonia is converted into urea which is excreted in urine [14–16]. Increased levels of ammonia in plasma are detrimental due to its involvement in various metabolic interactions: reducing efficiency of the citric acid cycle, inhibiting protein synthesis, exacerbating oxidative stress, inducing neurotoxicity, and disturbing acid-base balance, leading to metabolic acidosis [17–21]. Due to its toxic effects, ammonia produced during anaerobic exercise exacerbates muscle cell damage, leading to muscle soreness and

delaying the regeneration of muscle cells. Citrulline supplementation is expected to accelerate ammonia metabolism, thereby reducing post-exercise pain and promoting muscle regeneration [22]. Additionally, citrulline is implicated in nitric oxide (NO) synthesis, which modulates muscle function by enhancing vasodilation and blood flow during exercise. The primary substrate for this reaction is l-arginine, which is metabolized into nitric oxide (NO) and l-citrulline [23]. However, citrulline supplementation may enhance NO synthesis, as excess cutrulline is converted back to arginine in kidneys [24]. The remaining citrulline is utilized in the urea cycle, with less than 5% excreted unchanged in urine [25]. Recent studies indicate that elevated serum citrulline levels were associated with an increased risk of chronic kidney disease (CKD) progression and accelerated decline in glomerular filtration rate (GFR) [26]. Higher serum citrulline concentrations are attributed to impaired NO metabolism in individuals with reduced GFR. NO deficiency induces endothelial dysfunction, which contributes to CKD pathophysiology. Thus some authors have suggested citrulline as a potential biomarker for proximal tubular dysfunction and CKD incidence [27,28]. Studies conducted in diabetic mice demonstrated that citrulline supplementation exerted a nephroprotective effect, reducing urinary albumin excretion, tubulointerstitial fibrosis, and kidney hypertrophy [29].

L-arginine: Aerobic Performance Gains, Supplementation, and Renal Impacts in Athletic and Clinical Settings

L-arginine supplementation has been shown to improve aerobic performance, which makes it a popular supplement among athletes and bodybuilders. A 6-week supplementation with 2 grams of L-arginine daily significantly improves sport performance (VO_2 max). However, the study observed no effects on body mass index (BMI), body fat mass (BFM), or lean body mass (LBM) [30]. Other studies have shown that supplementing with 6 grams daily, including a dose taken three hours before exercise, enhances physical performance and delays the onset of fatigue [31,32]. Human studies have employed a wide range of L-arginine dosing strategies, typically involving daily intakes of 2–30 grams in adults [30,33]. Bode-Böger et al. investigated the pharmacokinetics of L-arginine administered intravenously at doses of 6 g/day and 30 g/day, as well as orally at 6 g/day. They observed that the half-life of L-arginine following a 6 g intravenous infusion most closely mirrored its physiological half-life, prompting their recommendation for oral 6 g doses in L-arginine research protocols. The physiological daily requirement for L-arginine is estimated at 4–6 grams [33]. However, oral L-arginine undergoes significant degradation in the gastrointestinal tract, with only ~70% of the ingested dose reaching systemic circulation. Consequently, many researchers advocate for L-citrulline supplementation as a superior method to enhance systemic L-arginine bioavailability [33–35]. Furthermore, clinical studies demonstrate that combining oral L-arginine and L-citrulline synergistically improves exercise performance metrics [36]. Beyond its ergogenic effects, L-arginine exhibits broad therapeutic potential, enhancing endothelial function, improving insulin sensitivity, and reducing oxidative stress and inflammatory markers in conditions like cardiovascular disease and diabetes [37–40]. While the precise mechanisms underlying these health benefits remain unclear, current hypotheses emphasize its role in nitric oxide (NO) production. L-arginine serves as the primary substrate for nitric oxide synthase (NOS), an enzyme that catalyzes its conversion into NO and L-citrulline. Supplementation with L-arginine has been shown to elevate plasma NO concentrations and reduce systolic blood pressure [32]. Higher NO levels boost blood flow to muscles, improving the delivery of essential nutrients and promoting the removal of anaerobic waste products, thereby accelerating post-exercise recovery [41,42]. NO also serves as a critical signaling molecule in the kidneys, regulating renal tubule function, renal vasculature, and glomerular activity. Studies have shown that NO bioavailability and biological activity are significantly reduced during acute kidney injury (AKI). Schramm et al. investigated the effects of L-arginine supplementation on renal function during the first four days following transplantation. The authors hypothesized that stress and ischemia linked to transplantation mimic AKI, providing a controlled model to study L-arginine's impact on human kidney function. In recipients of kidneys with short ischemic times from donors younger than 45 years, early L-arginine supplementation improved glomerular filtration rate (GFR) and renal plasma flow (RPF) compared to placebo [43]. This finding aligns with earlier observations by Kopp et al., who reported that adding L-arginine to kidney preservation solutions prolongs graft survival [44]. Prior research suggests potential benefits of L-arginine supplementation in AKI [43,45]. In contrast to these findings, supplementation with this amino acid in chronic kidney disease (CKD) does not demonstrate significant clinical effects [46]. Recent animal studies suggest a negative impact of long-term L-arginine supplementation on renal health. A four-month regimen of this amino acid failed to reduce inflammation or fibrosis in murine kidney models. Furthermore, older subjects exhibited increased mortality and elevated albuminuria following supplementation [47]. Additional studies have documented adverse effects associated with chronic L-arginine supplementation on overall health [48,49].

