



DESAFIE-SE



INSPIRE-SE



MOVA-SE



CENTRAL  
- nutrition -

# Otimização do metabolismo energético e a importância do catabolismo de gordura para o desempenho físico.

**Gabriel de Carvalho**

Nutricionista e Farmacêutico Bioquímico

Introdutor da Nutrição Funcional no Brasil em 1999

Co-fundador da Faculdade de Saúde Avançada

# A Teia de Inter Relações Metabólicas da Nutrição Funcional

Fisiologia e Função: Organizando os Desequilíbrios Clínicos do Paciente



Gabriel de Carvalho  
CRN-2 3945

**Histórico do Paciente**

Nome: \_\_\_\_\_

Data: \_\_\_\_/\_\_\_\_/\_\_\_\_

**Antecedentes**

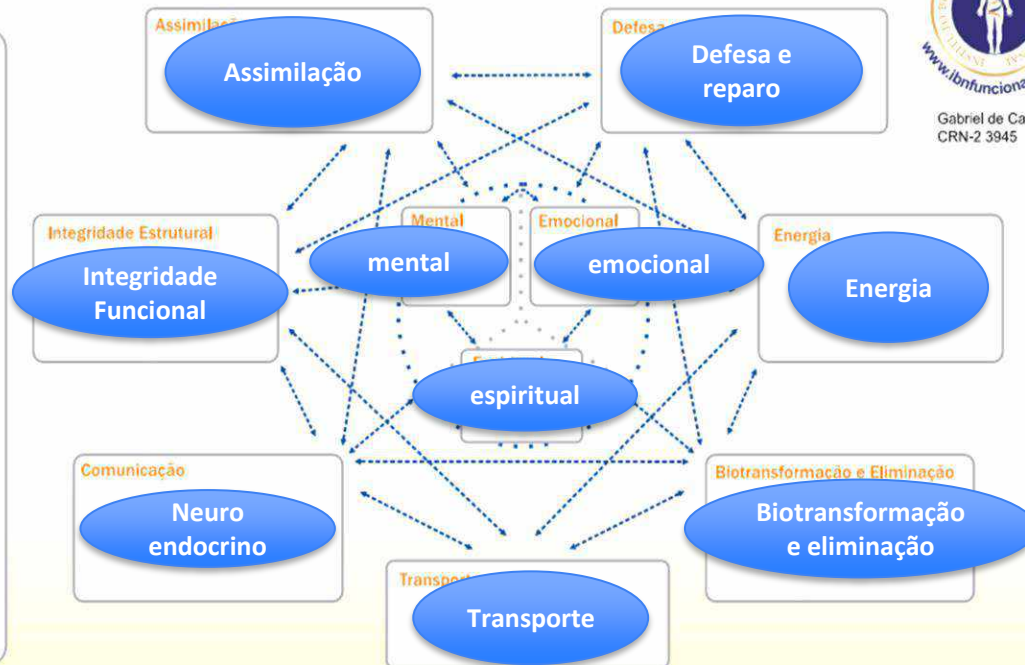
**Genes**  
**Dieta**  
**hábitos**

**Gatilhos**

**Iniciadores**

**Mediadores e Perpetuadores**

**Mediadores**



## Fatores de Estilo de Vida Personalizados

Sono e Relaxamento

Sono e relaxamento

Exercício e Movimento

Exercício e movimento

Nutrição e Hidratação

Nutrição e hidratação

Estresse e Resiliência

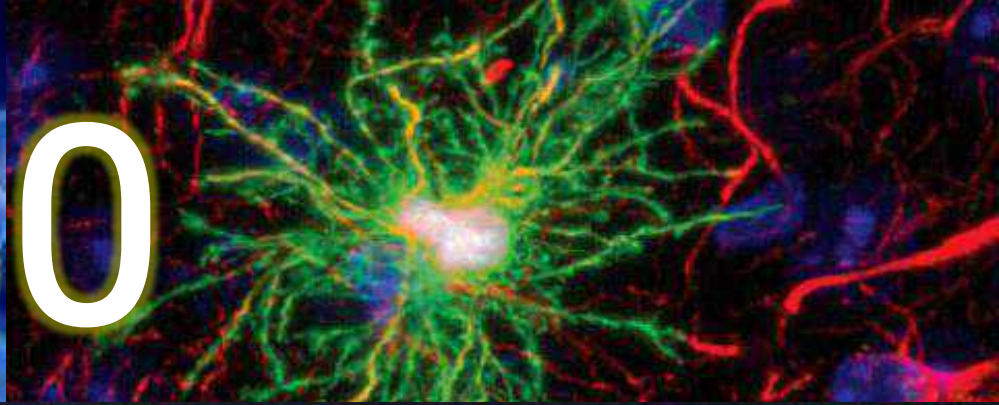
Estresse

Relacionamentos e Trabalho em Equipe

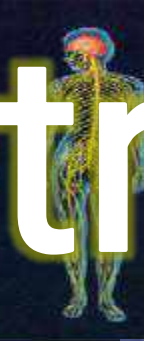
Relações / Equipe

Adaptado do Institute for Functional Medicine  
Todos os direitos reservados ao Instituto Brasileiro de Nutrição Funcional

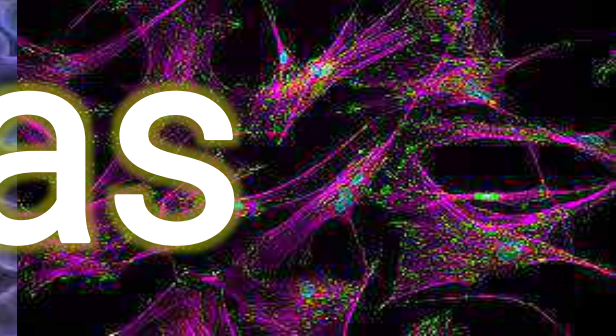
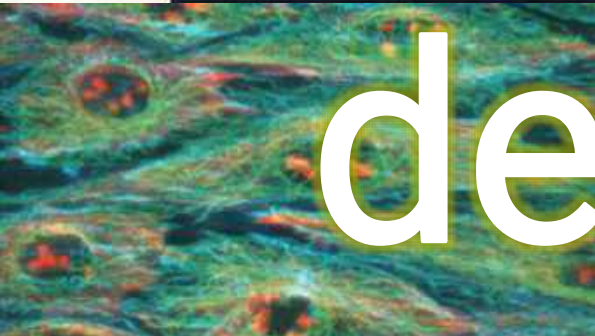
AGO 2015



30



trilhões



de células

The background of the slide is a grid of microscopic images showing cells with blue-stained mitochondria. The mitochondria are bean-shaped and contain internal folds called cristae. The text is overlaid on this grid.

40 quadrilhões  
de  
mitocôndrias

# Por que temos tantos problemas mitocondriais?

# Deficiências Nutricionais

# Deficiências de vitaminas e minerais: aceleram o enfraquecimento mitocondrial do envelhecimento

Review

Mineral and vitamin deficiencies can accelerate the mitochondrial decay of aging

Bruce N. Ames <sup>\*</sup>, Hani Atamna, David W. Killilea

Bruce N. Ames <sup>\*</sup>, Hani Atamna, David W. Killilea



# B3, B2, ferro, enxofre, Q10/Q10H, hemo, cobre

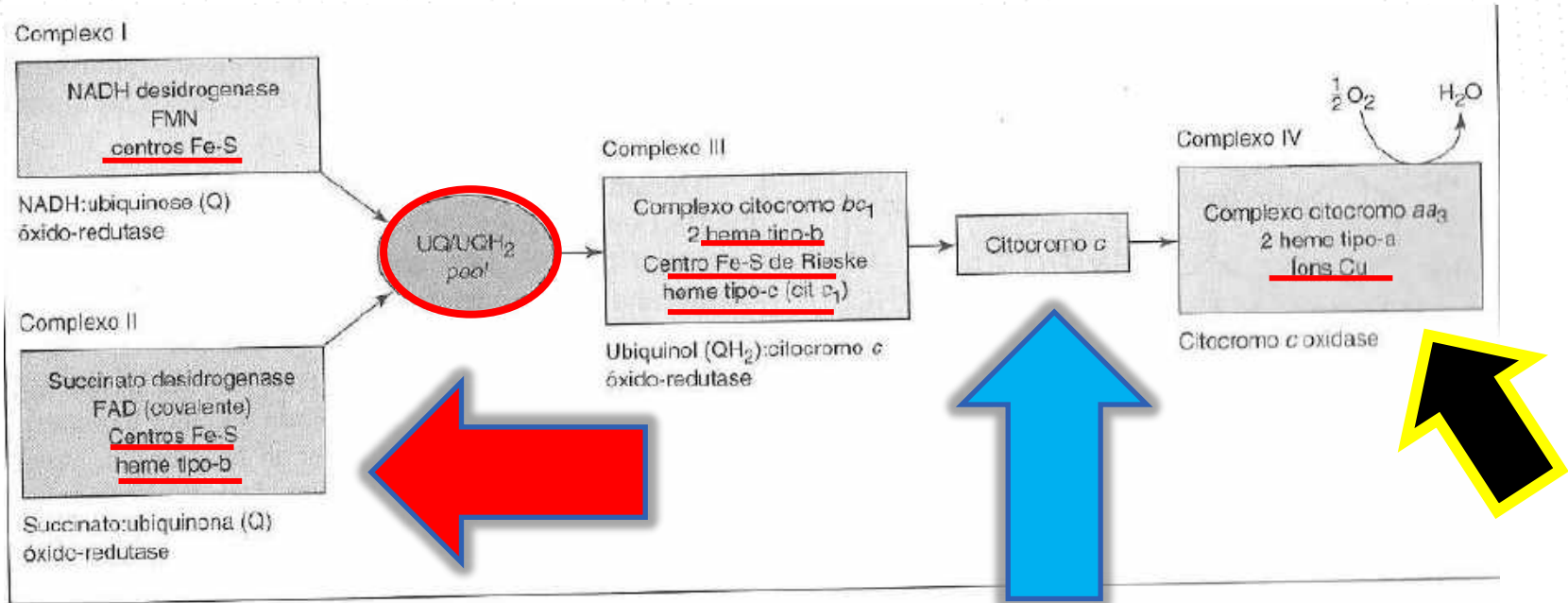
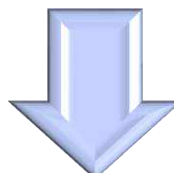


FIGURA 13.30  
Visão geral de complexos e vias de transferência de elétrons na cadeia mitocondrial de transporte de elétrons.

↓ síntese do hemo



↓ hemo-a (exclusivo  
complexo IV)



