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A Review: Role of Leucine as a Sports Supplement

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ABSTRACT Leucine is an essential amino acid that cannot be synthesised by the human body and so the body has to attain it from dietary sources. Besides its role in regulation of the blood-sugar level, wound healing and growth hormone production, it also helps in muscle protein synthesis and in decrease of muscle protein breakdown. L-Leucine, after exercise, stimulates recovery of muscle protein synthesis via translation regulation. Leucine supplementation during exercise is responsible for muscle growth, strength and enhanced performance. Studies recommend 4 grams per day of leucine supplementation for enhancing strength in male gymnasium goers. Leucine supplementation is currently in the scenario but more detailed studies are required on its effect on body composition, performance and health of a sports person. The paper includes comparison and review that will reveal the metabolic functions of leucine in human body, especially in sportspersons.

INTRODUCTION

A supplement is a synthetic item when taken by means of mouth as a pill, tablet, pill or liquid (Anonymous 2017). It offers vitamins, minerals and other food ingredients either extracted from food sources or organised synthetically, individually or in aggregate, as a way to increase their intake (Anonymous 2011). Supplements are widely used by elite players to maintain their health and to improve their activity level (Khelaifi et al. 2018). Supplements include protein, energy bars, vitamins, fat burners, weight gainers and Branched Chain Amino Acids (BCAA) (Anonymous 2017). Among them, BCAAs are an important class, which includes Leucine, Isoleucine and Valine (Starkie 2009). It is estimated that three percent to eighteen percent of all workout energy is provided by the BCAAs. Out of these three, Leucine is an essential amino acid that cannot be synthesised by the body and must be attained from food sources (Layman 2003). Like all 'amino acids', the crucial amino acid leucine incorporates a charged 'amino group ($-NH_3^+$)' and negatively charged 'carboxyl group ($-COO^-$)' connected to the identical carbon atom, the alpha-carbon.

Leucine not only regulates blood-sugar levels, supports muscle and bone tissue, wound healing and growth hormone production, but also has numerous metabolic roles in cellular oxidation rate (Sweatt et al. 2014). Leucine is usable to 'skeletal muscle' where it acts as a nutrient signal and is used for protein synthesis. It behaves as a metabolic fuel or a nitrogen donor for the synthesis of glutamine and alanine (Pitkanen et al. 2003). Blood amino acid concentration gets elevated when leucine is consumed before and during exercise (Bruce et al. 1997). Leucine supplementation during exercise is responsible for muscle growth, strength and performance (Layne et al. 2009). After the exercise, both blood and muscle level of BCAAs decrease, after which leucine is used as fuel by muscles (Layman 2003). During physical activity, it can be transaminated and oxidised to get 'acetyl-CoA' in muscles. Leucine in the diet helps to boost muscle anabolism after resistance activity (Layman 2003). Leucine is available in natural food sources and nowadays available in the market in synthetic form (Ananieva et al. 2016).

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MATERIAL AND METHODS

For this study, the researchers collected the review from Google Scholar, Web of Science and literature was compiled under different sections.

OBSERVATIONS AND DISCUSSION

Leucine and Its Metabolism

For protein synthesis, the first step is initiation of mRNA (messenger ribonucleic acid), that is, translation by which leucine generates protein. Adjustment of mRNA translation is done by leucine, which is based on 'mTOR (mammalian target of rapamycin)', as 'rapamycin', a specific mTOR inhibitor, as it is ready to sharpen the changes of leucine (Vianna et al. 2010). Initially, cytosolic and mitochondrial branched chain amino transferase metabolises the leucine into α-ketoisocaproate by carrying nitrogen from leucine to 'α-ketoglutarate' to get glutamate and KIC. α- KIC is metabolised into Iso-valeryl-CoA by branched chain α-keto acid dehydrogenase complex or into β-hydroxyl β-methylbutyrate by KIC di-oxygenase (Rosenthal et al. 1974). One derivative of isovaleryl-CoA, β-methyl-crotonyl forms HMB. Ultimately, these metabolites harvest 'acetoacetyl-CoA' and aceto-acetate, which are utilised in energy generation. Thus, leucine stimulates protein synthesis by activating the mTORC1 'signalling pathway' (Elia et al. 1980; Harper et al. 1984; Ali et al. 2009).