Beta-alanine: Supplementation Practices, Metabolic Mechanisms in Exercise Performance, and Renal Implications

Beta-alanine is a supplement used by athletes and bodybuilders, commonly known for its exercise capacity enhancing properties. Research has shown that a daily beta-alanine intake of 4-6 grams over 4 weeks improves exercise capacity. While some studies have proposed doses as high as 20 grams daily, no direct correlation between dosage and effectiveness has been established [50,51]. Beta-alanine is a non-proteinogenic amino acid involved in the synthesis of carnosine, a dipeptide composed of beta-alanine and histidine. Carnosine is predominantly found in skeletal muscles, and its levels in the body are directly influenced by dietary intake of beta-alanine [52]. Research demonstrates that four weeks of beta-alanine supplementation significantly increases muscle carnosine concentrations [53]. The role of carnosine in muscle physiology has not been fully discovered. It is hypothesized to contribute to maintaining intramuscular homeostasis through four primary mechanisms: proton buffering capacity, protection against reactive oxygen species (ROS), preventing protein glycoxidation and regulating calcium sensitivity. High-intensity muscle contractions stimulate anaerobic glycolysis and increase lactic acid production. This disrupts the acid-base balance, leading to acidosis which has often been associated with exercise-induced muscle fatigue. Carnosine contains a histidine subunit capable of binding protons (H+), thereby acting as a proton buffer and delaying the decline in muscle pH [52]. Individuals with greater muscle carnosine levels resulting from beta-alanine supplementation, have lower degree of acidosis in the blood during high-intensity exercise [54]. Carnosine also plays a role in neutralizing reactive oxygen species (ROS). ROS are mostly generated in mitochondria as byproducts of the electron transport chain. Excessive ROS levels may be harmful to cells due to their uncontrolled oxidation properties, leading to cellular damage and oxidative stress. Carnosine is responsible for ROS neutralization through its redox activity, enabling it to neutralize hydroxyl radicals and form stable complexes with superoxide radicals [55–57]. These properties also enable carnosine to act as an effective chelator, binding transition metals (Cu^{2+},Zn^{2+},Fe^{2+}) and preventing their participation in ROS-driven harmful reactions [58]. Carnosine's ability to chelate metals has been proposed by Nagai et al. as a potential mechanism involved in suppressing the formation of advanced glycation end-products (AGEs) [59]. Carnosine can inhibit AGE generation at multiple stages of their formation cascade. It demonstrates particular efficacy in preventing protein glycation and reversing glycation-induced damage [52]. Glycated proteins represent an early step in the complex cascade leading to AGEs—a group of compounds implicated in aging processes. These include glycated proteins, lipids, and nucleic acids [60]. Similarly, advanced lipoxidation end-products (ALEs) are another class of aging-related compounds [61]. In both in vitro and in vivo studies, carnosine has shown the ability to prevent the formation of ALEs and AGEs [62–64]. This has direct implications for maintaining muscle cell homeostasis, as AGEs and ALEs can destabilize muscle protein structures and accelerate their degradation [65]. Furthermore, carnosine enhances muscle contractility by increasing the sensitivity of the contractile apparatus to Ca^{2+} ions during contraction-relaxation cycles [66]. However, the precise mechanism underlying this relationship requires further investigation.

Given that beta-alanine is an endogenously produced compound required for carnosine synthesis, its supplementation is unlikely to pose harm to the body. Numerous studies support this claim. The most widely recognized side effect of beta-alanine supplementation is paresthesia, which is a transient tingling sensation, affecting the face, neck, and back of the hands. This effect occurs only in sensitive individuals and is dose-dependent, with higher doses typically intensifying the tingling sensation [67,68]. Another potential side effect is a reduction in taurine levels due to beta-alanine supplementation. This hypothesis arises from the fact that beta-alanine and taurine compete for the same transporter (TauT) in skeletal muscles, meaning increased beta-alanine intake could theoretically lower intramuscular taurine concentrations [50]. While this relationship has been confirmed in animal models, human studies have not observed significant decreases in muscle taurine levels following beta-alanine supplementation [69,70].

Studies have not identified adverse effects of beta-alanine supplementation on renal function [71]. Furthermore, due to carnosine's role as a natural antioxidant, beta-alanine supplementation has demonstrated potential benefits in kidney disease management. For example, carnosine suppresses GPX4-dependent ferroptosis in ischemia-induced acute kidney injury. This inhibition reduces inflammation in renal tubular epithelial cells, thereby mitigating ischemic kidney damage [72]. Another example of carnosine's nephroprotective action is its ability to reduce reactive oxygen species (ROS) by downregulating NADPH oxidase 4 (NOX4) expression and enhancing total superoxide dismutase (T-SOD) activity. This mechanism suppresses mitochondrial apoptosis and protects hydrogen peroxide-exposed human kidney cells from oxidative damage [73]. These findings highlight potential beta-alanine supplementation as a therapeutic agent

for diabetic nephropathy, ischemia-induced acute kidney injury and other diseases associated with ferroptosis or oxidative stress [72,73]. Furthermore, studies in animal models have demonstrated that carnosine reduces obesity-related disorders, such as dyslipidemia, hypertension, and kidney damage, in obese Zucker rats [74].