= liberação de oxidantes +  
dano mitocondrial

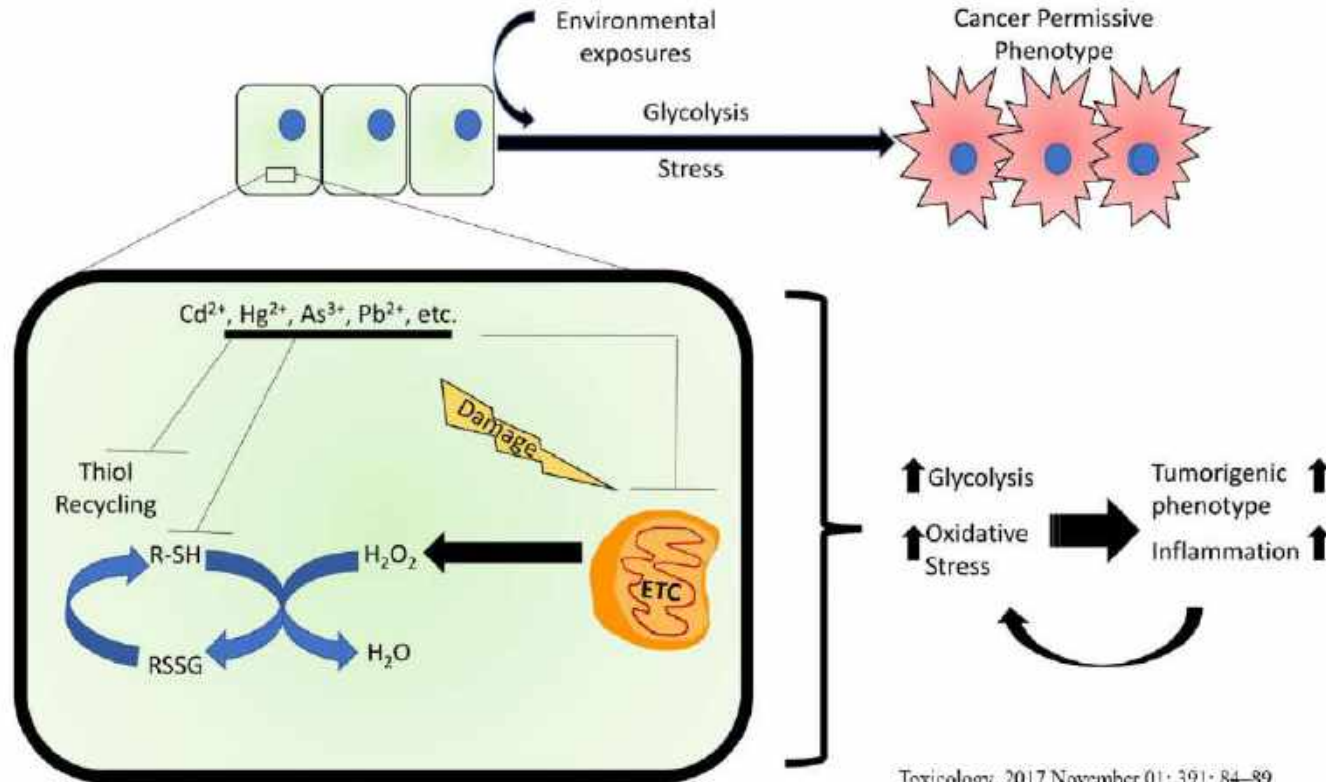
# Assim

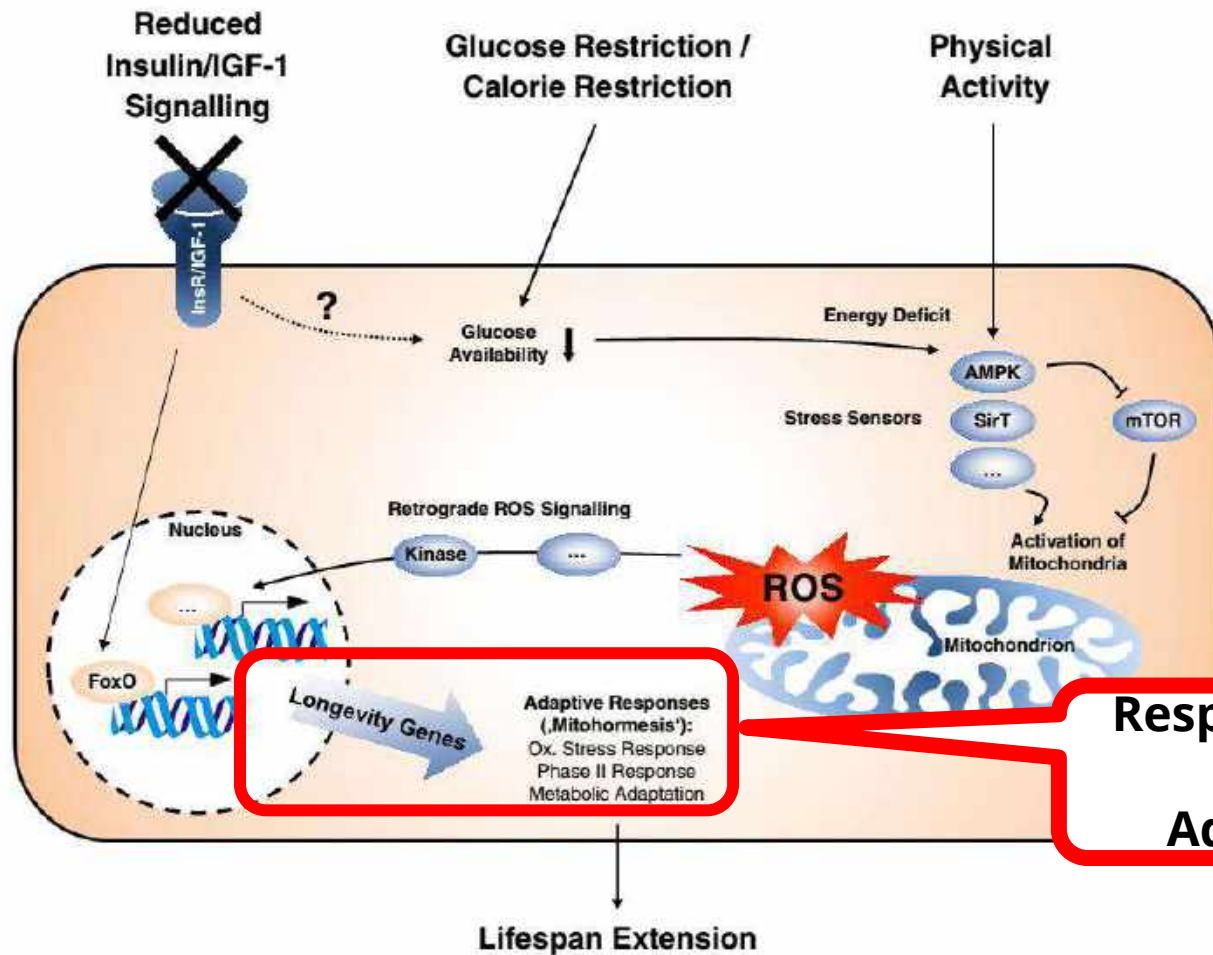
... ↓ síntese do hemo  
causa dano mitocondrial e  
dano ao DNA

antes de haver anemia!

# Algo mais??

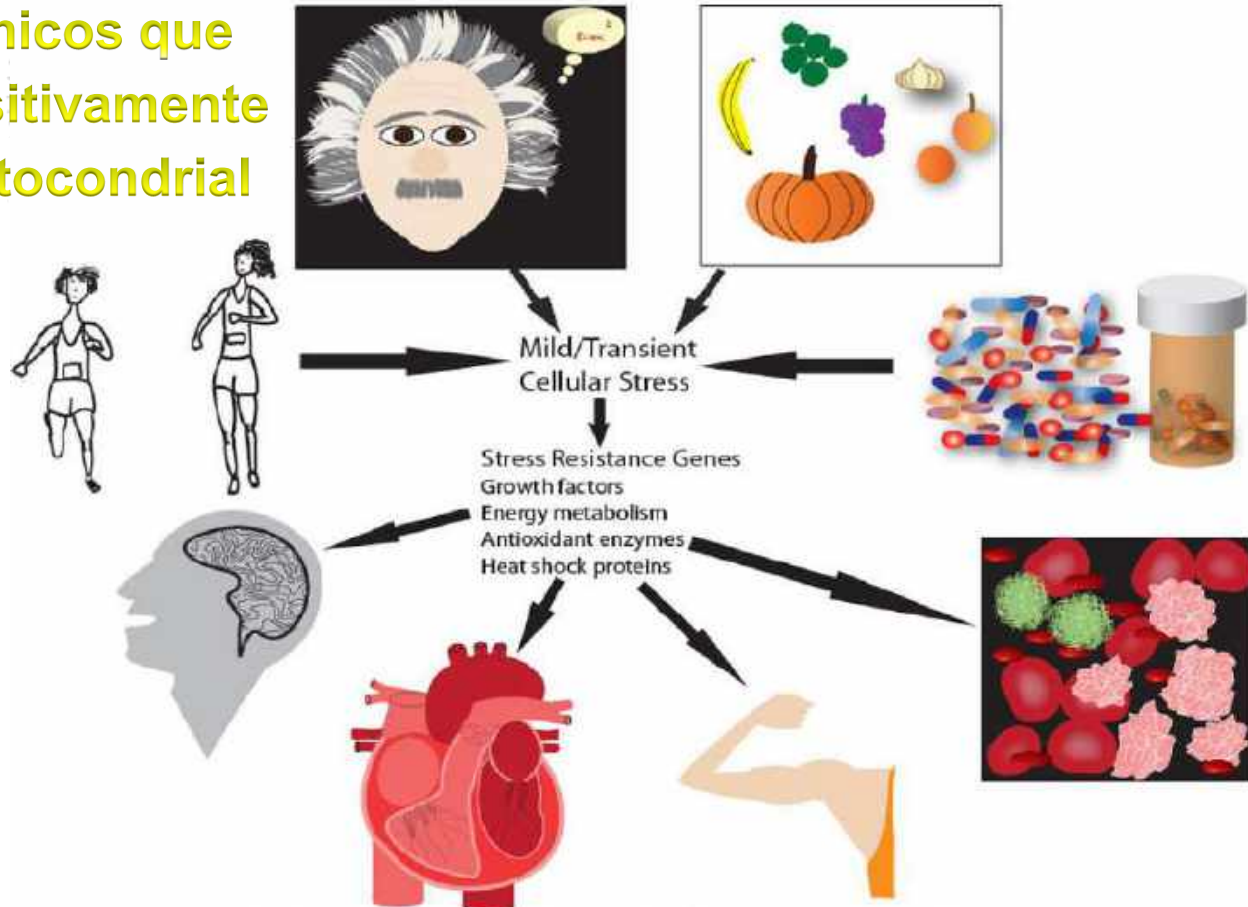
# Metais tóxicos danificam a mitocôndria





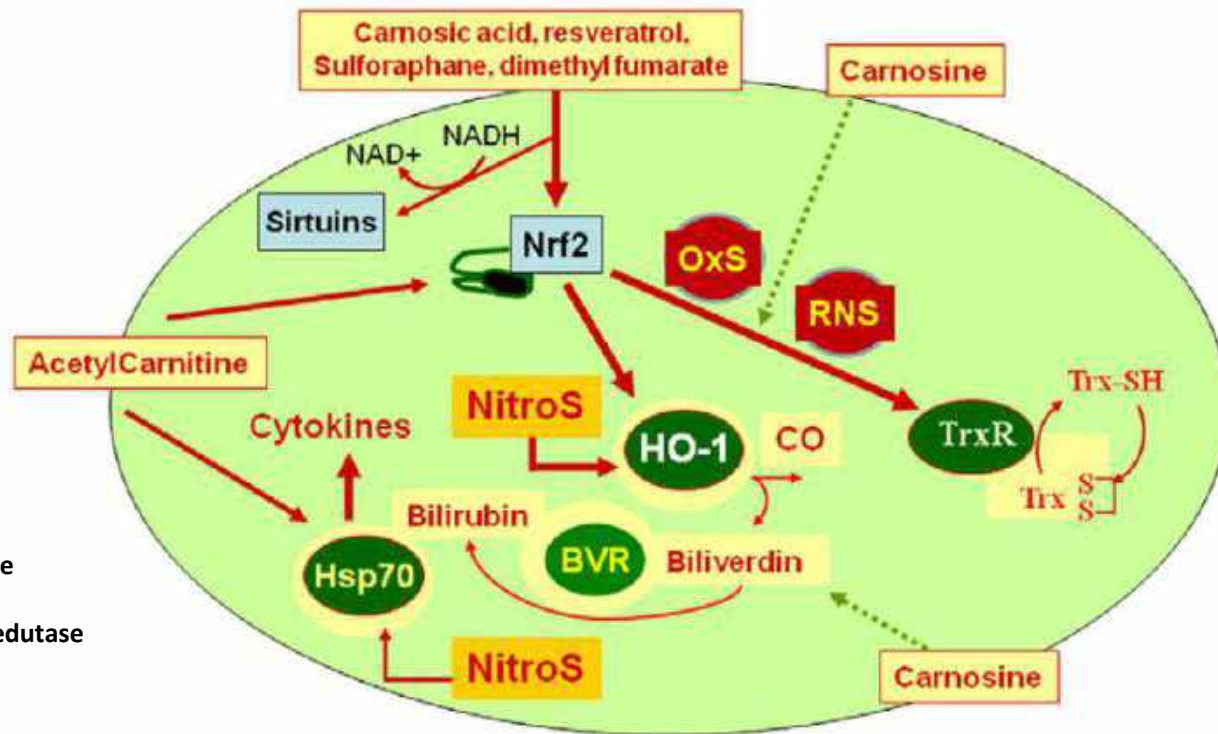
**Resposta ao Estr. oxidativo**  
**Enzimas de Fase II**  
**Adaptação Metabólica**

# Alguns fitoquímicos que impactam positivamente na função mitocondrial



Optimum Mental, Cardiovascular, Neuromuscular and Immune  
Function Resistance to Diseases Including Diabetes, Cardiovascular and Neurological Disorders

# Resveratrol, sulforafano, ácido carnosóico, acetil-L-carnitina, dimetil fumarato e carnosina ativam vitagenes!



Alguns Vitagenes:  
 HO = hemo oxigenase  
 Hsp70,  
 TrxR = tioredoxina redutase  
 Sirtuínas





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## Clinical Nutrition

journal homepage: <http://www.elsevier.com/locate/clnu>



### Review

## Feeding mitochondria: Potential role of nutritional components to improve critical illness convalescence

E. Wesselink<sup>a</sup>, W.A.C. Koekkoek<sup>b</sup>, S. Grefte<sup>c</sup>, R.F. Witkamp<sup>a</sup>, A.R.H. van Zanten<sup>b,\*</sup>

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**Alimentando a mitocôndria:  
possível papel de componentes nutricionais**

# Alimentando a mitocôndria: possível papel de componentes nutricionais



## Review

## Feeding mitochondria: Potential role of nutritional components to improve critical illness convalescence

E. Wesselink<sup>a</sup>, W.A.G. Koekkoek<sup>b</sup>, S. Greffe<sup>c</sup>, R.F. Witkamp<sup>d</sup>, A.H.H. van Zanten<sup>b,\*</sup><sup>a</sup> Division of Human Nutrition and Health, Wageningen University, Wageningen, 6500 ZD, The Netherlands<sup>b</sup> Department of Intensive Care Medicine, University Medical Center Groningen, 3000 RB, The Netherlands<sup>c</sup> Maxon and Austri Physiology, Wageningen University, 6500 ZD, The Netherlands<sup>d</sup> Mucosa and Axonal Physiology, Wageningen University, 6500 ZD, The Netherlands

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Mitochondria

## SUMMARY

Persistent physical impairment is frequently encountered after critical illness. Recent data point towards mitochondrial dysfunction as a frequent determinant of this phenomenon. This narrative review provides a comprehensive overview of the present knowledge of mitochondrial function during and after critical illness and the role and potential (in)specific application of specific nutritional inputs to restore mitochondrial function.