Role of Leucine in Exercise and Sports

The sports industry around the world has grown many fold from the last decade. Many supplements are available in the market claiming that they will improve strength and performance. Leucine is one of them. Many scientific studies on leucine are going on to see its impact on strength and performance of sports people. There are several studies, which reveal that leucine has the capacity to build up muscles. All these aspects of leucine are further reviewed under the following sections.

a. Leucine Supplementation and Exercise

L-Leucine can be used as a nutritional supplement to increase the strength performance during resistance training program (Ispoglou et al. 2011). The response of total muscle protein balance by ingestion of additional leucine with protein in association with resistance exercise was reported to be very beneficial. Whey protein plus leucine results in an anabolic response in muscle that is not greater than that of whey protein alone (Tipton et al. 2009). The upper intake level of Leucine supplements in healthy elderly men is similar as that of young men that is 500 mg/kg/day (Elango et al. 2016).

BCAA, especially leucine, have proved to be ergogenic for both endurance and performance. A study was done to investigate the effects of dietary leucine supplementation on the exercise performance of outrigger Australian canoeists. Thirteen (ten female, three male) competitive outrigger canoeists (aged 31.6 (2.2) year) underwent testing before and after a 6-week supplementation course with either capsulated L-leucine (45 mg kg (-1) d (-1); n = 6) or placebo (corn flour; n = 7). Testing comprised of anthropometry, upper body power and work and a row to exhaustion at seventy to seventy-five percent maximal aerobic power where perceived exertion (RPE), heart rate (HR) and plasma BCAA, and tryptophan concentrations were determined. Leucine supplementation showed that there was significant elevation in plasma leucine and total BCAA concentrations. Upper body power and work significantly marked up in both groups after supplementation, but power was positively greater after leucine supplementation compared to the placebo group. Rowing time was significantly increased and average RPE significantly decreased with leucine supplementation, while these variables were unaltered with the placebo group. Leucine supplementation had no effect on the plasma tryptophan to BCAA ratio, HR or anthropometric variables. Six weeks dietary leucine supplementation significantly corrected endurance performance and upper body power in outrigger canoeists without significant change in the plasma ratio of tryptophan to BCAA (Crowe et al. 2006).

The whole body leucine turnover increases by training. So, both by training and exercise, oxidation of leucine increases and gets acetyl-CoA, which produces energy (Crowe et al. 2006). This result is based on a study conducted during rest and exercise in young, post-absorptive female rats (Henderson et al. 1985). Leucine supplementation of 50 mg/kg of body weight per day appears to prevent the decrease in the serum leucine concentration during training (Mero et al. 1997).

Thirteen-month-old mice were subjected to moderate aerobic exercise (45 minutes swimming per day with 3% body weight workload) and provided with a chow diet with five percent leucine or 3.4 percent alanine for the time period of 8 weeks. Serum and plasma were adjusted for glucose, urea nitrogen, insulin and amino acid profile analysis. The white gastronomies muscles were used for identification of muscle size and signalling proteins involved in protein synthesis and degradation. The study showed that moderate aerobic training combined with five percent leucine supplementation has the potential to raise muscle size in fast-twitch skeletal muscle during aging, potentially through increased protein synthesis and decreased protein breakdown (Pedroso et al. 2015).

Positive results were obtained when Leucine was supplemented at the rate of 3 grams per day to male gym goers for 45 days. It enhanced their muscle growth and increased the strength performance of the gym persons (Saharan et al. 2019).

b. Leucine Supplementation and Muscle Mass

Leucine intake after exercise stimulates muscle protein synthesis and helps in recovery of skeletal muscle protein, independent of increased plasma insulin (Anthony et al. 1999; Mero 1999). To induce a maximal skeletal muscle protein anabolic response in young adults, 10 grams of essential amino acid with high leucine content (1.8 g) is required (Glynn et al. 1970). The inclusion of leucine to protein is greatest in liver, followed by adipose tissue, then muscle. The total leucine utilisation (conversion to CO_2 + total lipid + protein) in adipose tissue and muscle combined is seven times greater than that of liver. Adipose tissue and muscle play a major important role in peripheral utilisation of leucine (C). Skeletal muscle mass remains same but peri-renal adipose tissue mass accumulates (+45%) in leucine supplemented rats. Leucine modulates mTOR pathway in muscle and adipose tissue, when leucine supplementation is consumed for long-term. It promotes hypertrophy and hyperplasia of adipose tissue and does not increase muscle mass (Zeanandian et al. 2012).