Branched Chain Amino Acids (BCAAs): Supplementation, Metabolic Roles in Muscle Development, and Impact on Renal Function

BCAAs are a popular dietary supplement composed of three essential amino acids: isoleucine, leucine, and valine. These amino acids play a vital role in muscle protein synthesis and must be obtained through diet, as they cannot be synthesized endogenously [75]. For this reason, BCAAs are commonly used by athletes and bodybuilders aiming to optimize muscle development. They enhance post-exercise recovery by reducing the muscle damage caused by high-intensity exercise [76]. Taking more than 200 mg kg−1 day−1 of BCAAs daily, helps reduce muscle soreness [77]. Many bodybuilders add 5-10 grams of BCAAs before and after training sessions, which has also been incorporated into certain evidence-based supplementation strategies [78,79]. Research also indicates that BCAA supplementation preserves muscle mass during states of severe catabolism and protein loss [80]. While many studies have demonstrated that BCAA supplementation enhances athletic performance [81,82], the evidence remains inconsistent and further research is needed. A recent systematic review found no significant impact of BCAA supplementation on athletic performance [83]. Leucine, one of the tree amino acids in BCAAs, activates the mTORC1 complex. This complex regulates important cellular mechanisms, primarily protein synthesis and autophagy suppression. At the molecular level, leucine inactivates Sestrin2, a negative regulator of mTORC1. Functional role of Sestrin2 is to inhibit GATOR2, which is a positive regulator that facilitates mTORC1 activation. By blocking Sestrin2, leucine increases GATOR2 availability, thereby promoting mTORC1 activation [84]. This mechanism is thought to underlie BCAA supplementation's ability to enhance protein synthesis [85,86]. BCAAs also exhibit the ability to inhibit muscle protein breakdown. While the precise mechanism remains unclear, current evidence suggests this effect may involve the downregulation of BCAA-dependent ubiquitin ligases MAFbx and MuRF-1. These muscle-specific E3 ubiquitin ligases catalyze the ubiquitylation of proteins, marking them for proteasomal degradation. By suppressing the expression of these enzymes, BCAAs reduce muscle protein breakdown [87]. Despite their beneficial effects on post-exercise muscle recovery, elevated plasma BCAA levels have increasingly been linked to insulin resistance [84]. However, research indicates that leucine-specific supplementation may improve insulin sensitivity, in contrast to chronic supplementation with all three BCAAs. This phenomenon may arise from leucine's ability to stimulate insulin secretion by pancreatic β-cells. Therefore, leucine supplementation may contribute to enhanced postprandial glucose regulation through its insulinotropic properties. However, the exact mechanisms underlying this effect remain to be established [88]. Given the strong association between elevated plasma BCAA levels and diabetes, Deng et al. investigated the relationship between disrupted BCAA homeostasis and diabetic kidney disease (DKD). Their findings revealed that elevated plasma BCAA concentrations serve as an independent risk factor for DKD progression. Additionally, their murine studies demonstrated that a low-protein diet improved renal function in experimental models [89]. According to DiMartino et al., BT2, a compound that enhances BCAA breakdown, reduces kidney damage caused by nephrotoxic agents in murine models [90]. BCAA supplementation may be harmful to patients with autosomal dominant polycystic kidney disease (ADPKD). Yamamoto et al. demonstrated that mice genetically engineered to develop kidney cysts fed BCAA exhibited accelerated cyst formation [91].

Conclusions

This review examined the effects of five commonly used sports supplements: creatine, citrulline, L-arginine, beta-alanine and branched-chain amino acids (BCAAs). The analysis focused on their performance-enhancing properties and their potential impact on kidney function. Available evidence indicates that, when used appropriately, these supplements are generally safe for healthy individuals and do not impair renal function. Creatine does not compromise kidney health. Citrulline and L-arginine, both involved in nitric oxide synthesis, show beneficial effects on vascular and muscular performance, but their influence on kidney health varies with context. Citrulline appears metabolically safe and may even exert nephroprotective effects in certain animal models, although elevated serum levels in patients with chronic kidney disease could reflect underlying dysfunction rather than toxicity. L-arginine, while potentially beneficial in acute renal conditions, has shown mixed results in long-term use, with some studies indicating adverse effects, especially in older or chronically ill individuals. Beta-alanine, through its role in carnosine synthesis, enhances buffering capacity and antioxidative defense, with no known renal risks and potential benefits in oxidative kidney injuries. In

contrast, excessive or prolonged BCAA supplementation may pose risks for individuals with metabolic or genetic kidney disorders, as elevated BCAA levels have been linked to insulin resistance, diabetic nephropathy and accelerated cyst formation in polycystic kidney disease models. Overall, while these substances can support exercise performance and muscle recovery, their use should be approached with caution in individuals with preexisting kidney conditions or metabolic disease, and further research is needed to clarify their long-term safety and therapeutic potential in such populations.