Initiated target lines and decreased mitochondrial ATP production are common findings during critical illness and considered to be associated with decreased activity of muscle mitochondrial complexes in the electron transfer system.

Adequate nutrient levels are essential for mitochondrial function as several specific micronutrients play crucial roles in energy metabolism and ATP production. We have addressed the role of vitamins, zinc, iron and alpha-tocopherol, carnitine, zinc, coenzyme Q10, carnitine, creatinine, carnitine, creatine, tyrosine, creatine and leucine in mitochondrial function. If vitamins and zinc and iron are essential in the mitochondrial cell cycle while selenium, alpha-tocopherol, coenzyme Q10, carnitine, and creatinine are suggested to boost the electron transfer system function. Creatinine is involved in the fatty acid beta-oxidation. Selenium is involved in mitochondrial transport, normalizing the documented importance of several nutritional components for optimal mitochondrial function. At present, there are no studies providing direction for optimal measurement during or after critical illness although detection of these specific micronutrient deficiencies in mitochondrial dysfunction are common. Considerable knowledge between these specific micronutrients, future research should pay more attention to their potential supply to provide guidance for use in clinical practice.

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## 1. Introduction

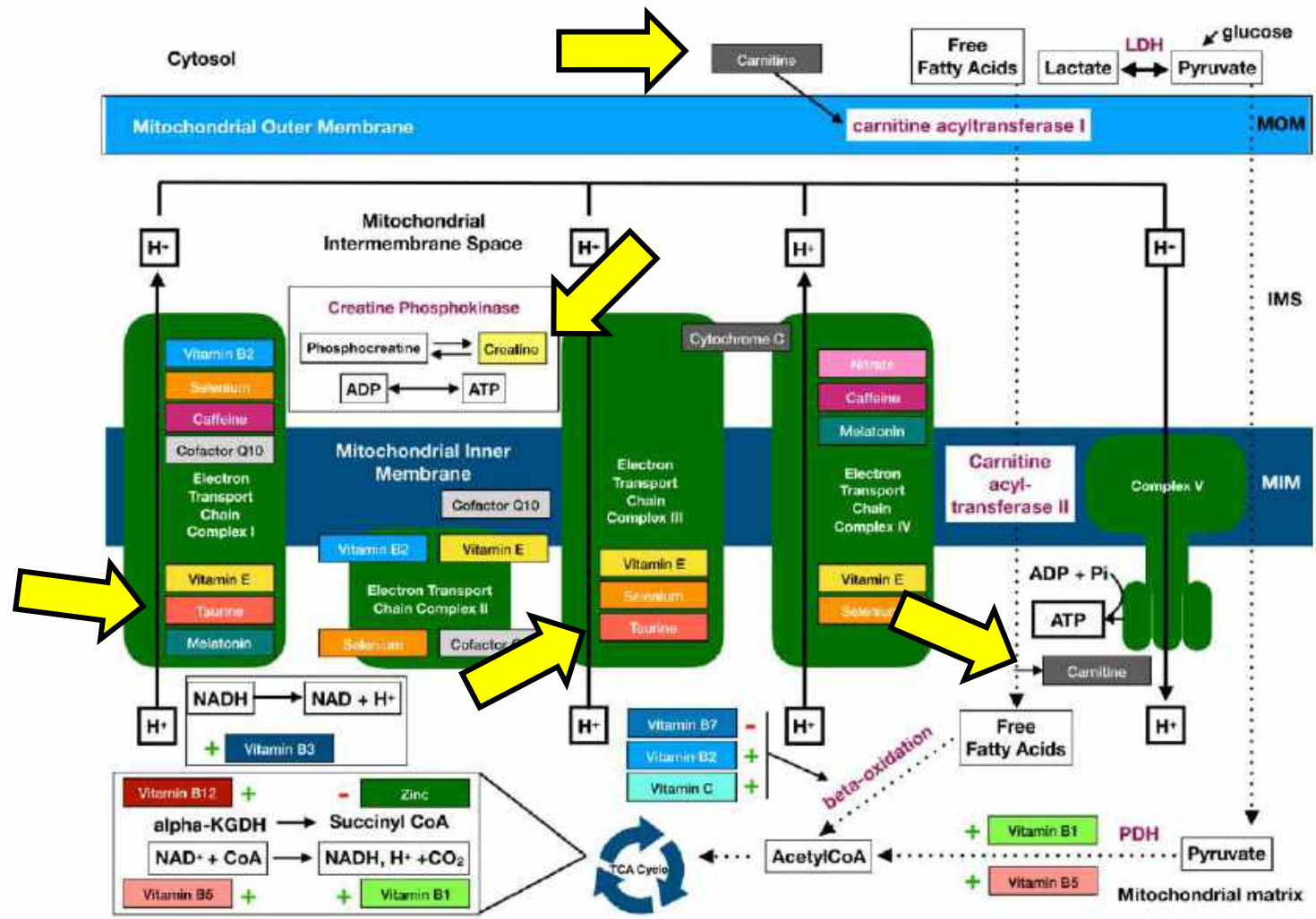
Due to improvements in clinical care and technological developments, the number of patients surviving critical illness continues to rise, since often at the expense of worse problems later in life [1]. Residual clinical issues and sensory, neurologic deficits are extremely common in long-term survivors of critical illness and mortality rates are higher compared to age-matched controls [2,3].

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Even five years after discharge from an intensive care unit (ICU), many patients suffer from impaired pulmonary function, muscle weakness and reduced ability to perform vigorous exercise [4,5]. Most of these physical limitations, many survivors complain about social isolation, sexual dysfunction, anxiety, depression and other mental health problems [6,7]. This spectrum of symptoms is known as post-intensive care syndrome [8]. As a consequence, ICU survivors are more likely to be readmitted to the hospital and ICU and demand more home care compared with non-ICU hospitalized patients [7]. This calls for further research into the aetiology, readjusting factors and possible ways for prevention or intervention of ICU syndrome.

An important cause of physical weakness is the loss of muscle mass and function during critical illness [9]. Interestingly, mitochondrial signalling pathways associated with increased muscle



E. Wesseling et al / Clinical Nutrition xxx (2018) 1–14

# L-carnitina

Review

## L-Carnitine Supplementation in Recovery after Exercise

Roger Fielding <sup>1</sup>, Linda Riede <sup>2</sup>, James P. Lugo <sup>3</sup> and Aouatef Bellamine <sup>3,\*</sup>

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Received: 22 January 2018; Accepted: 9 March 2018; Published: 13 March 2018

**Abstract:** Given its pivotal role in fatty acid oxidation and energy metabolism, L-carnitine has been investigated as ergogenic aid for enhancing exercise capacity in the healthy athletic population. Early research indicates its beneficial effects on acute physical performance, such as increased maximum oxygen consumption and higher power output. Later studies point to the positive impact of dietary supplementation with L-carnitine on the recovery process after exercise. It is demonstrated that L-carnitine alleviates muscle injury and reduces markers of cellular damage and free radical formation associated by aftermath of exercise stress. The supplementation-based increase in serum and muscle L-carnitine contents is suggested to enhance blood flow and oxygen supply to the muscle tissue via improved endothelial function thereby reducing heparin-induced cellular and biochemical disruptions. Studies in older adults further showed that L-carnitine intake can lead to increased muscle mass accompanied by a decrease in body weight and reduced physical and mental fatigue. Based on current animal studies, a role of L-carnitine in the prevention of age-associated muscle protein degradation and regulation of mitochondrial homeostasis is suggested.

**Keywords:** L-carnitine; exercise recovery; physical performance; muscle metabolism; aging

### 1. Introduction

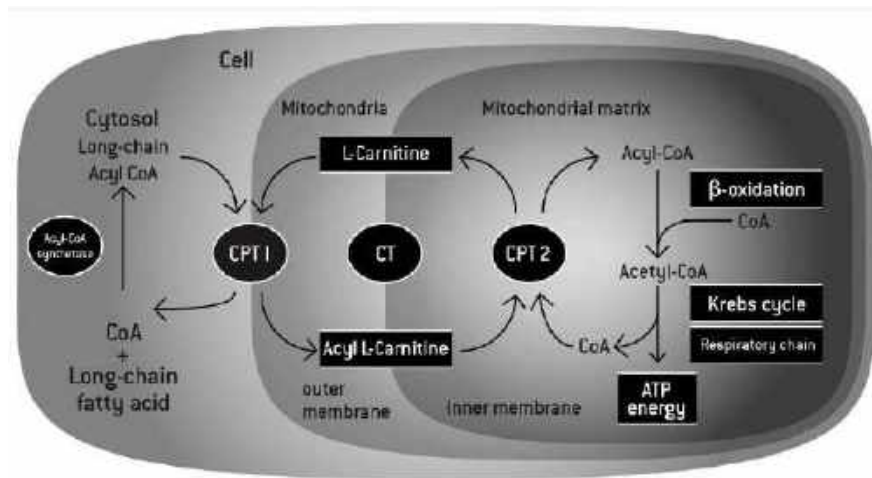
Naturally occurring, L-carnitine is a quaternary amine (3-hydroxy-4-N-trimethylaminobutyl) found in all mammalian species. After the discovery of L-carnitine in muscle extracts in 1935 [1] and its structural identification in 1927 [2], the importance of L-carnitine in fatty acid oxidation in the liver and the heart was first described by Fizz in 1969 [3]. An intracellular membrane, an impermeable to coenzyme A (CoA) enters and long-chain fatty acids, binding of L-carnitine to acetyl groups via carnitine acyltransferase is essential for the shuttle of the acetylated fatty acids into the mitochondria and for their subsequent  $\beta$ -oxidation in the matrix (Figure 1) [4]. The products of the oxidation (two-carbon molecules) are then used by the Krebs cycle to produce Adenosine triphosphate (ATP) as form of energy. L-carnitine has also been recognized for its crucial biological function in buffering the free CoA/acetyl-CoA ratio. Under conditions of stress with excess formation of acyl-CoA, transamination with L-carnitine potentially promotes the substrate movement in the Krebs cycle.

L-carnitine is synthesized endogenously in the liver, the kidney, and the brain from the essential amino acids lysine and methionine [5,6] or ingested via animal-based food products. Its synthesis is catalyzed by four sequential reactions, reviewed by Vaz et al. [7] and requires vitamins C, vitamin B<sub>6</sub>, niacin, and reduced iron as cofactors [8]. Biochemistry of L-carnitine accounts only for 25% of the daily needs [7,8]. Thus, supplementation either in the diet or as a nutritional supplement is required. At the tissue levels, the primary storage of L-carnitine is in the heart and the skeletal muscle with an estimated 95%, while much lower concentrations are found in the liver, the kidney, and the plasma [10]. It is estimated that the muscle content is about 70-fold higher than the blood plasma

### Review

# L-Carnitine Supplementation in Recovery after Exercise

Roger Fielding <sup>1</sup>, Linda Riede <sup>2</sup>, James P. Lugo <sup>3</sup> and Aouatef Bellamine <sup>3,\*</sup>



# L-carnitina

- **Alivia o dano** muscular
- **Reduz** marcadores de **dano celular** (CK e mioglobina)
- **Reduz** a formação de **radicais livres**
- **Atenua a dor** muscular
- Aumenta os **níveis séricos**
- Aumenta os níveis musculares\*
  - Provavelmente depende do conteúdo muscular prévio.
- Melhora o **fluxo sanguíneo** e o **fornecimento de O2** ao músculo (melhora endotelial)
- Aumenta o **receptor androgênico** muscular Molecules 2020, 25, 182
- **Nos mais velhos:** aumento da massa muscular, redução peso corporal e da fadiga física e mental
- **Mecanismo:** previne degradação de proteínas musculares e regulação mitocondrial

# Detalhes importantes:

## Review Carnitine in Human Muscle Bioenergetics: Can Carnitine Supplementation Improve Physical Exercise?

Antonio Gómez <sup>1</sup>, Soera Longo <sup>2</sup>, Gabriel V. Grand <sup>2</sup> and Ana M. Ciudad <sup>1,4,\*</sup>

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Academic Editor: Cesare Trafimetti and Luca Grassi



Molecules 2020, 25, 182; doi:10.3390/molecules25010182

**Abstract:** Carnitine is an amino acid derivative widely known for its involvement in the transport of long chain fatty acids into the mitochondrial matrix where fatty acid oxidation occurs. Moreover, carnitine protects the cell from acyl-CoA depletion through the generation of acylcarnitines. Circulating carnitine is mainly supplied by animal-based food products and to a lesser extent by endogenous biosynthesis in the liver and kidney. Human muscle contains high amounts of carnitine but it depends on the uptake of this compound from the blood stream, due to muscle inability to synthesize carnitine. Mitochondrial and fatty acid oxidation represents an important energy source for muscle metabolism, particularly during physical exercise. However, especially during high-intensity exercise, this process seems to be limited by the mitochondrial availability of the carnitine. Hence, fatty acid oxidation rapidly declines, increasing exercise intensity from moderate to high. Considering the important role of fatty acids in muscle bioenergetics, and the limiting effect of the carnitine on fatty acid oxidation during exercise, carnitine supplementation has been hypothesized to improve exercise performance. Under the assumption of the role of carnitine supplementation on muscle performance has not definitively been clarified. Differences in exercise intensity, timing of carnitine loading of the subject, amount of carnitine administered, route and timing of administration relative to the muscle to be fed, influence reported results. In this review, we will describe the role of carnitine in muscle energetics and the main issues that led to conflicting data on the use of carnitine as a supplement.

