**Universidade Estadual Paulista**

**“Júlio de Mesquita Filho”**

**Faculdade de Ciências Farmacêuticas**

# Efeitos da suplementação de taurina sobre biomarcadores de estresse oxidativo em mulheres com idade de 55 a 70 anos

**Gabriela Ferreira Abud**

Dissertação apresentada ao Programa de Pós-graduação em Alimentos e Nutrição para obtenção do título de Mestre em Alimentos e Nutrição.

Área de concentração: Ciências Nutricionais.

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TÍTULO DA DISSERTAÇÃO: Efeitos da suplementação de taurina sobre biomarcadores de estresse oxidativo em mulheres com idade de 55 a 70 anos

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Araraquara, 07 de março de 2022

# Dedicatória

*Aos meus pais Cristina e Michel (in memoriam), por dedicarem suas vidas pela minha. A eles, devo tudo o que sou hoje.*

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# *Epígrafe*

*“O conhecimento exige uma presença curiosa do sujeito em face do mundo. Requer uma ação transformadora sobre a realidade. Demanda uma busca constante. Implica em invenção e em reinvenção.”*

*Paulo Freire*

**Resumo**

**Objetivo:** Avaliar os efeitos da suplementação de taurina sobre biomarcadores de estresse oxidativo em mulheres com idade de 55 a 70 anos. **Métodos:** Participaram do estudo 24 mulheres com idade variando de 61,4 ± 4,2 anos, índice de massa corporal (IMC) 31,4 ± 5,1 kg / m², que foram submetidas ou não a suplementação de taurina. As participantes foram distribuídas aleatoriamente em dois grupos: grupo controle (GC, n = 11), suplementado com placebo (1,5 g de amido); e grupo taurina (GTAU, n = 13), suplementado com taurina (1,5 g), durante 16 semanas. Foram realizadas avaliações de antropometria, testes de capacidade funcional, níveis de minerais, taurina e os níveis de marcadores de estresse oxidativo determinados no plasma no período pré e pós intervenção nutricional, assim como foi realizada análise da ingestão alimentar antes, durante e após o período de intervenção nutricional. Os resultados foram analisados por ANOVA *two way* medidas repetidas modelo misto, com post hoc Sidak ($p < 0,05$). **Resultados:** Os níveis plasmáticos de taurina e superóxido dismutase (SOD, enzima antioxidante) aumentaram no GTAU quando comparados aos resultados obtidos no GC após a suplementação. Os níveis de glutationa redutase (GR) diminuíram em ambos os grupos de intervenção. Os níveis de malondialdeído (MDA) aumentaram no GC quando comparado com o GTAU. **Conclusão:** A suplementação de taurina evitou a diminuição da enzima antioxidante SOD, sugerindo a suplementação de taurina como uma estratégia no controle do estresse oxidativo durante o processo de envelhecimento.

**Palavras-chave:** Envelhecimento; estresse oxidativo; taurina; estratégia terapêutica.

**Abstract**

**Objective:** To evaluate the effects of taurine supplementation on oxidative stress biomarkers in women aged 55 to 70 years. **Methods:** The study included 24 women aged 61.4 ± 4.2 years, body mass index (BMI) 31.4 ± 5.1 kg / m², who was submitted or not to taurine supplementation. Participants were randomly assigned to two groups: control group (CG, n = 11), supplemented with placebo (1.5 g starch); and taurine group (GTAU, n = 13), supplemented with taurine (1.5 g), for 16 weeks. Anthropometry assessments, functional capacity tests, minerals levels, taurine, and oxidative stress markers levels were determined in plasma sample pre and post nutritional intervention period, as well as an analysis of food intake before, during, and after the nutritional intervention period. The results were analyzed by an ANOVA two-way repeated measures mixed model, with post hoc Sidak ($p < 0.05$). **Results:** Taurine and superoxide dismutase (SOD, antioxidant enzyme) plasma levels were increased in GTAU when compared to the results obtained in GC after supplementation. Glutathione reductase (GR) levels decreased regardless intervention groups. Malondialdehyde (MDA) levels increased in GC when compared to GTAU. **Conclusion:** Taurine supplementation prevented the decrease in the antioxidant enzyme SOD, suggesting taurine supplementation as a strategy to control oxidative stress during the aging process.