Disclosures

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REFERENCES

1. R. Cooper, F. Naclerio, J. Allgrove, and A. Jimenez, "Creatine supplementation with specific view to exercise/sports performance: an update.," *J Int Soc Sports Nutr*, vol. 9, no. 1, p. 33, Jul. 2012, doi: 10.1186/1550-2783-9-33.
2. J. S. VOLEK *et al.*, "Performance and muscle fiber adaptations to creatine supplementation and heavy resistance training," *Med Sci Sports Exerc*, vol. 31, no. 8, pp. 1147–1156, Aug. 1999, doi: 10.1097/00005768-199908000-00011.
3. V. Pirola, L. Pisani, and P. Teruzzi, "[Evaluation of the recovery of muscular trophicity in aged patients with femoral fractures treated with creatine phosphate and physiokinesitherapy].," *Clin Ter*, vol. 139, no. 3–4, pp. 115–9.
4. M. B. Cooke, E. Rybalka, A. D. Williams, P. J. Cribb, and A. Hayes, "Creatine supplementation enhances muscle force recovery after eccentrically-induced muscle damage in healthy individuals," *J Int Soc Sports Nutr*, vol. 6, no. 1, Jan. 2009, doi: 10.1186/1550-2783-6-13.
5. J. Mielgo-Ayuso, J. Calleja-Gonzalez, D. Marqués-Jiménez, A. Caballero-García, A. Córdova, and D. Fernández-Lázaro, "Effects of Creatine Supplementation on Athletic Performance in Soccer Players: A Systematic Review and Meta-Analysis.," *Nutrients*, vol. 11, no. 4, Mar. 2019, doi: 10.3390/nu11040757.
6. M. Wyss and R. Kaddurah-Daouk, "Creatine and Creatinine Metabolism," *Physiol Rev*, vol. 80, no. 3, pp. 1107–1213, Jul. 2000, doi: 10.1152/physrev.2000.80.3.1107.
7. R. B. Kreider *et al.*, "International Society of Sports Nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine," *J Int Soc Sports Nutr*, vol. 14, no. 1, Jan. 2017, doi: 10.1186/s12970-017-0173-z.
8. I. Longobardi, B. Gualano, A. C. Seguro, and H. Roschel, "Is It Time for a Requiem for Creatine Supplementation-Induced Kidney Failure? A Narrative Review," *Nutrients*, vol. 15, no. 6, p. 1466, Mar. 2023, doi: 10.3390/nu15061466.
9. A. de Souza E Silva *et al.*, "Effects of Creatine Supplementation on Renal Function: A Systematic Review and Meta-Analysis.," *J Ren Nutr*, vol. 29, no. 6, pp. 480–489, Nov. 2019, doi: 10.1053/j.jrn.2019.05.004.

10. R. Lugaresi *et al.*, “Does long-term creatine supplementation impair kidney function in resistance-trained individuals consuming a high-protein diet?,” *J Int Soc Sports Nutr*, vol. 10, no. 1, p. 26, May 2013, doi: 10.1186/1550-2783-10-26.
11. B. Gualano *et al.*, “Creatine supplementation does not impair kidney function in type 2 diabetic patients: a randomized, double-blind, placebo-controlled, clinical trial.,” *Eur J Appl Physiol*, vol. 111, no. 5, pp. 749–56, May 2011, doi: 10.1007/s00421-010-1676-3.
12. J. Pérez-Guisado and P. M. Jakeman, “Citrulline Malate Enhances Athletic Anaerobic Performance and Relieves Muscle Soreness,” *J Strength Cond Res*, vol. 24, no. 5, pp. 1215–1222, May 2010, doi: 10.1519/JSC.0b013e3181cb28e0.
13. A. Viribay, J. Fernández-Landa, A. Castañeda-Babarro, P. S. Collado, D. Fernández-Lázaro, and J. Mielgo-Ayuso, “Effects of Citrulline Supplementation on Different Aerobic Exercise Performance Outcomes: A Systematic Review and Meta-Analysis,” *Nutrients*, vol. 14, no. 17, p. 3479, Aug. 2022, doi: 10.3390/nu14173479.
14. H. Zhang *et al.*, “The cyanobacterial ornithine–ammonia cycle involves an arginine dihydrolase,” *Nat Chem Biol*, vol. 14, no. 6, pp. 575–581, Jun. 2018, doi: 10.1038/s41589-018-0038-z.
15. V. Walker, “Ammonia Metabolism and Hyperammonemic Disorders,” 2014, pp. 73–150. doi: 10.1016/bs.acc.2014.09.002.
16. G. S. Ribas, F. F. Lopes, M. Deon, and C. R. Vargas, “Hyperammonemia in Inherited Metabolic Diseases,” *Cell Mol Neurobiol*, vol. 42, no. 8, pp. 2593–2610, Nov. 2022, doi: 10.1007/s10571-021-01156-6.