c. Leucine Supplementation and Body Composition

A combination of moderate energy restriction and BCAA supplementation induces significant and preferential losses of visceral adipose tissue (VAT), and maintain a high level of performance. A study was conducted in which 25 competitive wrestlers restricted their caloric intake (28 kcal/kg/d) for 19 days, using a hypo-caloric control (hC, n=6), hypo-caloric high-protein (hHP, n=7), hypo-caloric high-branched-chain that the combination of moderate energy restriction and BCAA supplementation amino acid (hBCAA, n=6), and hypo-caloric low-protein (hLP, n=6) diet. There was significant and preferential loss of visceral adipose tissue (VAT). With this, a high level of performance was also maintained (Mourier et al. 1997). In another study, AIN-93M diet (rodent diet) was given to a control group and the same diet supplemented with 5.9 g l-leucine/kg was given to a leucine group for 6 weeks. It was found that there was no difference in final body weight but the liver protein concentration was higher in the leucine group. After 40 weeks of supplementation, body weight and fat were lower in the leucine group than that of control group but still higher from the adult group (Vianna et al. 2010).

d. Leucine and Muscle Protein Synthesis

The most effective amino acid in stimulation of protein synthesis is leucine. It also helps in promoting positive nitrogen balance, by the activation of the protein. It serves as a stimulus on muscle protein synthesis, thus decreases muscle protein breakdown (Vianna et al. 2010). Leucine directly and indirectly stimulates the synthesis and secretion of insulin, raising its anabolic cellular effects. By modulating, the elements which are involved in the insulin signalling pathway translation, it also stimulates protein synthesis and inhibits insulin signalling. A study concluded that to sustain basal rates of protein synthesis, availability of all amino acids is necessary to prevent hypo amino-academia. It activates signalling factor of mammalian target of rapamycin (mTOR) to promote synthesis in skeletal muscle and in adipose tissue (Frexes et al. 1992).

Liver protein status and the capacity of muscle protein synthesis are also improved by low-dose leucine supplementation (Donato et al. 2006). Leucine supplementation raised time of exhaustion and the upper body power of rowers at the time of 6 weeks of supplementation (Crowe et al. 2006) to a larger extent than a placebo group, at the same time, co-ingestion of protein and leucine for 8 weeks of resistance training has proven to bring out more gains in one repetition maximum strength than a placebo (CHO) and a control group (Coburn et al. 2006).

In a randomised study, 10 healthy young men (age 25 ± 1 years, height 1.73 ± 0.02 m, weight 65.8 ± 1.5 kg) were put into different conditions. One, with intake of 2 grams of leucine (LEU), intake of a mixed meal (protein 27.5 grams, including 2.15 grams of leucine, and protein to fat to carbohydrate ratio of 22:25:53) only (MEAL), intake of 2 gram of leucine immediately after a mixed meal (MEAL-LEU) and intake of 2 gram of leucine 180 minutes after a mixed meal (MEAL-LEU180). Blood samples were collected within 420 minutes (240 minutes for LEU only) after intake and modifications in amino acid concentrations were checked out. Although the top most plasma leucine concentration rose to 442 ± 24 μM for LEU, it was lower at 347 ± 16 μM ($p < 0.05$ vs. LEU) for MEAL-LEU, 205 ± 8 μM ($p < 0.05$ vs. LEU) for MEAL. The maximum plasma leucine concentration for MEAL-LEU180 increased to 481 ± 27 μM and compared to LEU there was no significant difference ($p > 0.1$). The estimation that rapid elevations in plasma leucine concentrations are suppressed when leucine is ingested at the same time as a meal suggests that the timing of its intake must be considered to maximise the anabolic response (Yoshi et al. 2018).

Health Consequences

- In case of obesity, leucine supplementation performs as a support in the treatment of insulin resistance (Macotela et al. 2011).
- A study concluded that when leucine supplementation associated with high fat diet is consumed then there is a reduction in weight gain of thirty-two percent and a decrease of twenty-five percent in adiposity levels (Zhang et al. 2007).
- Leucine supplementation also contributes to the process of muscle anabolism in skin wounds and muscle injuries (Zhang et al. 2004).
- Leucine supplementation reduces the risk of hardening of the arteries (atherosclerosis) (Zhao et al. 2016).
- Several studies suggested that leucine supplementation reduces food intake (Pedroso et al. 2015).

CONCLUSION

The available data simultaneously shows that leucine supplementation before and after resistance exercise significantly increases endurance performance and upper body power and thus helps in recovery process. However, more research is required to support these effects of leucine supplementation as a sport supplement. Although the number of studies determining the effect of leucine on muscle mass and exercise training is limited, it shows that adding leucine supplements to a resistance exercise provides further benefits. Many studies have been carried out to see the effect of Leucine but the safe level recommendations are still under trial. Practically, more research should be carried to understand the effectiveness of leucine supplementation on the body composition and study of negative effects should also be carried out.

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