**Keywords:** Aging; oxidative Stress; taurine; therapeutic strategy.

# Lista de abreviaturas e siglas

ANOVA = Análise de variância
CAPES = Coordenação de Aperfeiçoamento de Pessoal de Nível Superior
CAT = Catalase
CC = Circunferência da Cintura; waist circumference
CDO = Cisteína dioxigenase
COVID-19 = Coronavírus
CQ = Circunferência do Quadril; hip circumference
CSAD = Cisteína sulfinato descarboxilase
Cu = Cobre
DRIs = Dietary Reference Intake
EROS = Espécies reativas de oxigênio; reactive oxygen species
FAPESP = Fundação de Amparo à Pesquisa do Estado de São Paulo
Fe2+ = íons ferro; iron ions
GC = Grupo Controle; control group
GPx = Glutationa peroxidase; glutathione peroxidase
GR = Glutathione reductase
GSH = Reduced glutathione
GSSG = Oxidized glutathione
GTAU = Grupo Taurina; taurine group
$H_2O$ = Water
$H_2O_2$ = Peróxido de hidrogénio; hydrogen peroxide
HDL-C = High-density lipoprotein cholesterol
HGS = Handgrip strength test
HGSL = Handgrip strength left
HGSR = Handgrip strength right
HPLC = high-performance liquid chromatography
IBGE = Instituto Brasileiro de Geografia e Estatística
IMC = Índice de Massa Corporal; Body Mass Index
Ir = Iridium
KGF = highest peak force
LDL-C = Low-density lipoprotein cholesterol
MDA = Malondialdeído; malondialdehyde
Mn = Manganês
MPO = Myeloperoxidase
NADPH = Nicotinamida adenina dinucleotídeo fosfato
ND = Value not determined
$O_2$- = Ânion superóxido; superoxide anion
OH- = Radical hidroxila; hydroxyl radicals
PKA = Proteína quinase A
PKC = Proteína quinase C
PUFAs = Polyunsaturated fatty acids

q-ICP-MS = Quadrupole inductively coupled plasma mass spectrometry
Rh = Rhodium
RMR = Resting metabolic rate
SOD = Superóxido dismutase; superoxide dismutase
Tau-Cl= Chloramine taurine
TAUT = Taurine transporter
TBARS = ácido tiobarbitúrico
TC = Total cholesterol
TG = Triglycerides
UL = Upper tolerable intake level
$VO_2$máx = volume máximo de oxigênio
WHO = World Health Organization
Zn = Zinco
η2 = Eta squared

# Sumário

## Introdução

Atualmente observa-se que o panorama do envelhecimento populacional aumentou substancialmente em grande parte do mundo (1). Do ponto de vista demográfico, mesmo com o aumento avassalador nas taxas de mortalidade e morbidade por consequência da COVID-19, os dados populacionais apontam que nas próximas décadas a sociedade será representada por um público mais envelhecido (2). No Brasil, segundo o Instituto Brasileiro de Geografia e Estatística (IBGE) as expectativas do número de idosos, para o ano de 2060 é de 25,5% (3).

Em virtude do processo de senescência é esperado que ocorram alterações fisiológicas em tecidos, órgãos e sistemas (4). Tais alterações envolvem mudanças na composição corporal como perdas ósseas, catabolismo muscular, aumento de gordura corporal, alterações digestivas e absortivas de nutrientes, além do acúmulo de danos celulares ao longo do tempo (4, 5).

Principalmente, esses danos celulares estão associados com o desequilíbrio entre os sistemas pró-oxidante e antioxidante do organismo, com predominância do primeiro, refletindo no aumento do estresse oxidativo. Esse desequilíbrio favorece a produção aumentada de espécies reativas de oxigênio (EROs), moléculas altamente reativas que em altas concentrações pode resultar no mal funcionamento do sistema de reparo celular, contribuindo para o desenvolvimento de doenças crônicas degenerativas não transmissíveis (6, 7) como alguns tipos de câncer, Alzheimer, Parkinson, esclerose múltipla, distúrbios cardiovasculares, osteoporose, diabetes Mellitus tipo 2, hipertensão arterial (8)

sendo essas, algumas das grandes preocupações associadas ao processo de envelhecimento.