17. M. Zielonka, J. Probst, M. Carl, G. F. Hoffmann, S. Kölker, and J. G. Okun, “Bioenergetic dysfunction in a zebrafish model of acute hyperammonemic decompensation,” *Exp Neurol*, vol. 314, pp. 91–99, Apr. 2019, doi: 10.1016/j.expneurol.2019.01.008.
18. G. Davuluri *et al.*, “Metabolic adaptation of skeletal muscle to hyperammonemia drives the beneficial effects of l-leucine in cirrhosis,” *J Hepatol*, vol. 65, no. 5, pp. 929–937, Nov. 2016, doi: 10.1016/j.jhep.2016.06.004.
19. C. R. Bosoi *et al.*, “Systemic oxidative stress is implicated in the pathogenesis of brain edema in rats with chronic liver failure,” *Free Radic Biol Med*, vol. 52, no. 7, pp. 1228–1235, Apr. 2012, doi: 10.1016/j.freeradbiomed.2012.01.006.
20. C. Bachmann, “Mechanisms of Hyperammonemia,” *Clin Chem Lab Med*, vol. 40, no. 7, Jan. 2002, doi: 10.1515/CCLM.2002.112.
21. K. Nakamura *et al.*, “Hyperammonemia in idiopathic epileptic seizure,” *Am J Emerg Med*, vol. 31, no. 10, pp. 1486–1489, Oct. 2013, doi: 10.1016/j.ajem.2013.08.003.
22. L. A. Gough *et al.*, “A critical review of citrulline malate supplementation and exercise performance,” *Eur J Appl Physiol*, vol. 121, no. 12, pp. 3283–3295, Dec. 2021, doi: 10.1007/s00421-021-04774-6.
23. T. Allerton, D. Proctor, J. Stephens, T. Dugas, G. Spielmann, and B. Irving, “l-Citrulline Supplementation: Impact on Cardiometabolic Health,” *Nutrients*, vol. 10, no. 7, p. 921, Jul. 2018, doi: 10.3390/nu10070921.
24. S. J. Bailey, J. R. Blackwell, T. Lord, A. Vanhatalo, P. G. Winyard, and A. M. Jones, “<scp>l</scp> -Citrulline supplementation improves O $_2$ uptake kinetics and high-intensity exercise performance in humans,” *J Appl Physiol*, vol. 119, no. 4, pp. 385–395, Aug. 2015, doi: 10.1152/japplphysiol.00192.2014.
25. C. Moinard, I. Nicolis, N. Neveux, S. Darquy, S. Bénazeth, and L. Cynober, “Dose-ranging effects of citrulline administration on plasma amino acids and hormonal patterns in healthy subjects: the Citrudose pharmacokinetic study,” *British Journal of Nutrition*, vol. 99, no. 4, pp. 855–862, Apr. 2008, doi: 10.1017/S0007114507841110.
26. N. B. Rinde, I. T. Enoksen, T. Melsom, O. M. Fuskevåg, B. O. Eriksen, and J. V. Norvik, “Nitric Oxide Precursors and Dimethylarginines as Risk Markers for Accelerated Measured GFR Decline in the General Population,” *Kidney Int Rep*, vol. 8, no. 4, pp. 818–826, Apr. 2023, doi: 10.1016/j.ekir.2023.01.015.
27. O. Levillain, P. Parvy, and C. Hassler, “Amino acid handling in uremic rats: Citrulline, a reliable marker of renal insufficiency and proximal tubular dysfunction,” *Metabolism*, vol. 46, no. 6, pp. 611–618, Jun. 1997, doi: 10.1016/S0026-0495(97)90002-0.
28. H. Lee, H. B. Jang, M.-G. Yoo, S. I. Park, and H.-J. Lee, “Amino Acid Metabolites Associated with Chronic Kidney Disease: An Eight-Year Follow-Up Korean Epidemiology Study,” *Biomedicines*, vol. 8, no. 7, p. 222, Jul. 2020, doi: 10.3390/biomedicines8070222.
29. M. J. Romero *et al.*, “l-Citrulline Protects from Kidney Damage in Type 1 Diabetic Mice,” *Front Immunol*, vol. 4, 2013, doi: 10.3389/fimmu.2013.00480.
30. N. Pahlavani *et al.*, “The effect of l-arginine supplementation on body composition and performance in male athletes: a double-blinded randomized clinical trial,” *Eur J Clin Nutr*, vol. 71, no. 4, pp. 544–548, Apr. 2017, doi: 10.1038/ejcn.2016.266.
31. Z. Kavcı, M. Ozan, Y. Buzdağlı, A. Savaş, and H. Uçar, “Investigation of the effect of nitrate and L-arginine intake on aerobic, anaerobic performance, balance, agility, and recovery in elite taekwondo athletes,” *J Int Soc Sports Nutr*, vol. 22, no. 1, Dec. 2025, doi: 10.1080/15502783.2024.2445609.
32. S. J. Bailey *et al.*, “Acute <scp>l</scp> -arginine supplementation reduces the O $_2$ cost of moderate-intensity exercise and enhances high-intensity exercise tolerance,” *J Appl Physiol*, vol. 109, no. 5, pp. 1394–1403, Nov. 2010, doi: 10.1152/japplphysiol.00503.2010.