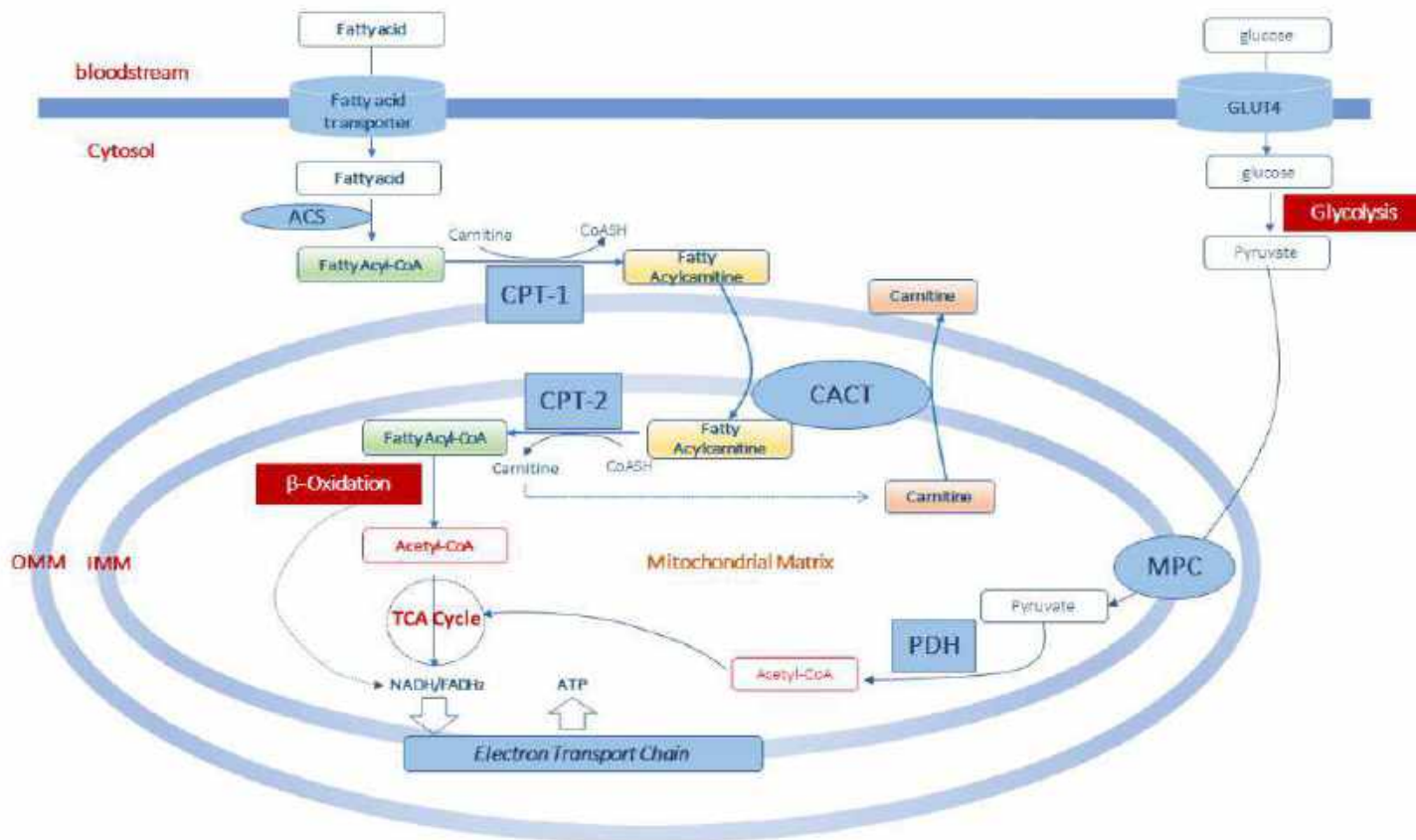
**Keywords:** carnitine; fatty acid oxidation; muscle energetics; physical exercise

### 1. Introduction

Carnitine (3-hydroxy-4-N-(trimethylammonio)butyryl-L-glutamate or L-carnitine) is a zwitterion that plays a key role in intermediary metabolism with the main function being the transport of long-chain fatty acids from the cytosol to the mitochondrial matrix where fatty acid  $\beta$ -oxidation occurs. Other established functions of carnitine are the preservation of acetylcholine integrity [1], the stimulation of a physiologic coenzyme A (CoA) acetyl-CoA entry in mitochondria, and the reduction of lactate production [2].

Carnitine is present in meat, liver oil, animal species and in several micro-organisms and plants. In the human body, carnitine is mainly found as a free form (free carnitine) and in the form of acylcarnitines, a pair of carnitine bonded to various acyl groups that are released throughout the body for a wide range of functions [3]. At rest, the skeletal muscle carnitine pool is distributed as

- **Conteúdo corporal:  $\approx 20\text{g}$**
- **Biodisponibilidade: 5-15%**
- **Limiar renal: próximo a nível plasmático usual**
- **Suplementação de “grandes doses”: quase o total é recuperado na urina**
- **Conclusão: longo período é necessário para mudanças na concentração muscular de carnitina**





## CARNITINA

A L-carnitina é encontrada predominantemente nos músculos e sintetizada endogenamente pelo nosso organismo no fígado e nos rins, a partir de aminoácidos essenciais, como a lisina, metionina e serina.

Pode ser encontrada em muitos alimentos, mas as carnes vermelhas, como carne bovina e de cordeiro, são as melhores opções para adicionar carnitina à dieta.

Funções:

- Ligada no processo de formação de energia (ATP) pois é essencial no transporte de ácidos graxos de cadeia longa para oxidação na mitocôndria
- Antioxidante

### SUPLEMENTAÇÃO

- L-carnitina
- Acetil-L-carnitina
- Propionil-L-carnitina

Dose usual – 1 g  
Dose mínima – 500 mg  
Dose máxima – 3000 mg



### PRINCIPAIS APLICAÇÕES CLÍNICAS

- Fadiga crônica
- Depressão
- Atividade física
- Doença cardiovascular
- Síndrome metabólica
- Fibromialgia

### EFEITOS ADVERSOS

• Não há evidências de efeitos colaterais descritos pela literatura

### CONTRAINDICAÇÃO

- Não há evidências

# Creatina

Sintetizada a partir de **glicina, arginina e metionina**

Tem um papel chave **no metabolismo celular**

**95% é armazenada no músculo** →  
restante em outros tecidos (coração e cérebro)

REVIEW

Open Access



# International Society of Sports Nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine

Richard B. Kreider<sup>1\*</sup>, Douglas S. Kalman<sup>2</sup>, Jose Antonio<sup>3</sup>, Tim N. Ziegenfuss<sup>4</sup>, Robert Wildman<sup>5</sup>, Rick Coffino<sup>6</sup>, Owen Li, Cardow<sup>7</sup>, Sarah M. Heine<sup>8</sup>, Anthony L. Almada<sup>9</sup> and Hector L. Lopez<sup>10</sup>

## Abstract

Creatine is one of the most popular nutritional ergogenic aids for athletes. Studies have consistently shown that creatine supplementation increases intramuscular creatine concentrations which may help support the development of improvements in high intensity exercise performance leading to greater training adaptations. In addition to athletic and exercise performance, research has shown that creatine supplementation may enhance cardiovascular recovery, injury prevention, thermoregulation, rehabilitation, and concussion and/or spinal cord reabsorption. Additionally, a number of clinical applications of creatine supplementation have been studied involving neurodegenerative diseases (e.g., muscular dystrophy, Huntington's disease), diabetes, osteoporosis, brain aging, brain and heart ischemia, adolescent depression, and pregnancy. These studies provide a large body of evidence that creatine can not only improve exercise performance but also play a role in promoting and/or reducing the severity of injury, enhancing rehabilitation from injury, and helping athletes tolerate heavy training loads. Additionally, research has confirmed a number of other body wide clinical uses of creatine supplementation. These studies demonstrate that creatine supplementation (up to 20 g/day for 5 years) is safe and well tolerated in healthy individuals and in a number of patient populations ranging from infants to the elderly. Moreover, significant health benefits may be provided by ensuring habitual low dietary creatine ingestion (e.g., 3 g/day) throughout the lifespan. The purpose of this review is to provide an update to the current literature regarding the role and safety of creatine supplementation in exercise, sport, and medicine and to update the position stand of International Society of Sports Nutrition (ISSN).

**Keywords:** Ergogenic aids, Performance enhancement, Sport nutrition, Athletes, Muscular strength, Muscle power, Clinical applications, Safety, Children, Adolescence

## Background

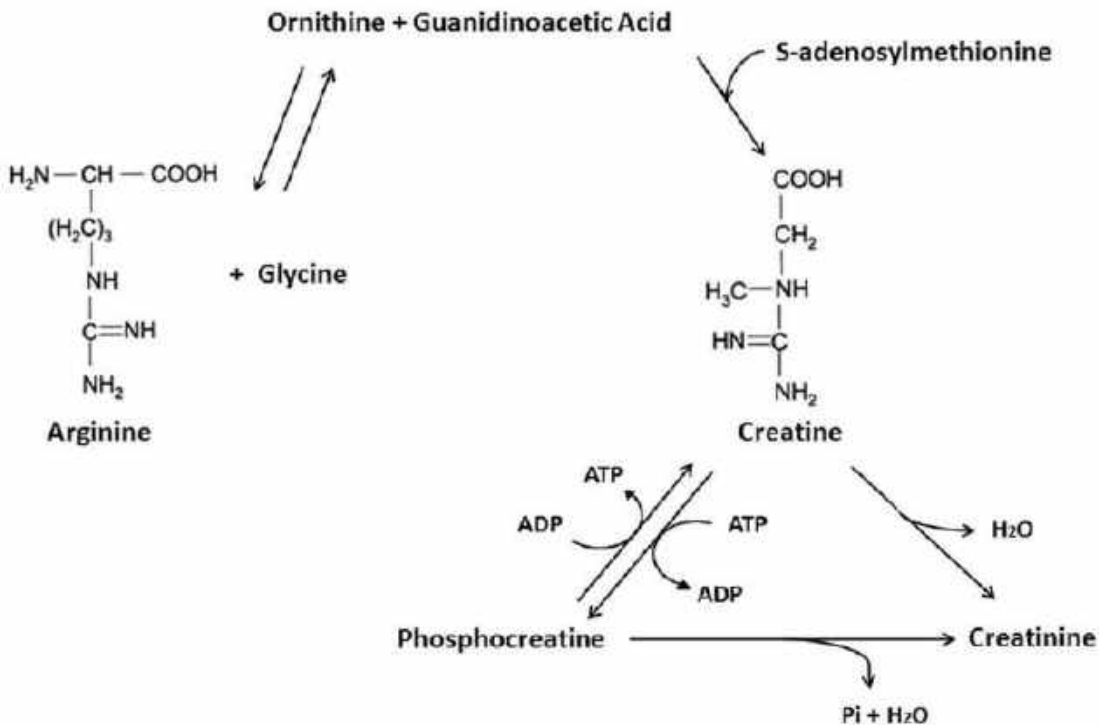
Creatine is one of the most popular nutritional ergogenic aids for athletes. Studies have consistently shown that creatine supplementation increases intramuscular creatine concentrations, can improve exercise performance, and/or improve training adaptations. Research has indicated that creatine supplementation may enhance post-exercise recovery, train prevention, thermoregulation, rehabilitation, and

rehabilitation and/or spinal cord reabsorption. A number of clinical applications of creatine supplementation have also been studied involving neurodegenerative diseases (e.g., muscular dystrophy, Huntington's disease), diabetes, osteoporosis, brain aging, brain and heart ischemia, adolescent depression, and pregnancy. The purpose of this review is to provide an update to the current literature regarding the role and safety of creatine supplementation in exercise, sport, and medicine and to update the position stand of International Society of Sports Nutrition (ISSN) related to creatine supplementation.

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<sup>1</sup>Richard B. Kreider, Department of Health, Behavior, and Society, Johns Hopkins University, College Park, MD, 20742-5241, USA  
Full list of author information is available at the end of the article



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Review

## Role of Creatine Supplementation in Conditions Involving Mitochondrial Dysfunction: A Narrative Review

Robert Percy Marshall <sup>1,\*</sup>, Jan-Niklas Droste <sup>1</sup>, Jürgen Giessing <sup>2</sup> and Richard B. Kreider <sup>3</sup>

Nutrients 2022, 14, 529



“A suplementação de **creatina** pode ter um papel **na melhoria da bioenergética celular** em várias doenças relacionadas à **disfunção mitocondrial, condições isquêmicas e patologia de lesão**, podendo **fornecer benefícios terapêuticos**”

Review > J Int Soc Sports Nutr. 2023 Dec;20(1):2204071. doi: 10.1080/15502783.2023.2204071.

