

## MULTI-INGREDIENT SUPPLEMENTATION IN PHYSICALLY ACTIVE INDIVIDUALS

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Recibido el 17 de noviembre de 2023 / Aceptado el 7 de diciembre de 2023 / DOI: 10.24310/riccafd.12.3.2023.17761  
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### Responsabilidades

<sup>A</sup>Diseño de la investigación, <sup>B</sup>Recolector de datos, <sup>C</sup>Redactor del trabajo, <sup>D</sup>Tratamiento estadístico, <sup>E</sup>Idea original y coordinador de toda la investigación.

### ■ RESUMEN

Los preparados que combinan múltiples ingredientes (MTN) constituyen una amplia gama de suplementos dietéticos que aportan simultáneamente macronutrientes, micronutrientes, aminoácidos, derivados (p. ej., L-Carnitina, β-HMB) o estimulantes (p. ej., cafeína) que pueden favorecer el rendimiento físico y la recuperación post-esfuerzo. Dependiendo de su formulación, los MTN se ingieren antes (pre-entreno), durante o después (post-entreno) del entrenamiento o competición. Las formulaciones pre-entreno están diseñadas para estimular un mejor rendimiento tanto físico como mental. Por otro lado, los suplementos post-entreno tienen como objetivo acelerar la recuperación entre sesiones y maximizar los resultados del entrenamiento (por ejemplo, hipertrofia, fuerza, etc.). La literatura científica disponible parece abogar por el uso de MTN tanto para mejorar el rendimiento durante la sesión de entrenamiento (pre-entreno) como para favorecer la recuperación (post-entreno) luego de realizar diferentes tipos de ejercicio (p. ej., fuerza, resistencia, etc.). El presente comentario describe los nutrientes más comúnmente incluidos en los MTN comercializados para ser ingeridos antes y después del ejercicio. Además, se brindan recomendaciones para seleccionar los MTN adecuados en cada caso, y se indican pautas para diseñar protocolos de suplementación basados en cantidades de nutrientes por kg de masa



corporal, como es el caso de la cafeína (pre-entreno) o de proteínas, carbohidratos y creatina (post-entreno).

### ■ PALABRAS CLAVE

Multi ingredientes, suplementos, cafeína, proteínas, carbohidratos, rendimiento físico, recuperación.

### ■ ABSTRACT

Multi-ingredients (MTN) are specialised dietary supplements containing macronutrients, micronutrients, amino acids, derivatives (e.g., L-Carnitine,  $\beta$ -HMB) or stimulants (e.g., caffeine) which may favour exercise performance. Depending on their unique formulation, MTN are ingested before (pre-workouts), during, or after (post-workout) training or competitions. Pre-workout formulations are designed to boost energy levels and acutely increase performance. On the other hand, post-workout supplements aim to accelerate recovery between sessions and maximise training outcomes (e.g., hypertrophy or strength enhancement) when regularly administered for several weeks. The revised literature seems to advocate for using both pre- and post-workout MTN to enhance exercise capacity and hasten post-exercise recovery under different training modalities (e.g., strength or endurance). The present commentary describes the most common ingredients including in pre- and post-workout MTN formulations. Additionally, recommendations for selecting appropriate MTN supplements are provided, along with guidelines for designing supplementation protocols based on amounts per kg of body mass of the most important ingredients, such as caffeine, in case of pre-workouts or protein, carbohydrates, and creatine for post-workouts.

### ■ KEY WORDS

Multi-nutrient supplement, caffeine, protein-based admixtures, exercise performance, recovery.

### ■ DEFINING MULTI-INGREDIENTS

Multi-ingredients (MTN) are specialised dietary supplements containing macronutrients, micronutrients (e.g., minerals, vitamins, or probiotics) and other nutritional substances like amino acids (e.g., Leucine) and derivatives (e.g., L-Carnitine,  $\beta$ -HMB) or stimulants (usually caffeine) which may maximise exercise outcomes (1). MTN are administered



before, during, or after an exercise session (2) depending on their unique formulation and sport context. Pre-workout MTN are ingested to acutely enhance motivation to train, perceived alertness, focus on the task and boost energy levels (3) to eventually achieve the best possible performance during workouts or competitions (4,5). On the other hand, post-workout MTN are used to speed up recovery (6) and eventually maximise the effects of physical training (e.g., gaining muscle mass, increasing strength, and overall functional capacity) (1).

Most MTN contain a proprietary blend of ingredients expected to promote benefits when taken as described. Even though physical training is the most efficient stimulus to increase performance, the addition of some nutritional strategies (e.g., pre-, or post-workout MTN) has proven to maximise exercise outcomes in physically active individuals (7).