33. S. M. Bode-Böger, R. H. Böger, A. Galland, D. Tsikas, and J. C. Frölich, "L-arginine-induced vasodilation in healthy humans:pharmacokinetic–pharmacodynamic relationship," *Br J Clin Pharmacol*, vol. 46, no. 5, pp. 489–497, Nov. 1998, doi: 10.1046/j.1365-2125.1998.00803.x.
34. I. Suzuki *et al.*, "A combination of oral l-citrulline and l-arginine improved 10-min full-power cycling test performance in male collegiate soccer players: a randomized crossover trial," *Eur J Appl Physiol*, vol. 119, no. 5, pp. 1075–1084, May 2019, doi: 10.1007/s00421-019-04097-7.
35. E. Schwedhelm *et al.*, "Pharmacokinetic and pharmacodynamic properties of oral L-citrulline and L-arginine: impact on nitric oxide metabolism," *Br J Clin Pharmacol*, vol. 65, no. 1, pp. 51–59, Jan. 2008, doi: 10.1111/j.1365-2125.2007.02990.x.
36. H. Speer, N. M. D'Cunha, M. J. Davies, A. J. McKune, and N. Naumovski, "The Physiological Effects of Amino Acids Arginine and Citrulline: Is There a Basis for Development of a Beverage to Promote Endurance Performance? A Narrative Review of Orally Administered Supplements," *Beverages*, vol. 6, no. 1, p. 11, Feb. 2020, doi: 10.3390/beverages6010011.
37. M. Settergren, F. Böhm, R. E. Malmström, K. M. Channon, and J. Pernow, "L-arginine and tetrahydrobiopterin protects against ischemia/reperfusion-induced endothelial dysfunction in patients with type 2 diabetes mellitus and coronary artery disease.," *Atherosclerosis*, vol. 204, no. 1, pp. 73–8, May 2009, doi: 10.1016/j.atherosclerosis.2008.08.034.
38. T. C. Wascher *et al.*, "Effects of low-dose L-arginine on insulin-mediated vasodilatation and insulin sensitivity.," *Eur J Clin Invest*, vol. 27, no. 8, pp. 690–5, Aug. 1997, doi: 10.1046/j.1365-2362.1997.1730718.x.
39. P. Lucotti *et al.*, "Oral l-arginine supplementation improves endothelial function and ameliorates insulin sensitivity and inflammation in cardiopathic nondiabetic patients after an aortocoronary bypass," *Metabolism*, vol. 58, no. 9, pp. 1270–1276, Sep. 2009, doi: 10.1016/j.metabol.2009.03.029.
40. P. Lucotti *et al.*, "Beneficial effects of a long-term oral L-arginine treatment added to a hypocaloric diet and exercise training program in obese, insulin-resistant type 2 diabetic patients.," *Am J Physiol Endocrinol Metab*, vol. 291, no. 5, pp. E906-12, Nov. 2006, doi: 10.1152/ajpendo.00002.2006.
41. Jonathan. P. Little, S. C. Forbes, D. G. Candow, S. M. Cornish, and P. D. Chilibeck, "Creatine, Arginine α-Ketoglutarate, Amino Acids, and Medium-Chain Triglycerides and Endurance and Performance," *Int J Sport Nutr Exerc Metab*, vol. 18, no. 5, pp. 493–508, Oct. 2008, doi: 10.1123/ijsnem.18.5.493.
42. G. Angeli, T. L. de Barros, D. F. L. de Barros, and M. Lima, "Investigação dos efeitos da suplementação oral de arginina no aumento de força e massa muscular," *Revista Brasileira de Medicina do Esporte*, vol. 13, no. 2, pp. 129–132, Apr. 2007, doi: 10.1590/S1517-86922007000200012.
43. L. Schramm *et al.*, "L-Arginine deficiency and supplementation in experimental acute renal failure and in human kidney transplantation," *Kidney Int*, vol. 61, no. 4, pp. 1423–1432, Apr. 2002, doi: 10.1046/j.1523-1755.2002.00268.x.
44. J. B. Kopp and P. E. Klotman, "Cellular and molecular mechanisms of cyclosporin nephrotoxicity.," *Journal of the American Society of Nephrology*, vol. 1, no. 2, pp. 162–179, Aug. 1990, doi: 10.1681/ASN.V12162.
45. R. Schneider *et al.*, "L-Arginine counteracts nitric oxide deficiency and improves the recovery phase of ischemic acute renal failure in rats," *Kidney Int*, vol. 64, no. 1, pp. 216–225, Jul. 2003, doi: 10.1046/j.1523-1755.2003.00063.x.
46. L. De Nicola *et al.*, "Randomized, double-blind, placebo-controlled study of arginine supplementation in chronic renal failure," *Kidney Int*, vol. 56, no. 2, pp. 674–684, Aug. 1999, doi: 10.1046/j.1523-1755.1999.00582.x.
47. J. Huang, D. Ladeiras, Y. Yu, X.-F. Ming, and Z. Yang, "Detrimental Effects of Chronic L-Arginine Rich Food on Aging Kidney," *Front Pharmacol*, vol. 11, Jan. 2021, doi: 10.3389/fphar.2020.582155.
48. A. M. Wilson, R. Harada, N. Nair, N. Balasubramanian, and J. P. Cooke, "<scp>l</scp> -Arginine Supplementation in Peripheral Arterial Disease," *Circulation*, vol. 116, no. 2, pp. 188–195, Jul. 2007, doi: 10.1161/CIRCULATIONAHA.106.683656.
49. S. P. Schulman *et al.*, "L-Arginine Therapy in Acute Myocardial Infarction," *JAMA*, vol. 295, no. 1, p. 58, Jan. 2006, doi: 10.1001/jama.295.1.58.
50. E. T. Trexler *et al.*, "International society of sports nutrition position stand: Beta-Alanine," *J Int Soc Sports Nutr*, vol. 12, no. 1, Oct. 2015, doi: 10.1186/s12970-015-0090-y.
51. V. Ávila-Gandía, A. Torregrosa-García, S. Pérez-Piñero, R. Ortolano, M. S. Abellán-Ruiz, and F. J. López-Román, "One-Week High-Dose β-Alanine Loading Improves World Tour Cyclists' Time-Trial Performance," *Nutrients*, vol. 13, no. 8, p. 2543, Jul. 2021, doi: 10.3390/nu13082543.
52. A. A. Boldyrev, G. Aldini, and W. Derave, "Physiology and Pathophysiology of Carnosine," *Physiol Rev*, vol. 93, no. 4, pp. 1803–1845, Oct. 2013, doi: 10.1152/physrev.00039.2012.
53. R. C. Harris *et al.*, "The absorption of orally supplied β-alanine and its effect on muscle carnosine synthesis in human vastus lateralis," *Amino Acids*, vol. 30, no. 3, pp. 279–289, May 2006, doi: 10.1007/s00726-006-0299-9.
54. A. Baguet, K. Koppo, A. Pottier, and W. Derave, "β-Alanine supplementation reduces acidosis but not oxygen uptake response during high-intensity cycling exercise," *Eur J Appl Physiol*, vol. 108, no. 3, pp. 495–503, Feb. 2010, doi: 10.1007/s00421-009-1225-0.