## **Creatine supplementation and endurance performance: surges and sprints to win the race**

Scott C Forbes<sup>1</sup>, Darren G Candow<sup>2</sup>, Joao Henrique Falk Neto<sup>3</sup>, Michael D Kennedy<sup>3</sup>, Jennifer L Forbes<sup>1</sup>, Marco Machado<sup>4</sup>, Erik Bustillo<sup>5</sup>, Jose Gomez-Lopez<sup>6</sup>, Andres Zapata<sup>7</sup>, Jose Antonio<sup>8</sup>

**“Dada a capacidade da creatina de umentar a capacidade de trabalho anaeróbico, a suplementação pode ser benéfica para esportes, como esqui cross-country, mountain bike, ciclismo, triatlo e para eventos de curta duração em que os surtos finais são críticos para desempenho, como remo, caiaque e ciclismo de pista”**

- Melhora o desempenho nos exercícios
- Melhora a reabilitação de lesões
- Pode melhorar a recuperação pós-exercício, prevenir ou reduzir gravidade de lesões
- Ajuda atletas a tolerar cargas pesadas de treinamento
- Melhora a termorregulação
- Útil na reabilitação e concussão e/ou neuro proteção da medula espinal
- Útil em doenças neurodegenerativas (ex.: distrofia muscular, Parkinson, doença de Huntington)
- Diabetes
- Osteoartrite
- Fibromialgia
- Gestação, envelhecimento, isquemia cerebral e cardíaca, depressão na adolescência.

REVIEW

Open Access



## International Society of Sports Nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine

Richard B. Kreider<sup>1†</sup>, Douglas S. Kalman<sup>2</sup>, Jose Antonio<sup>3</sup>, Tim N. Ziegenfuss<sup>4</sup>, Robert Wilmore<sup>5</sup>, Rick Collins<sup>6</sup>, Daniel G. Candow<sup>7</sup>, Susan M. Heine<sup>8</sup>, Anthony L. Almada<sup>9</sup> and Hector L. Lopez<sup>10\*</sup>

### Abstract

Creatine is one of the most popular nutritional ergogenic aids for athletes. Studies have consistently shown that creatine supplementation increases intramuscular creatine concentrations which may help explain the observed improvements in high intensity exercise performance leading to greater training adaptations. In addition to effects on exercise performance, research has shown that creatine supplementation may increase antioxidant enzymes, injury prevention, thermoregulation, rehydration, and concussion and/or spinal cord neuroprotection. Additionally, a number of clinical applications of creatine supplementation have been studied involving neurodegenerative diseases (e.g., muscle atrophy, Alzheimer's, Huntington's, stroke, diabetes), osteoarthritis, osteomyelitis, aging, brain and heart ischemia, adolescent depression, and pregnancy. These studies provide a large body of evidence that creatine can not only improve exercise performance but can play a role in preventing and/or reducing the severity of injury, enhancing rehabilitation from injury, and helping athletes tolerate heavy training loads. Additionally, researchers have identified a number of potentially beneficial clinical uses of creatine supplementation. These studies show that creatine is a safe supplement (up to 30 g/day for 5 years) in male and well-hydrated in healthy individuals and in a number of patient populations ranging from infants to the elderly. Moreover, significant health benefits may be provided by ensuring adequate daily energy intake, regular sleep, and sleep stress about the disease. The purpose of this review is to provide an update to the current literature regarding the role and safety of creatine supplementation in exercise, sport, and medicine and to update the position stand of International Society of Sports Nutrition (ISSN).

**Keywords:** Ergogenic aids, Performance enhancement, Sport nutrition, Athletes, Muscular strength, Muscle power, Clinical applications, Safety, Children, Adolescence

### Background

Creatine is one of the most popular nutritional ergogenic aids for athletes. Studies have consistently shown that creatine supplementation increases intramuscular creatine concentrations, can improve exercise performance, and/or improve training adaptations. Research has indicated that creatine supplementation may enhance post-exercise recovery, injury prevention, thermoregulation, rehabilitation, and

rehydration and/or spinal cord neuroprotection. A number of clinical applications of creatine supplementation have also been studied involving neurodegenerative diseases (e.g., muscular atrophy, Parkinson's, Huntington's disease, diabetes, osteoarthritis, osteomyelitis, aging, brain and heart ischemia, adolescent depression, and pregnancy). The purpose of this review is to provide an update to the current literature regarding the role and safety of creatine supplementation in exercise, sport, and medicine and to update the position stand of International Society of Sports Nutrition (ISSN) related to creatine supplementation.

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- **Suplementação** de até 30g por dia, por 5 anos, **é segura e bem tolerada**, em indivíduos saudáveis e em pacientes (de crianças a idosos)
- **Efeitos significativos** podem ser alcançados pela ingestão de doses como 3g por dia, ao longo da vida.

Kreider et al. *Journal of the International Society of Sports Nutrition* (2017) 14:18

REVIEW

Open Access



## International Society of Sports Nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine

Richard B. Kreider<sup>1†</sup>, Douglas S. Kalman<sup>2</sup>, Jose Antonio<sup>3</sup>, Tim N. Ziegenfuss<sup>4</sup>, Robert Wildman<sup>5</sup>, Rick Collins<sup>6</sup>, Damien G. Candow<sup>7</sup>, Susan M. Iliesiu<sup>8</sup>, Anthony L. Almada<sup>9</sup> and Hector L. Lopez<sup>10\*</sup>

### Abstract

Creatine is one of the most popular nutritional ergogenic aids for athletes. Studies have consistently shown that creatine supplementation increases intramuscular creatine concentrations which may help explain the observed improvements in high intensity muscle performance leading to greater training adaptations. In addition to athletic and exercise applications, research has shown that creatine supplementation may be helpful in various disease states, injury prevention, thermoregulation, rehabilitation, and concussion and/or spinal cord neuroprotection. Additionally, a number of clinical applications of creatine supplementation have been studied involving neurodegenerative diseases (e.g., muscular dystrophy, Parkinson's, Huntington's, amyotrophic lateral sclerosis, schizophrenia, aging, brain and spinal cord trauma, and breast depression, and pregnancy). These studies provide a large body of evidence that creatine can not only improve exercise performance but can play a role in preventing and/or reducing the severity of injury enhancing rehabilitation from injury, and helping athletes obtain faster training gains. Additionally, research has also identified a number of potentially beneficial clinical uses of creatine supplementation. These studies show that short and long-term supplementation (up to 30 g/day for 5 years) is safe and well-tolerated in healthy individuals and in a number of patient populations ranging from infants to the elderly. Moreover, significant health benefits may be produced by ensuring minimal low-dose creatine ingestion (e.g., 3 g/day) throughout the lifespan. The purpose of this review is to provide an update to the current literature regarding the role and safety of creatine supplementation in exercise, sport and medicine and to update the position stand of International Society of Sports Nutrition (ISSN).

**Keywords:** Ergogenic aids, Performance enhancement, Sport nutrition, Athletes, Muscular strength, Muscle power, Clinical applications, Safety, Children, Adolescence

### Background

Creatine is one of the most popular nutritional ergogenic aids for athletes. Studies have consistently shown that creatine supplementation increases intramuscular creatine concentrations, can improve exercise performance, and/or improve training adaptations. Research has indicated that creatine supplementation may enhance post-exercise recovery, injury prevention, thermoregulation, rehabilitation and

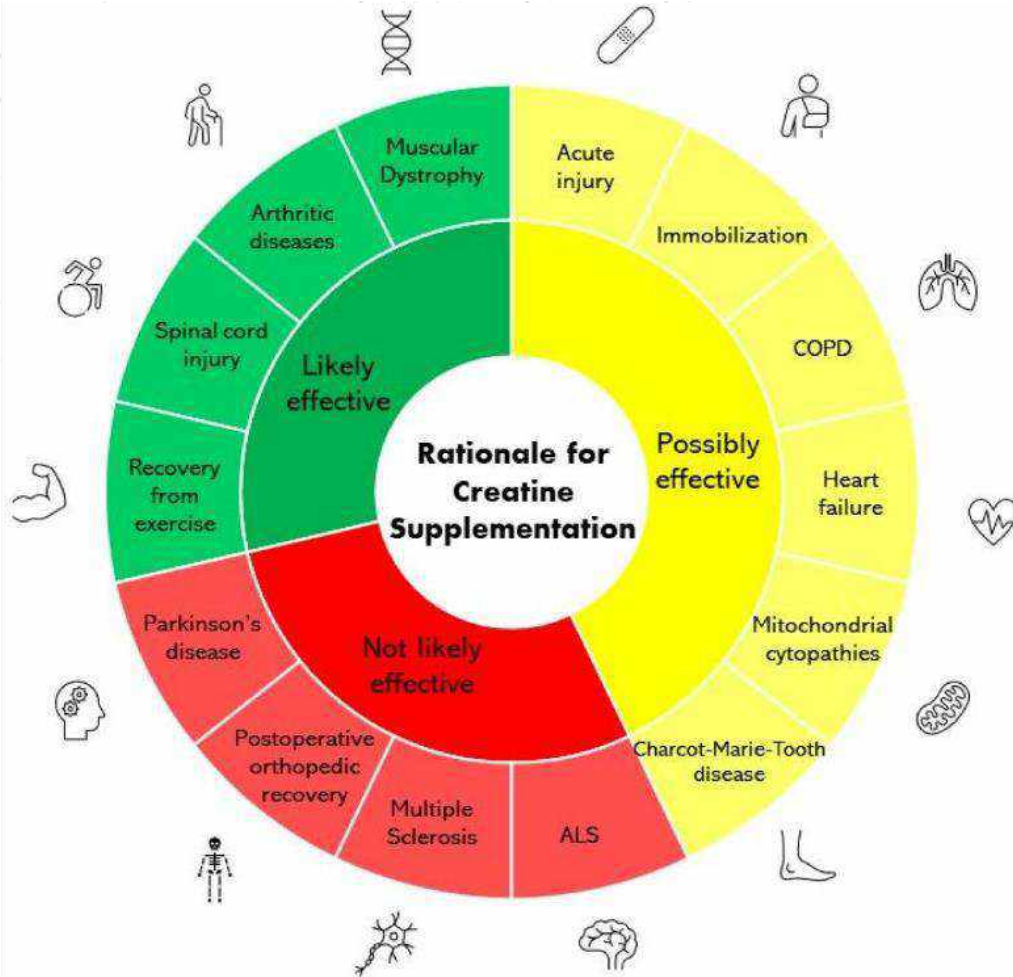
concession and/or spinal cord neuroprotection. A number of clinical applications of creatine supplementation have also been studied including neurodegenerative diseases (e.g., muscular dystrophy, Parkinson's, Huntington's, amyotrophic lateral sclerosis, schizophrenia, aging, brain and spinal cord trauma, and breast depression, and pregnancy). The purpose of this review is to provide an update to the current literature regarding the role and safety of creatine supplementation in exercise, sport, and medicine and to update the position stand of International Society of Sports Nutrition (ISSN) related to creatine supplementation.

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# Visão geral dos usos da suplementação de creatina

## CREATINA

A creatina desempenha um papel integral no metabolismo celular.

Cerca de 95% da creatina é armazenada no músculo, com a quantidade restante encontrada em outros tecidos como coração e cérebro.

Sintetizada a partir de glicina, arginina e metionina.

- O principal papel: se liga ao fosfato inorgânico (Pi) para formar fosfocreatina (PCr) e, assim, serve como uma fonte fosfato para conversão de ADP em ATP
- Níveis aumentados de creatina melhoram o desempenho do exercício de alta intensidade e as adaptações do treinamento físico

### SUPLEMENTAÇÃO

Creatina monohidratada

Dose mínima: 3 g  
Dose máxima: 30 g

Dose usual: 5 g



### PRINCIPAIS APLICAÇÕES CLÍNICAS

- Diabetes
- Hipertrofia, Força Muscular e Sarcopenia
- Doenças neurodegenerativas
- Fibromialgia
- Depressão
- Performance física

### EFEITOS ADVERSOS

- O uso desse produto pode provocar diarreia, dor de estômago e distensão abdominal.