## ■ EFFECTS OF MULTI-INGREDIENT SUPPLEMENTATION TO SUPPORT HEALTH AND ADAPTATION TO EXERCISES IN PHYSICALLY ACTIVE INDIVIDUALS

*Pre-workout:* Most pre-workout supplements include caffeine along with amino acids (e.g., L-Citrulline, L-Tyrosine, L-Taurine) and derivatives such as citrulline-malate, betaine, and L-carnitine (8), which may also be combined with modest to small amounts of carbohydrates and proteins (Puente-Fernández et al. 2020).

Pre-workout supplementation has been used to delay fatigue (9) and improve training capacity in strength-power and endurance athletes (10). Particularly, caffeine has been shown to promote greater strength or power (11) endurance (12) exercise capacity. The ergogenic effect of caffeine has been attributed to its action as an adenosine receptor blocker(13), which may serve to decrease the perception of fatigue (14), stimulates the release of excitatory neurotransmitters (acetylcholine), and eventually increase motor neuron excitability (15). Furthermore, ingesting caffeine may also prolong fat oxidation with a concomitant saving of glycogen during long-duration exercise sessions (16). A recent study from our laboratory found beneficial effects of ingesting a single dose of a pre-workout MTN to increase resistance training volume in middle-aged, physically active males and females (5). The administered MTN provided 400 mg (~5.2 mg/kg of body mass), and of caffeine, 16 g (0.21 g/kg of body mass) of carbohydrates with a high proportion of isomaltulose (slow-release disaccharide), 9 g (0.12 g/kg of body mass) of protein along with citrulline-malate, L-leucine, L-tyrosine, L-aurine, and betaine. It is worth noticing that when the MTN was consumed prior to endurance training sessions, a significant increase in fat oxidation was also observed (5).



The available evidence suggests that pre-workout MTN providing caffeine and other caffeinated ingredients (e.g., Yerba Mate extract, Guarana) combined with amino acids such as L-leucine, L-arginine, L-tyrosine, or L-taurine and other nutritional derivatives (e.g., citrulline-malate, betaine, and L-carnitine) may be beneficial for enhancing exercise capacity and delaying fatigue under different exercise modalities, such as lifting weights (5), cycling or running at moderate to low intensities (17).

*Post-workout:* MTN post-workout supplements contain high-quality protein (e.g., whey, casein, beef), carbohydrates, and a variety of synergic ingredients such as creatine (18), vitamin D(19), long-chain omega-3 fatty acids (2), essential amino acids, particularly Leucine (19) and derivatives such as  $\beta$ -HMB and L-Carnitine (20). Post-workout formulations are used to speed up post-exercise recovery and maximise training outcomes (e.g., muscle mass gain, strength, or endurance performance) (21).

The claimed superior effects of MTN compared to the intake of each ingredient in isolation are based on their synergistic interaction once the included ingredients are ingested as a component of a special formulation (22). Nevertheless, the expected outcomes are based on the proven effects of each singular ingredient examined separately. For instance, creatine has been shown to optimise recovery and amplify training capacity maximizing training outcomes in strength and endurance athletes (23). Vitamin D is a cofactor associated with optimal muscular function and growth (24). Long-chain omega-3 fatty acids promote muscle membrane sensitivity which facilitates amino acid uptake and improve muscle protein synthesis (25). High-quality protein extracts such as whey or casein with a high concentration of essential amino acids (>40%), particularly the branched-chain amino acids, including leucine, maximise muscle protein synthesis and attenuate muscle protein breakdown during exercise and resting conditions (18). Additionally,  $\beta$ -HMB, a Leucine metabolite, would also attenuate catabolism while favouring muscular anabolism (26), whereas L-Carnitine optimises recovery by attenuating membrane disruption and consequently increases oxygen delivery to the working muscles (27).

Two recent studies reported superior strength and power performance regain in recreationally trained young men by ingesting a post workout MTN providing whey and beef protein (6) or plant-based protein from rice fortified with amino acids (e.g., Leucine) and derivatives (e.g.,  $\beta$ -HMB) (21) instead of an isocaloric supplement providing only carbohydrates. It seems that regardless of the protein source (animal or plant) when equivalent amounts of essential amino acids (particularly leucine) are included in the MTN, similar effects on exercise-induced outcomes (e.g.,



increase of post-exercise muscle protein synthesis and performance regain) could be expected (28). Along these lines, a meta-analysis suggested superior gains in strength and fat-free mass in resistance-trained individuals who ingested MTN containing whey protein and creatine vs. a comparator supplement providing only carbohydrates or protein.

The available evidence advocates for the use of post-workout MTN admixtures containing protein extracts from animals (whey, casein, or beef) or plant sources (fortified with essential amino acids like leucine), creatine, carbohydrates, and small amounts of fat to promote recovery and maximise exercise-induced outcomes in physically active, healthy individuals.