55. D. B. Zorov, M. Juhaszova, and S. J. Sollott, “Mitochondrial Reactive Oxygen Species (ROS) and ROS-Induced ROS Release,” *Physiol Rev*, vol. 94, no. 3, pp. 909–950, Jul. 2014, doi: 10.1152/physrev.00026.2013.
56. A. R. Pavlov, A. A. Revina, A. M. Dupin, A. A. Boldyrev, and A. I. Yaropolov, “The mechanism of interaction of carnosine with superoxide radicals in water solutions,” *Biochimica et Biophysica Acta (BBA) - General Subjects*, vol. 1157, no. 2, pp. 304–312, Jun. 1993, doi: 10.1016/0304-4165(93)90114-N.
57. M. T. A. Torreggiani, “A pulse radiolysis study of carnosine in aqueous solution,” *Int J Radiat Biol*, vol. 74, no. 3, pp. 333–340, Jan. 1998, doi: 10.1080/095530098141474.
58. I. Jukić *et al.*, “Carnosine, Small but Mighty—Prospect of Use as Functional Ingredient for Functional Food Formulation,” *Antioxidants*, vol. 10, no. 7, p. 1037, Jun. 2021, doi: 10.3390/antiox10071037.
59. R. Nagai, D. B. Murray, T. O. Metz, and J. W. Baynes, “Chelation: A Fundamental Mechanism of Action of AGE Inhibitors, AGE Breakers, and Other Inhibitors of Diabetes Complications,” *Diabetes*, vol. 61, no. 3, pp. 549–559, Mar. 2012, doi: 10.2337/db11-1120.
60. A. Twarda-Clapa, A. Olczak, A. M. Białkowska, and M. Koziołkiewicz, “Advanced Glycation End-Products (AGEs): Formation, Chemistry, Classification, Receptors, and Diseases Related to AGEs,” *Cells*, vol. 11, no. 8, p. 1312, Apr. 2022, doi: 10.3390/cells11081312.
61. A. Negre-Salvayre, C. Coatrieux, C. Ingueneau, and R. Salvayre, “Advanced lipid peroxidation end products in oxidative damage to proteins. Potential role in diseases and therapeutic prospects for the inhibitors,” *Br J Pharmacol*, vol. 153, no. 1, pp. 6–20, Jan. 2008, doi: 10.1038/sj.bjp.0707395.
62. E. D. Pepper, M. J. Farrell, G. Nord, and S. E. Finkel, “Antiglycation Effects of Carnosine and Other Compounds on the Long-Term Survival of *Escherichia coli*,” *Appl Environ Microbiol*, vol. 76, no. 24, pp. 7925–7930, Dec. 2010, doi: 10.1128/AEM.01369-10.
63. I. Rashid, D. M. van Reyk, and M. J. Davies, “Carnosine and its constituents inhibit glycation of low-density lipoproteins that promotes foam cell formation in vitro,” *FEBS Lett*, vol. 581, no. 5, pp. 1067–1070, Mar. 2007, doi: 10.1016/j.febslet.2007.01.082.
64. J. Pietkiewicz, A. Bronowicka-Szydełko, K. Dzierzba, R. Danielewicz, and A. Gamian, “Glycation of the Muscle-Specific Enolase by Reactive Carbonyls: Effect of Temperature and the Protection Role of Carnosine, Pirydoxamine and Phosphatidylserine,” *Protein J*, vol. 30, no. 3, pp. 149–158, Mar. 2011, doi: 10.1007/s10930-011-9307-3.
65. B. RAMAMURTHY, P. HÖÖK, A. D. JONES, and L. LARSSON, “Changes in myosin structure and function in response to glycation,” *The FASEB Journal*, vol. 15, no. 13, pp. 2415–2422, Nov. 2001, doi: 10.1096/fj.01-0183com.
66. T. L. Dutka and G. D. Lamb, “Effect of Carnosine on Excitation–Contraction Coupling in Mechanically-Skinned Rat Skeletal Muscle,” *J Muscle Res Cell Motil*, vol. 25, no. 3, pp. 203–213, Apr. 2004, doi: 10.1023/B:JURE.0000038265.37022.c5.
67. P. M. Bellinger and C. L. Minahan, “Performance effects of acute ***β*** -alanine induced paresthesia in competitive cyclists,” *Eur J Sport Sci*, vol. 16, no. 1, pp. 88–95, Feb. 2016, doi: 10.1080/17461391.2015.1005696.
68. S. MacPhee, I. N. Weaver, and D. F. Weaver, “An Evaluation of Interindividual Responses to the Orally Administered Neurotransmitter ***β*** -Alanine,” *J Amino Acids*, vol. 2013, pp. 1–5, Jun. 2013, doi: 10.1155/2013/429847.
69. Jr. , R. Dawson, M. Biasetti, S. Messina, and J. Dominy, “The cytoprotective role of taurine in exercise-induced muscle injury,” *Amino Acids*, vol. 22, no. 4, pp. 309–324, Jun. 2002, doi: 10.1007/s007260200017.
70. R. C. Harris *et al.*, “The absorption of orally supplied β-alanine and its effect on muscle carnosine synthesis in human vastus lateralis,” *Amino Acids*, vol. 30, no. 3, pp. 279–289, May 2006, doi: 10.1007/s00726-006-0299-9.
71. J. J. Matthews *et al.*, “*β* -alanine supplementation in adults with overweight and obesity: a randomized controlled feasibility trial,” *Obesity*, vol. 33, no. 2, pp. 278–288, Feb. 2025, doi: 10.1002/oby.24204.
72. H. Wang *et al.*, “Carnosine attenuates renal ischemia–reperfusion injury by inhibiting GPX4-mediated ferroptosis,” *Int Immunopharmacol*, vol. 124, p. 110850, Nov. 2023, doi: 10.1016/j.intimp.2023.110850.
73. Y. Cao *et al.*, “Protective effect of carnosine on hydrogen peroxide–induced oxidative stress in human kidney tubular epithelial cells,” *Biochem Biophys Res Commun*, vol. 534, pp. 576–582, Jan. 2021, doi: 10.1016/j.bbrc.2020.11.037.
74. G. Aldini *et al.*, “The carbonyl scavenger carnosine ameliorates dyslipidaemia and renal function in Zucker obese rats,” *J Cell Mol Med*, vol. 15, no. 6, pp. 1339–1354, Jun. 2011, doi: 10.1111/j.1582-4934.2010.01101.x.
75. T. Bo and J. Fujii, “Primary Roles of Branched Chain Amino Acids (BCAAs) and Their Metabolism in Physiology and Metabolic Disorders,” *Molecules*, vol. 30, no. 1, p. 56, Dec. 2024, doi: 10.3390/molecules30010056.
76. G. Howatson, M. Hoad, S. Goodall, J. Tallent, P. G. Bell, and D. N. French, “Exercise-induced muscle damage is reduced in resistance-trained males by branched chain amino acids: a randomized, double-blind, placebo controlled study,” *J Int Soc Sports Nutr*, vol. 9, no. 1, Feb. 2012, doi: 10.1186/1550-2783-9-20.
77. A. Fouré and D. Bendahan, “Is Branched-Chain Amino Acids Supplementation an Efficient Nutritional Strategy to Alleviate Skeletal Muscle Damage? A Systematic Review,” *Nutrients*, vol. 9, no. 10, p. 1047, Sep. 2017, doi: 10.3390/nu9101047.