### CONTRAINDICAÇÃO

- Pode prejudicar alguns pacientes com transtorno bipolar, mas auxilia a maioria

\*DOSES USUAIS PARA ADULTOS

# Taurina

```
graph TD; Taurina --> Citoprotetora; Taurina --> Fase2[Fase 2 de detoxificação];
```

**Taurina**

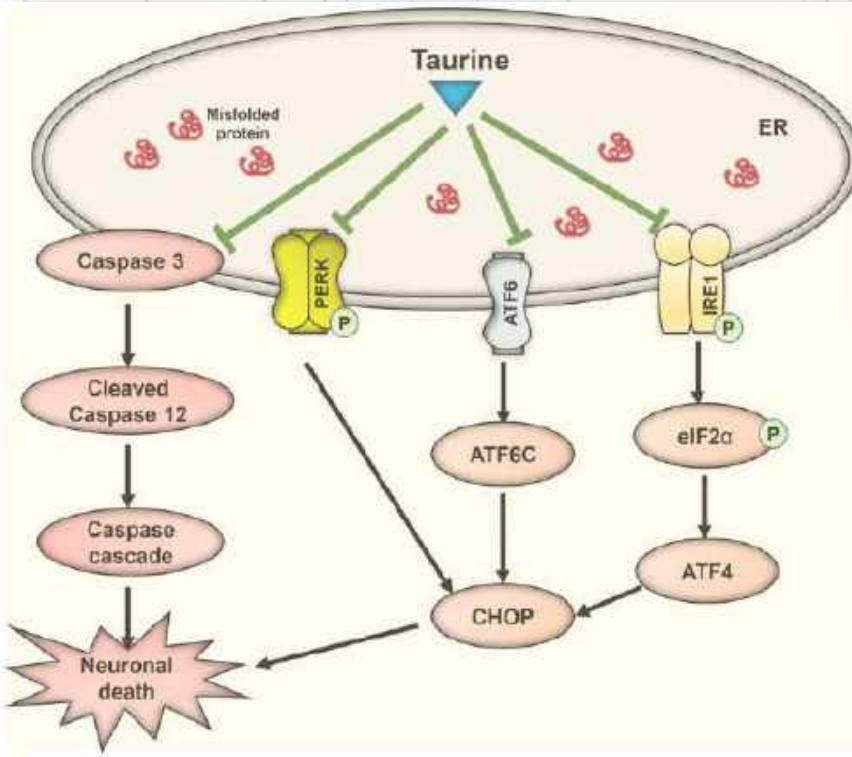
**Citoprotetora**

**Fase 2 de  
detoxificação**

# Situações de alta demanda / necessidade de L-taurina

**Ansiedade**

**Neuro proteção**



Review article

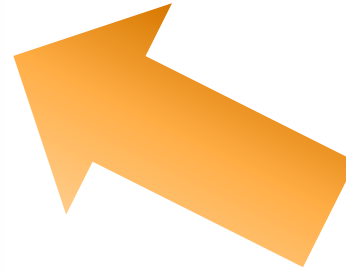
## Taurine and its analogs in neurological disorders: Focus on therapeutic potential and molecular mechanisms

Md. Jakaria<sup>a</sup>, Shofiqul Azam<sup>a</sup>, Md. Ezazul Haque<sup>a</sup>, Song-Hee Jo<sup>b</sup>, Md. Sahab Uddin<sup>b</sup>, In-Su Kim<sup>a,c</sup>, Dong-Kug Choi<sup>a,c,\*</sup>

<sup>a</sup>Department of Applied Life Sciences and Integrated Bioscience, Graduate School, Konkuk University, Chungju, South Korea

<sup>b</sup>Department of Pharmacy, Southeast University, Dhaka, Bangladesh

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# Taurina é essencial a função mitocondrial normal

Hansen et al. *Journal of Biomedical Science* 2010, **17**(Suppl 1):S23

Hansen et al. *Journal of Biomedical Science* 2010, **17**(Suppl 1):S23  
<http://www.jbiomedsci.com/content/17/S1/S23>



The cost of publication in *Journal of Biomedical Science*  
is borne by the National Science Council, Taiwan



JOURNAL OF  
BIOMEDICAL SCIENCE

REVIEW

Open Access

## A role for taurine in mitochondrial function

Svend Heime Hansen<sup>1\*</sup>, Mogens Larsen Andersen<sup>2</sup>, Claus Cornett<sup>3</sup>, Robert Gradinaru<sup>4</sup>, Niels Grunnet<sup>5</sup>

From 17<sup>th</sup> International Meeting of Taurine  
Fort Lauderdale, FL, USA, 14-19 December 2009

### Abstract

The mitochondrial pH gradient across the inner-membrane is stabilised by buffering of the matrix. A low-molecular mass buffer compound has to be localised in the matrix to maintain its alkaline pH value. Taurine is found ubiquitously in animal cells with concentrations in the millimolar range and its pKa value is determined to 9.0 (25°C) and 8.6 (37°C), respectively. Localisation of such a low-molecular buffer in the mitochondrial matrix, transforms the matrix into a biochemical reaction chamber for the important matrix-localised enzyme systems. Three acyl-CoA dehydrogenase enzymes, which are pivotal for beta-oxidation of fatty acids, are demonstrated to have optimal activity in a taurine buffer. By application of the model presented, taurine depletion caused by hyperglycemia could provide a link between mitochondrial dysfunction and diabetes.



CENTRAL  
- nutrition -

## Prolonging healthy aging: Longevity vitamins and proteins

Bruce N. Ames<sup>\*1</sup>

Edited by Cynthia Kenyon, Calico Labs, San Francisco, CA, and approved September 13, 2018; received for review May 30, 2018

It is proposed that proteins/enzymes be classified into two classes according to their essentiality for immediate survival/reproduction and their function in long-term health: that is, survival proteins versus longevity proteins. As proposed by the triage theory, a modest deficiency of one of the nutrients/cofactors triggers a built-in rationing mechanism that favors the proteins needed for immediate survival and reproduction (survival proteins) while sacrificing those needed to protect against future damage (longevity proteins). Impairment of the function of longevity proteins results in an insidious acceleration of the risk of diseases associated with aging. I also propose that nutrients required for the function of longevity proteins constitute a class of vitamins that are here named "longevity vitamins." I suggest that many such nutrients play a dual role for both survival and longevity. The evidence for classifying taurine as a conditional vitamin, and the following 10 compounds as putative longevity vitamins, is reviewed: the fungal antioxidant ergothioneine; the bacterial metabolites pyrroloquinoline quinone (PQQ) and queuine; and the plant antioxidant carotenoids lutein, zeaxanthin, lycopene,  $\alpha$ - and  $\beta$ -carotene,  $\beta$ -cryptoxanthin, and the marine carotenoid astaxanthin. Because nutrient deficiencies are highly prevalent in the United States (and elsewhere), appropriate supplementation and/or an improved diet could reduce much of the consequent risk of chronic disease and premature aging.

vitamins | essential minerals | aging | nutrition

I propose that an optimal level of many of the known 30 vitamins and essential minerals/elements (VME), plus that of 11 new putative vitamins described herein, is necessary for promoting healthy aging. The "triage theory" (1) had previously introduced the concept that proteins/enzymes that are sacrificed on a VME shortage are necessary for supporting long-term health. This insight is being broadened here to classify also many VME as necessary for supporting long-term health. I present evidence that the deficiency of many VME specifically increases the risk of future disease

adverse health effects. They include vitamins A, B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, B<sub>12</sub>, biotin, C, choline, D, E, folic acid, K, niacin, pantothenate, and minerals/elements calcium, chloride, chromium, cobalt, copper, iodine, iron, manganese, magnesium, molybdenum, phosphorus, potassium, selenium, sodium, sulfur, and zinc. Some additional important nutrients, the marine omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) and xanthopterin (2) are discussed here, although they are not known as vitamins. Nine essential dietary amino acids are also important for the synthesis of proteins and hormones (2) but

"Um ser humano de 70kg contém cerca de 70g de taurina"

"Taurina é particularmente importante na mitocôndria"

Proc Natl Acad Sci U S A. 2018 Oct 23;115(43):10836-10844





# Fontes de Taurina

A maior parte da taurina vem da dieta, principalmente de:

- Peixes e frutos do mar**
- Algas marinhas**
- Ovos**
- Carne escura da aves**

# The Beneficial Effects of Taurine to Counteract Sarcopenia

Special Issue for *Current Protein and Peptide Science*



REVIEW ARTICLE

Current Protein and Peptide Science 2018, 19, 673-680

## The Beneficial Effects of Taurine to Counteract Sarcopenia

Bianca Marie Scicchitano\* and Gigliola Sica

*Istituto di Biologia ed Embriologia, Università Cattolica del Sacro Cuore, Fondazione Policlinico Universitario Agostino Gemelli, Largo Francesco Pio 1, 00168, Roma, Italy*

### ARTICLE HISTORY

Received 20/07/2017  
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**Keywords:** Taurine, sarcopenia, nutrition, amino acids, oxidative stress, inflammation, protein metabolism.

### 1. INTRODUCTION

Ageing is an inevitable and complex biological process characterized by a gradual decline in the physiological and biochemical functions of the organism system, resulting in increasing risk of disability and loss of independence [1, 2]. During aging, several morphofunctional changes occur in skeletal muscle, such as the generalized loss of muscle mass, reduced muscle size, and the progressive reduction in muscle strength, leading to a pathological condition known as sarcopenia [3, 4] [9a, 4].

This progressive age-related muscle wasting process is associated with an increased prevalence of falls, a greater incidence of disease and the loss of functional independence [4-6]. Sarcopenia might also involve intramuscular fat accumulation, fibrosis, chronic inflammation, and a decreased ability of skeletal cells to contract and proliferate following injury, thus leading to impaired muscle regeneration [7, 8]. While there are many possible causes for the age-related decline in skeletal mass in man, it is generally accepted that changes in the regulation of skeletal muscle protein metabolism are responsible for the negative protein balance and the

Abstract: Ageing is a multifactorial process characterized by several factors including low-grade inflammation, increased oxidative stress and reduced regenerative capacity, which ultimately lead to alterations in muscle functional properties of skeletal muscle, thus promoting sarcopenia. This condition is characterized by a gradual loss of muscle mass due to an imbalance between protein synthesis and degradation, thereby resulting in functional decline and disability. The development of specific therapeutic approaches able to block or reverse this condition may represent an achievable goal for the prevention of a healthy aging among elderly people. It is well established that changes in the quantity and the quality of dietary proteins, as well as the intake of specific amino acids, are able to counteract some of the physiological processes related to the progression of this loss of muscle mass, and may have beneficial effects in improving the metabolic response of muscle in the elderly. Taurine is a non-essential amino acid essential to life; concentration in skeletal muscle mass and particularly in skeletal muscle where it is involved in the modulation of several cellular processes and in the control of apoptosis and where it also acts as an antioxidant and anti-inflammatory factor. The aim of this review is to summarize the pleiotropic effects of taurine on specific muscle targets used to discuss its role in regulating signaling pathways involved in the maintenance of muscle mass in man. We also highlight the potential use of taurine as a therapeutic molecule for the amelioration of skeletal muscle function and performance severely compromised during aging.

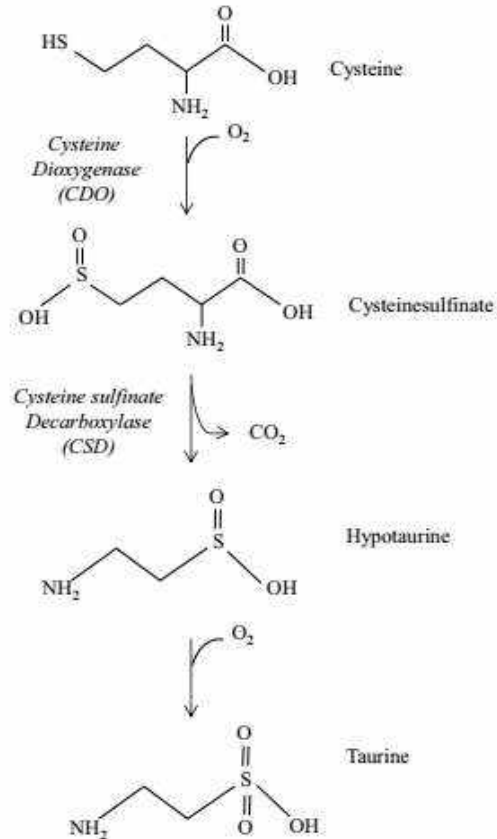


Fig. (1). Schematic representation of cellular processes involved in the onset of sarcopenia. During aging multifactorial events such as increased levels of intracellular  $Ca^{2+}$ , mitochondrial dysfunction, protein oxidation, oxidative stress and inflammation lead to the onset of sarcopenia.

the result of an alteration between protein synthesis and breakdown rates [9, 10]. Protein balance is regulated by many factors that are each susceptible to change during the

Current Protein & Peptide Science

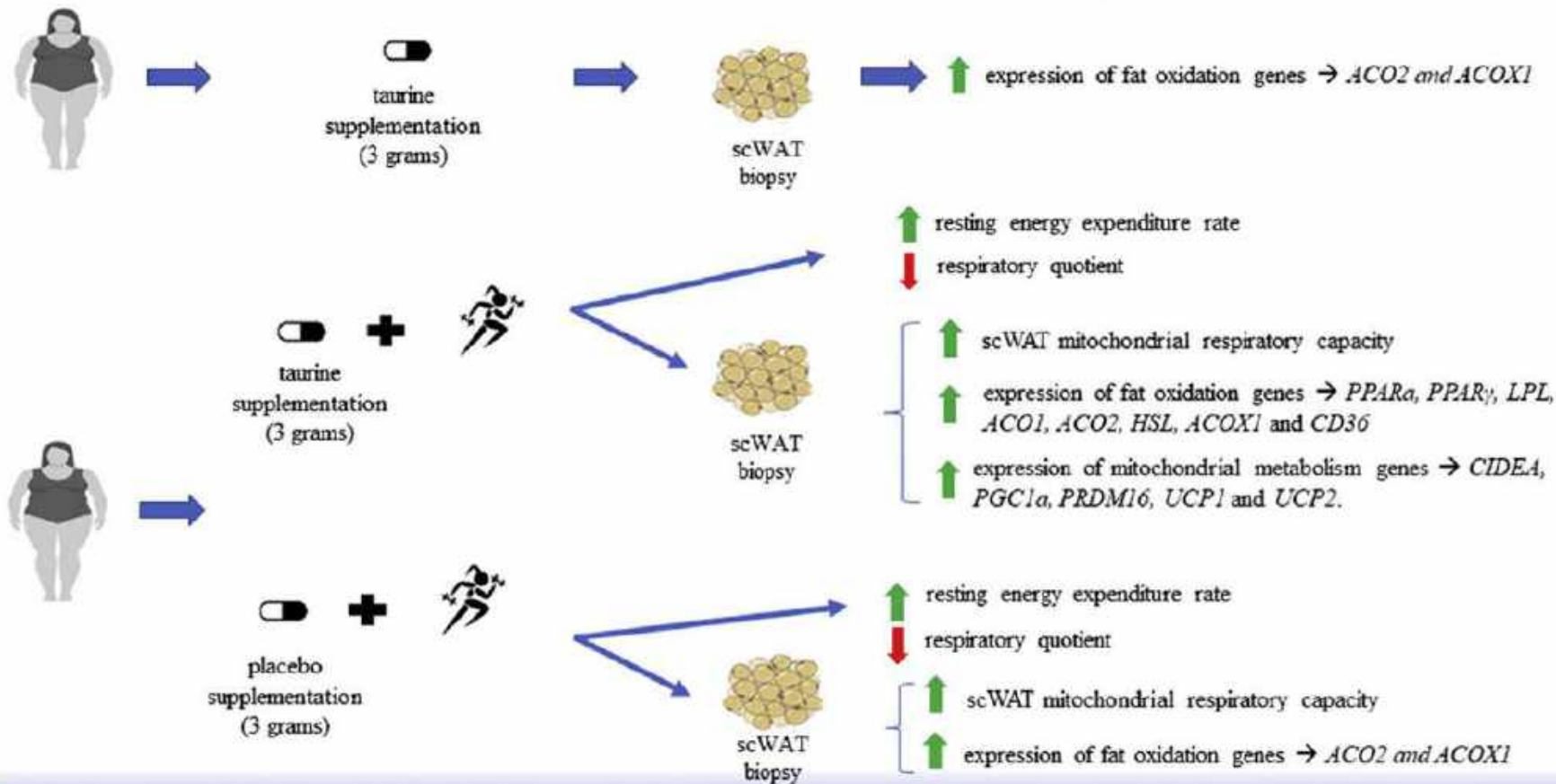
### Metabolic pathway of taurine synthesis