## ■ SUPPLEMENTATION PROTOCOLS AND PRACTICAL RECOMMENDATIONS

*Pre-workout supplementation:* The proposed protocol varies depending on the chosen formulation (e.g., the amount of caffeine per dose, grams of protein and carbohydrate per intake), the exercise modality (e.g., strength or endurance), and the length of workout sessions (e.g., shorter, or longer than 1 hour). Caffeine, the main component of most preworkout MTN (8) is rapidly absorbed (within 5 to 15 min), peaking between 40- and 80-min post ingestion (29). The ergogenic effects of MTN are expected noticeable within 15 minutes, lasting for up to 60 to 80 minutes post-ingestion. Therefore, for long-duration disciplines (e.g., marathons), administering caffeine-based pre-workout MTN immediately before starting or during exercise may be more advantageous than ingesting them 60 to 30 min beforehand (29). As such, for long-duration exercise sessions (>1 hour), pre-workout supplements can be ingested 1 hour (looking for earlier ergogenic effects) to immediately before (looking for ergogenic effects toward the middle and last segment of the workout) or at some point during the session, to maintain the expected performance enhancement effects in long-duration (> 90 min) exercise activities. Conversely, for shorter (~45 min to ~1 hour) training sessions, pre-workout supplements can be ingested between 1 hour, 30 or 15 minutes before training.

Typical dosages of pre-workout MTN should provide between 3 to 6 mg/kg of body mass of caffeine. This amount is within the range of caffeine ergogenic effects (30). Caffeinated MTN usually contain synergetic nutrients such as L-tyrosine. Furthermore, to favour a stable glycaemia and attenuate the exercise induced catabolic effects during workouts, some pre-workout MTN may also contain carbohydrates (~0.20 g/kg) and proteins (~0.15 g/kg) (5).



*Postworkout supplementation:* Although several studies have employed absolute doses (e.g., 30 to 60 g) (10), It is highly recommended to adjust the ingestion protocol based on each person's body mass (g/kg). The exact dose will rely on the supplement formulation considering the proportions of carbohydrates, protein, and other key ingredients such as creatine. For instance, postworkout MTN with 0.30 to 0.45 up to 0.60 g/kg of carbohydrates, 0.20-0.30 up to 0.50 g/kg of high-quality protein such as whey, beef or a complete plant protein source (such as rice or pea) administered with 1:1 or 2:1 ratio of CHO/protein and fortified with amino-acids, proven to be effective to optimise recovery and exercise outcomes in resistance training athletes (6,21). Furthermore, the minimum effective daily dose of creatine supplementation has been established at 0.03 g/kg of body mass (23). However, in order to maximize the physiological benefits attributed to creatine supplementation, higher daily doses of up to 0.1 grams per kilogram of body mass are currently recommended (23,31).

Overall, when ingesting consistently for at least four weeks, a single post-workout intake administered within 20 minutes after the training session would be adequate to accelerate and optimise performance outcomes. Additional intakes (such as those taken after breakfast, prior to sleep, and during non-training days) should be individually examined upon integration with the regular diet.

## ■ ADDITIONAL RECOMMENDATIONS

When considering MTN supplements, it is worth considering that many of the commercially available products are manufactured as part of a proprietary blend with undisclosed amounts of each ingredient. Nonetheless, a thorough analysis of the product's composition allows the consumer to disclose all ingredient amounts and therefore assess whether the product includes the right dosages for the claimed effects of each ingredient. Particular attention should be paid to specific ingredients that may be underdosed (e.g., creatine). In this regard, to achieve the expected benefits, consumers may have the option of combining MTN supplementation with other products. On the other hand, knowing the amount of ingredients (e.g., caffeine, proteins, PUFAs, or carbohydrates) will allow consumers to reconsider the diet design, including a more appropriate food selection and timing for each daily meal.

To date, the available scientific literature suggests that most commercially available MTN are safe with minimal, if any, reported adverse effects (32). Nonetheless, it is worth mentioning that most studies so far have analysed the impact of MTN on performance, muscle



function or general health indicators (e.g., haematological markers, blood pressure or heart rate) for relatively shorter periods (approximately eight weeks) with no exhaustive examination of the diet. Therefore, longer studies using an adequate integration of MTN in the diet and identification of the individual responses to various supplementation protocols administered in relative amounts (g/kg of body mass) should be considered for future studies.

### ■ ACKNOWLEDGMENTS

The author thanks the Sports Science Research Team at the Centre for Exercise Activity and Rehabilitation for their strong support and valuable cooperation to all sport nutrition projects conducted in the centre.

### ■ CONFLICTS OF INTEREST

The author declares no conflicts of interest relevant to the content of this manuscript.

### ■ FUNDING DETAILS

There is no funding associated with the production of the present manuscript.

**Data availability statement:** NA.

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