78. M. Waldron, K. Whelan, O. Jeffries, D. Burt, L. Howe, and S. D. Patterson, “The effects of acute branched-chain amino acid supplementation on recovery from a single bout of hypertrophy exercise in resistance-trained athletes,” *Applied Physiology, Nutrition, and Metabolism*, vol. 42, no. 6, pp. 630–636, Jun. 2017, doi: 10.1139/apnm-2016-0569.
79. T. I. Gee and S. Deniel, “Branched-chain aminoacid supplementation attenuates a decrease in power-producing ability following acute strength training.,” *J Sports Med Phys Fitness*, vol. 56, no. 12, pp. 1511–1517, Dec. 2016.
80. G. Bianchi, R. Marzocchi, F. Agostini, and G. Marchesini, “Update on nutritional supplementation with branched-chain amino acids,” *Curr Opin Clin Nutr Metab Care*, vol. 8, no. 1, pp. 83–87, Jan. 2005, doi: 10.1097/00075197-200501000-00013.
81. X.-N. Zhang *et al.*, “The effect of acute branched-chain amino acids ingestion on rate of force development in different time intervals: a controlled crossover study,” *Front Nutr*, vol. 11, Jan. 2025, doi: 10.3389/fnut.2024.1463202.
82. M. Gervasi *et al.*, “Effects of a commercially available branched-chain amino acid-alanine-carbohydrate-based sports supplement on perceived exertion and performance in high intensity endurance cycling tests,” *J Int Soc Sports Nutr*, vol. 17, no. 1, Jan. 2020, doi: 10.1186/s12970-020-0337-0.
83. D. V. Martinho, H. Nobari, A. Faria, A. Field, D. Duarte, and H. Sarmento, “Oral Branched-Chain Amino Acids Supplementation in Athletes: A Systematic Review,” *Nutrients*, vol. 14, no. 19, p. 4002, Sep. 2022, doi: 10.3390/nu14194002.
84. M. Neinast, D. Murashige, and Z. Arany, “Branched Chain Amino Acids.,” *Annu Rev Physiol*, vol. 81, pp. 139–164, Feb. 2019, doi: 10.1146/annurev-physiol-020518-114455.
85. S. Fujita *et al.*, “Nutrient signalling in the regulation of human muscle protein synthesis,” *J Physiol*, vol. 582, no. 2, pp. 813–823, Jul. 2007, doi: 10.1113/jphysiol.2007.134593.
86. H. C. Dreyer, S. Fujita, J. G. Cadenas, D. L. Chinkes, E. Volpi, and B. B. Rasmussen, “Resistance exercise increases AMPK activity and reduces 4E-BP1 phosphorylation and protein synthesis in human skeletal muscle,” *J Physiol*, vol. 576, no. 2, pp. 613–624, Oct. 2006, doi: 10.1113/jphysiol.2006.113175.
87. M. S. Kaspy, S. J. Hannaian, Z. W. Bell, and T. A. Churchward-Venne, “The effects of branched-chain amino acids on muscle protein synthesis, muscle protein breakdown and associated molecular signalling responses in humans: an update,” *Nutr Res Rev*, vol. 37, no. 2, pp. 273–286, Dec. 2024, doi: 10.1017/S0954422423000197.
88. J. Pedroso, T. Zampieri, and J. Donato, “Reviewing the Effects of l-Leucine Supplementation in the Regulation of Food Intake, Energy Balance, and Glucose Homeostasis,” *Nutrients*, vol. 7, no. 5, pp. 3914–3937, May 2015, doi: 10.3390/nu7053914.
89. X. Deng *et al.*, “Disruption of branched-chain amino acid homeostasis promotes the progression of DKD via enhancing inflammation and fibrosis-associated epithelial-mesenchymal transition,” *Metabolism*, vol. 162, p. 156037, Jan. 2025, doi: 10.1016/j.metabol.2024.156037.
90. S. DiMartino, M. P. Revelo, S. K. Mallipattu, and S. E. Piret, “Activation of branched chain amino acid catabolism protects against nephrotoxic acute kidney injury,” *American Journal of Physiology-Renal Physiology*, vol. 328, no. 1, pp. F152–F163, Jan. 2025, doi: 10.1152/ajprenal.00260.2024.
91. J. Yamamoto *et al.*, “Branched-chain amino acids enhance cyst development in autosomal dominant polycystic kidney disease,” *Kidney Int*, vol. 92, no. 2, pp. 377–387, Aug. 2017, doi: 10.1016/j.kint.2017.01.021.