# Taurina...

- ...tem feitos pleiotrópicos em **alvos musculares** específicos
- ... regula **rotas de sinalização envolvidas na manutenção muscular**
- Taurina **pode ser usada para melhora da função muscular e da performance**, comprometidas, por exemplo, pelo envelhecimento

## 8 weeks of taurine/placebo supplementation associated or not with exercise in obese women



ORIGINAL ARTICLE | VOLUME 40, ISSUE 4, P2180-2187, APRIL 2021

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## Taurine supplementation associated with exercise increases mitochondrial activity and fatty acid oxidation gene expression in the subcutaneous white adipose tissue of obese women

Flavia Giolo De Carvalho • Camila Fernanda Cunha Brandao • Gabriela Batitucci • ...

Marcia Varella Morandi Junqueira-Franco • Julio Sergio Marchini • Ellen Cristini de Freitas

[Show all authors](#)

Published: October 05, 2020 • DOI: <https://doi.org/10.1016/j.clnu.2020.09.044>



**Suplementação de taurina com exercício melhorou o metabolismo lipídico através da modulação de genes relacionados a atividade mitocondrial e a oxidação de gorduras, sugerindo um efeito “amarronzador” do tecido adiposo subcutâneo branco de mulheres obesas”**

# Taurina no exercício físico



## Efeitos da suplementação de taurina no exercício físico

Effects of taurine supplementation on physical exercise

Rocha, Gustavo Pedrosa

Ribeiro, Carlos Alberto Fomes

taurina; via aeróbia; via anaeróbia; suplementação; exercício físico; taurine; aerobic performance; anaerobic performance; supplementation; physical exercise

18-Jun-2018

Efeitos da suplementação de taurina no exercício físico

FMUC

- O principal efeito ergogênico observado no exercício aeróbio está centrado no aumento da capacidade cardiorrespiratória.
- Na atividade anaeróbia, teve como principal efeito a melhoria no dano muscular

## **TAURINA**

A taurina é um aminoácido que contém enxofre e está presente em altas concentrações no plasma e em muitos tecidos.

Possui propriedades citoprotetoras devido suas ações de destoxificação, especialmente na fase II e nas reações de conjugação dos ácidos biliares.

### Funções:

- Regulação da homeostase da glicose
- Modulação do cálcio
- Atividade antioxidante
- Estabilização das membranas;
- Reprodução e imunidade
- Restauração da função dos receptores do ácido  $\gamma$ -aminobutírico (GABA)
- Redução da neuroinflamação;
- Redução do estresse oxidativo
- Aumento da biogênese mitocondrial e da neurogênese

### SUPLEMENTAÇÃO

L-Taurina •

Dose mínima: 250 mg •  
Dose máxima: 5.000 mg •

Dose usual v.o: 500 mg/dia •

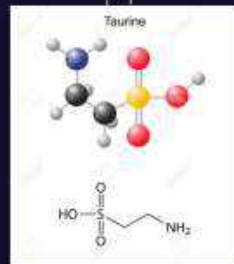
Dose usual sublingual: 50-75mg - várias vezes ao dia

Atletas: 1-3 g/dia, 1-3 h antes do treino

### EFEITOS ADVERSOS

Não há evidências de efeitos colaterais descritos pela literatura

**\*DOSES USUAIS PARA ADULTOS**



### PRINCIPAIS APLICAÇÕES CLÍNICAS

- Destoxificação
- Antioxidante
- Anti-inflamatório
- Saúde mitocondrial
- Cardioproteção
- Neuroproteção
- Imunoproteção
- Proteção ocular (retinopatia)
- Recurso ergogênico

### CONTRAINDICAÇÃO

- Não há evidências

# HMB

**hidroxi-beta-metil-butirato**





- **Suplementação de HMB leva a:**
- **Aumento da massa livre de gordura**
- **Redução da massa gorda**
- **Os efeitos variam conforme a população e a faixa etária, e tipo de atividade física.**

- Jakubowski, J., Nunes, E., Teixeira, F., Vescio, V., Morton, R., Banfield, L., & Phillips, S. (2020). Supplementation with the Leucine Metabolite  $\beta$ -hydroxy- $\beta$ -methylbutyrate (HMB) does not Improve Resistance Exercise-Induced Changes in Body Composition or Strength in Young Subjects: A Systematic Review and Meta-Analysis. *Nutrients*, 12.
- Kaczka, P., Michalczyk, M., Jastrząb, R., Gawelczyk, M., & Kubicka, K. (2019). Mechanism of Action and the Effect of Beta-Hydroxy-Beta-Methylbutyrate (HMB) Supplementation on Different Types of Physical Performance - A Systematic Review. *Journal of Human Kinetics*, 68, 211 - 222.
- Durkalec-Michalski, K., Jeszka, J., & Podgórski, T. (2017). The Effect of a 12-Week Beta-hydroxy-beta-methylbutyrate (HMB) Supplementation on Highly-Trained Combat Sports Athletes: A Randomised, Double-Blind, Placebo-Controlled Crossover Study. *Nutrients*, 9.

# L-tirosina

Article  
**Tyrosine Is a Booster of Leucine-Induced Muscle Anabolic Response**

Kotaro Tamura <sup>1,†</sup>, Hiroyuki Kitazawa <sup>1</sup>, Satoshi Sugita <sup>2</sup>, Kohjiro Hashizume <sup>1</sup>, Masaruji Iwashita <sup>1</sup>, Takashi Iibigami <sup>2</sup>, Yoshitaka Minegishi <sup>1,3,\*</sup>, Akira Shinozuyodome <sup>2</sup> and Noriyasu Ota <sup>1,§</sup>

<sup>1</sup> Biological Science Research, Neo Corporation, 568-1 Akihara, 1-1 Chiba-ku, Chiba City, Chiba 262-0492, Japan; hiroyuki.kitazawa@neo-corp.co.jp (H.K.); akira.shinozuyodome@neo-corp.co.jp (A.S.); masaruji.iwashita@neo-corp.co.jp (M.I.); kohjiro.hashizume@neo-corp.co.jp (K.H.); takashi.iibigami@neo-corp.co.jp (T.I.); yoshitaka.minegishi@neo-corp.co.jp (Y.M.); noriyasu.ota@neo-corp.co.jp (N.O.)

**Abstract:** Leucine (Leu), an essential amino acid, is known to stimulate protein synthesis in the skeletal muscle via mTORC1 activation. However, the intrinsic contribution of other amino acids to Leu-mediated activation of mTORC1 signaling remains unexplored. This study aimed to identify amino acids that can promote mTORC1 activity in combination with Leu and to assess the effectiveness of these amino acids in combination with Leu. We found that tyrosine (Tyr) enhanced Leu-induced phosphorylation of S6 kinase (S6K), an indicator of mTORC1 activity, although it exerted no such effect individually. This booster effect was observed in C2C12 cells isolated from muscle, and the skeletal muscles of mice orally administered the amino acids. To explore the molecular mechanism underlying this Tyr-mediated booster effect, the expression of the intracellular Leu sensors, Sestrin1 and 2, was suppressed, and the cells were treated with Leu and Tyr. The suppression modified Tyr alone to induce S6K phosphorylation and enhanced the booster effect, suggesting that Tyr possibly contributes to mTORC1 activation when Sestrin GAP activity is low (i.e., mTORC1 is dissociated through Sestrin knockdown or the limiting of Sestrin to Leu cellularity). These results indicate that Tyr is a key regulator of Leu-mediated protein synthesis.

**Keywords:** amino acids; mTORC1; muscle; tyrosine; Sestrin1/2

**1. Introduction**

Skeletal muscle mass is maintained through a balance between protein synthesis and degradation. Nutritional supplementation with proteins or amino acids activates anabolic responses in the skeletal muscle and may be important for counteracting muscle loss due to aging, sarcopenia, or frailty [1–3]. The intracellular signaling mechanism regulating muscle protein synthesis (MPS) is controlled by the activation of the mammalian target of rapamycin complex 1 (mTORC1), which directly stimulates the phosphorylation of S6 kinase (S6K) and endogenous translation initiation factor 4E-binding protein (4E-BP). Changes in the phosphorylation state of these key proteins affect mRNA translation initiation and elongation, thereby regulating MPS [4]. Essential amino acid (EAA) supplementation effectively stimulates MPS; however, non-essential amino acids (NEAA) are ineffective even at significant, high doses [4–6]. Among EAAs, leucine (Leu) has been shown to be particularly important for MPS, as it is the only stimulator of mTORC1 signaling identified in muscle cells over the physiological range of amino acid levels in blood [6]. The amount of Leu in ingested proteins or EAA mixtures determines the extent of the MPS response at rest and after exercise [7–11]. The amino acid composition of whey protein is considered to be suitable for stimulating MPS, owing to its high Leu content and absorbability [12,13]. Thus, Leu is widely accepted as being indispensable for stimulating mTORC1 signaling. Recently, the mechanism underlying Leu-mediated mTORC1 activation was elucidated using HEK293T cells [14,15]. In these studies, mTORC1 regulation by amino acids was found



Citation: Tamura, K.; Kitazawa, H.; Sugita, S.; Hashizume, K.; Iwashita, M.; Iibigami, T.; Minegishi, Y.; Shinozuyodome, A.; Ota, N. Tyrosine Is a Booster of Leucine-Induced Muscle Anabolic Response. *Nutrients* **2024**, *16*, 84. <https://doi.org/10.3390/nu16010084>

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“Descobrimos que a tirosina aumentou a fosforilação induzida por Leu da quinase S6, um indicador da atividade do mTORC1, embora não tenha exercido tal efeito individualmente”



Article

## Tyrosine Is a Booster of Leucine-Induced Muscle Anabolic Response

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**Abstract:** Leucine (Leu), an essential amino acid, is known to stimulate protein synthesis in the skeletal muscle via mTORC1 signaling. However, the intrinsic contribution of other amino acids to Leu-mediated activation of mTORC1 signaling remains unexplored. This study aimed to identify amino acids that can promote mTORC1 activity in combination with Leu and to assess the effectiveness of these combinations *in vitro* and *in vivo*. We found that tyrosine (Tyr) enhanced Leu-induced phosphorylation of S6 kinase (S6K), an indicator of mTORC1 activity, although it exerted no such effect individually. This booster effect was observed in C2C12 cells and in skeletal muscle, and the skeletal muscles of mice orally administered the amino acids. To explore the molecular mechanism underlying this Tyr-mediated booster effect, the expression of the intracellular Leu sensors, Sestrin1 and 2, was suppressed, and the cells were treated with Leu and Tyr. The suppression resulted in a loss to induce S6K phosphorylation and enhanced the booster effect, suggesting that Tyr possibly contributes to mTORC1 activation when Sestrin GAP activity is lost. ETags1 (E1TOR2) is downregulated through Sestrin knockdown or the binding of Sestrin to Leu. Collectively, these results indicate that Tyr is a key regulator of Leu-mediated protein synthesis.

**Keywords:** amino acids; mTORC1 complex; intracellular Sestrin1/2

### 1. Introduction

Skeletal muscle mass is maintained through a balance between protein synthesis and degradation. Nutritional supplementation with proteins or amino acids activates anabolic responses in the skeletal muscle and may be important for maintaining muscle loss due to aging, sarcopenia, or frailty [1–3]. The intracellular signaling mechanism regulating muscle protein synthesis (MPS) is controlled by the activation of the mammalian target of rapamycin complex 1 (mTORC1), which directly stimulates the phosphorylation of S6 kinase (S6K) and eukaryotic translation initiation factor 4E-binding protein (4E-BP). Changes in the phosphorylation state of these key proteins affect mRNA translation initiation and elongation, thereby regulating MPS [4]. Essential amino acids (EAAs) supplementations effectively stimulate MPS; however, non-essential amino acids (NEAAs) supplementations are significant at high doses [5,6]. Among EAAs, leucine (Leu) has been shown to be particularly important for MPS, as it is the only stimulator of mTORC1 signaling identified in muscle cells over the physiological range of amino acid levels in blood [4]. The amount of Leu in ingested proteins or EAA mixtures determines the extent of the MPS response at rest and after exercise [7–11]. The amino acid composition of dietary protein is considered to be suitable for stimulating MPS, owing to its high Leu content and absorbability [12,13]. Thus, Leu is widely accepted as being indispensable for stimulating mTORC1 signaling. Recently, the mechanism underlying Leu-mediated mTORC1 activation was elucidated using HEK293T cells [14,15]. In these studies, mTORC1 regulation by amino acids was found

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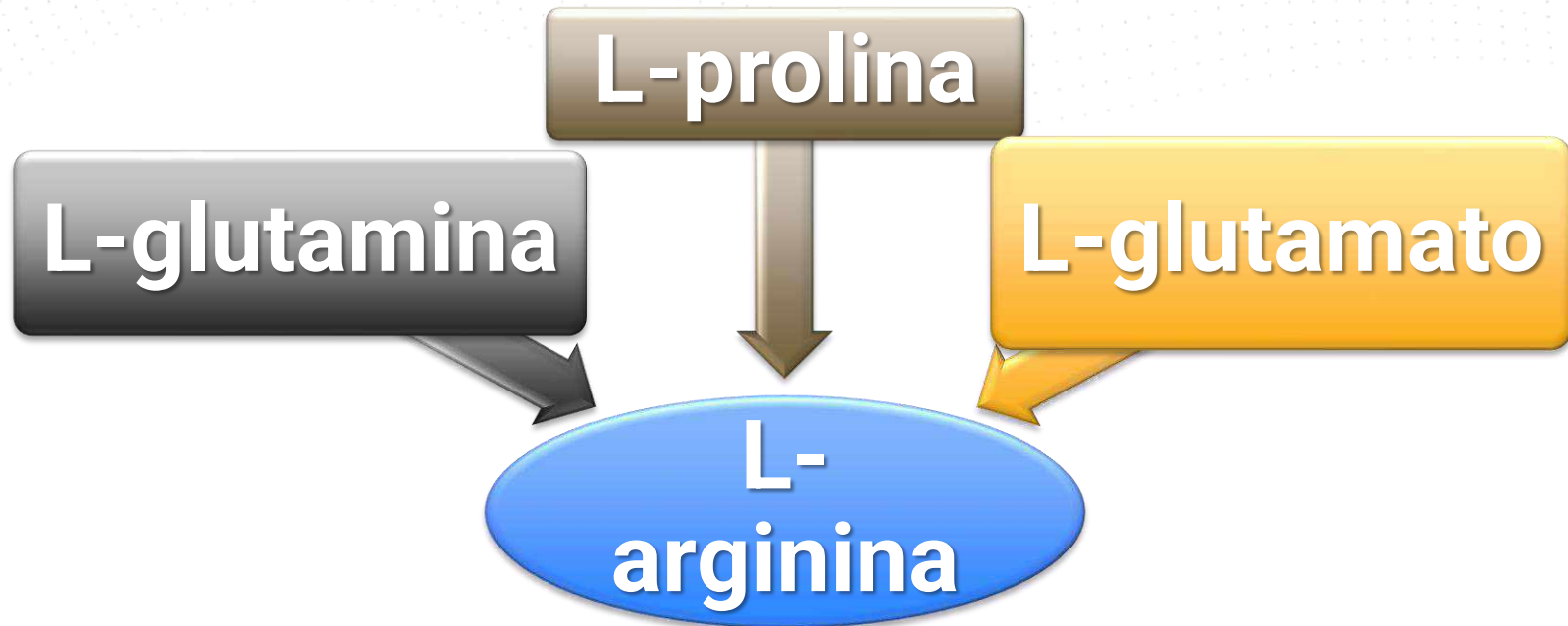
“Esse efeito booster foi observado em células C2C12, músculo murino isolado e músculos esqueléticos de camundongos que receberam os aminoácidos por via oral”

Estes resultados indicam que Tyr é um regulador chave da síntese proteica mediada por Leu”



# L-arginina

# Síntese endógena



# Situações de alta demanda / necessidade de L-arginina

**Crescimento  
na Infância**

**e Gestação**

**Queimaduras**

**Deficiência imunológica grave**

## ARGININA

Condicionalmente essencial. A síntese endógena pode não ser suficiente nas seguintes situações:

- crescimento durante a infância e gestação
- deficiência imunológica grave
- queimaduras

Biossintetizada a partir de glutamina, glutamato e prolina.

Funções:

- Síntese proteica (ativação m-TOR);
- Desintoxicação de amônia
- Antioxidante
- Liberação hormonal (GH, testosterona)
- Ativação da síntese de BH4 (=síntese neurotransmissores)

Via NO:

- regulação do tônus vascular
- biogênese mitocondrial
- função imune (macrófagos, células dendríticas e células T)
- neurotransmissão
- cicatrização
- espermatogênese, embiogênese e fertilidade

Precursora da creatina e ornitina, que gera poliaminas, prolina e glutamato

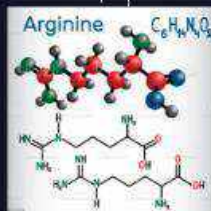
### SUPLEMENTAÇÃO

L-arginina: uso geral

Arginina Alpha Cetoglutarato (AAKG): utilizado na suplementação esportiva

Dose mínima: 500 mg  
Dose máxima: 3.500 mg

Dose usual: 1.000 mg/dia



### PRINCIPAIS APLICAÇÕES CLÍNICAS

- Imunomodulação
- GH e Testosterona
- Exercício físico
- Cicatrização
- HAS e disfunção endotelial

### EFEITOS ADVERSOS

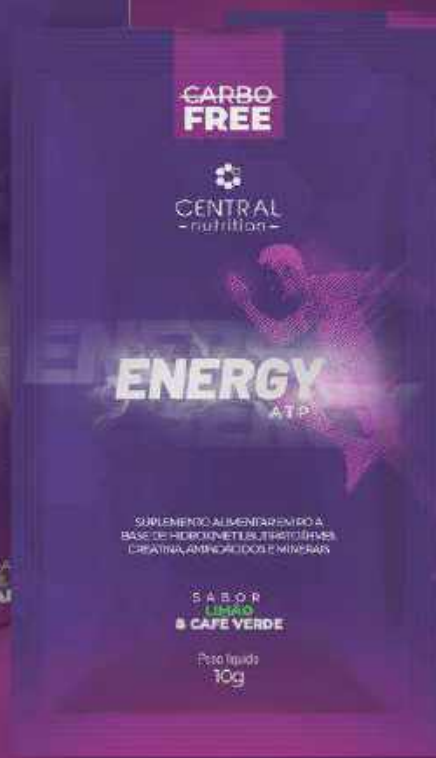
Em altas doses pode elevar os níveis de uréia no sangue e causar hipercalcemia, em pacientes com disfunção renal

### CONTRAINDICAÇÃO

- Em longo prazo: pacientes com alergias respiratórias, asma e cirrose
- Infecções por herpes: estimula a replicação do vírus
- Hipotensão arterial
- Pode potencializar fármacos hipotensores

\*DOSES USUAIS PARA ADULTOS





# ATIVOS **ENERGY**<sup>®</sup> ATP

- **HMB:** Promove rápida queima de gordura, transformando-a em energia para os treinos.
- **Creatina:** Aumenta a energia em 20% e melhora o desempenho atlético.
- **L-Alanina:** Ativa o metabolismo muscular, gerando força, ganho de massa magra e definição.
- **L-Arginina:** Melhora a oxigenação celular, acelera a recuperação muscular e reduz a fadiga.
- **L-Tirosina:** Aumenta o foco e a concentração, e melhora o desempenho físico e mental.
- **L-Taurina:** Melhora a resistência, performance e o metabolismo muscular.
- **L-Carnitina:** Reduz a gordura corporal, a fadiga e os danos ao tecido muscular.
- **Magnésio:** Colabora para maior nutrição e reduz as dores nos músculos.
- **Extrato de Café Verde:** Contribui para perda do peso de forma natural.



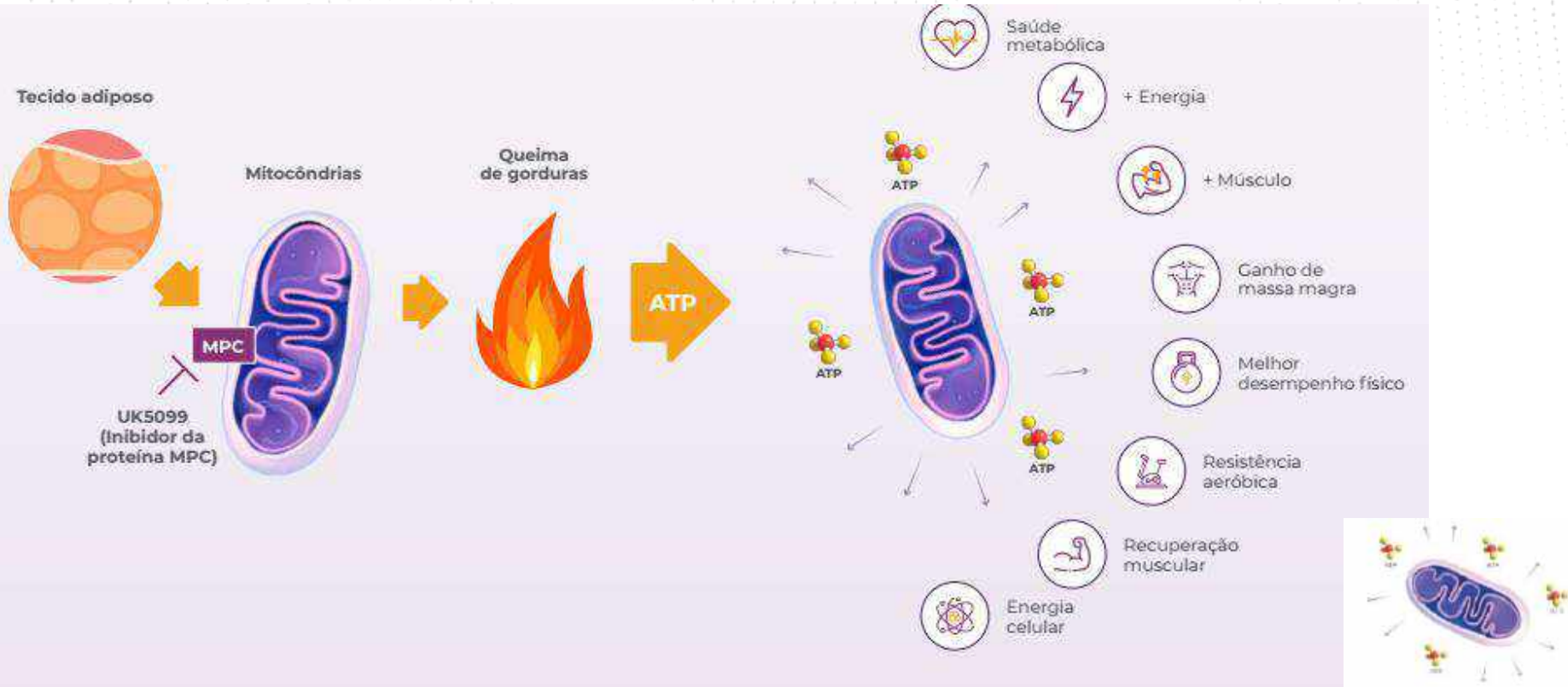
O QUE É O  
**ENERGY**<sup>®</sup>  
ATP

SUPLEMENTO IDEAL PARA  
PROPORCIONAR **MAIS ENERGIA!**

A sinergia dos ativos presente no ENERGY ATP proporciona ativação mitocondrial para aumentar a produção de ATP, contribuindo para melhora da performance no treino e fadiga muscular. A combinação de nutrientes auxilia a  $\beta$ -oxidação lipídica, promovendo maior energia corporal e cognitiva.



# Usos / benefícios



## INFORMAÇÃO NUTRICIONAL

porção de 20 g (2 sachês)

Quantidade por porção

%VD\*

HMB (Hidroximetilbutirato de cálcio)

2990 mg

\*\*

Creatina Monohidratada

3000 mg

\*\*

L-Alanina

1000 mg

\*\*

L-Arginina

1500 mg

\*\*

L-Carnitina

500 mg

\*\*

L-Taurina

2000 mg

\*\*

L-Tirosina

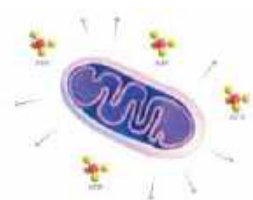
500 mg

\*\*

Magnésio

100 mg

38%



  
CENTRAL  
- nutrition -

# 1 sachê

- HMB 1500mg
- Creatina 1500mg
- Taurina 1000mg
- L-arginina 750mg
- L-alanina 500mg
- L-carnitina 250mg
- L-tirosina 250mg
- Magnésio 50mg (+malato)





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- nutrition -

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é **ciência!**

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