Esses malefícios são provenientes de uma condição predominantemente multifatorial que envolvem desde aspectos genéticos (5), estilo de vida que impera da alimentação inadequada como exemplo, o consumo frequente de alimentos ricos em açúcar e gordura saturada e pobres em componentes antioxidantes presentes nas frutas, legumes e vegetais (9), além da exposição a outros múltiplos fatores de estresse como a poluição do ar, radiação, tabagismo e etilismo, prevalecendo a geração e acúmulo de EROs (8,10), conforme demonstrado na figura 1.

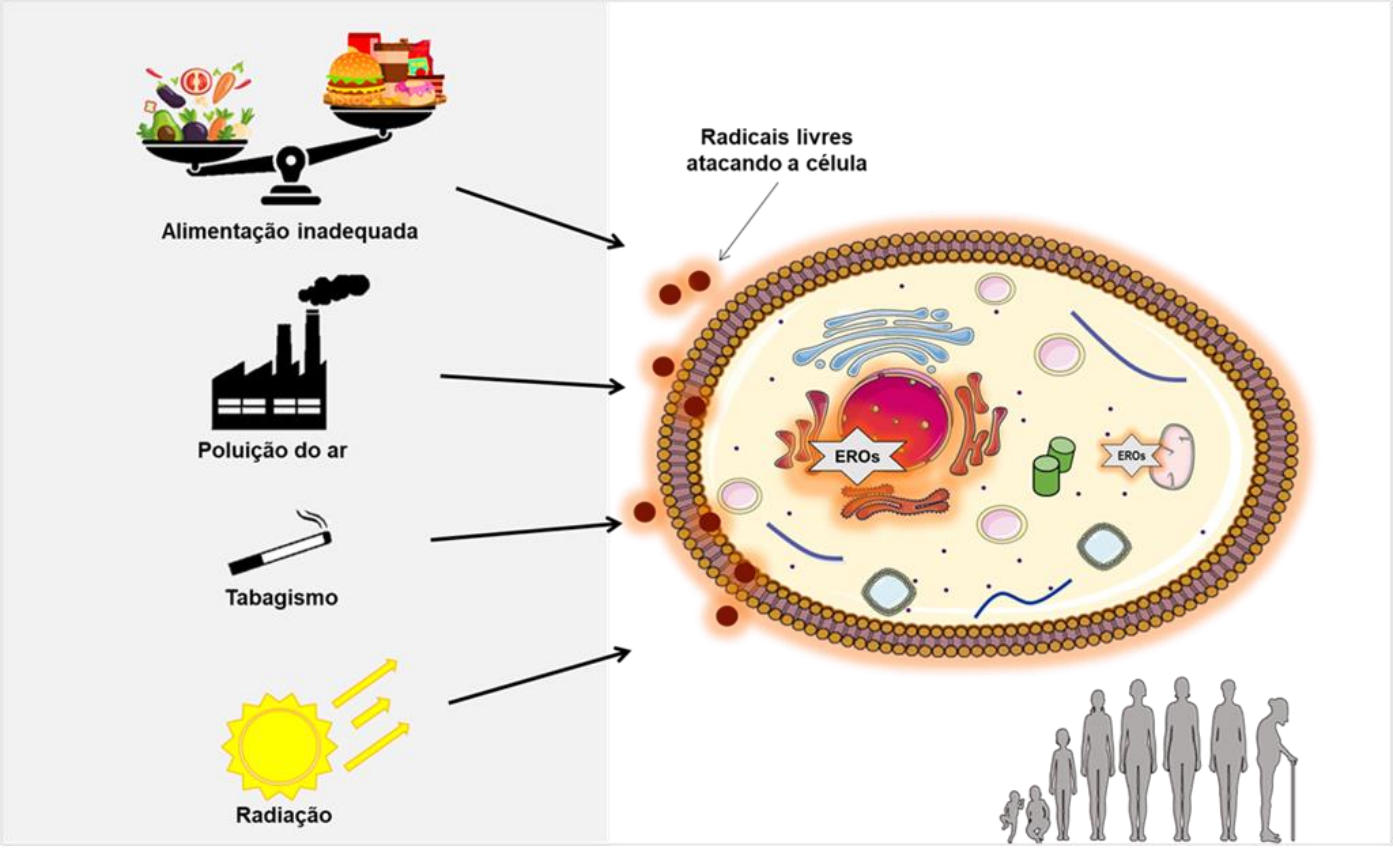

**Figura 1.** Fatores exógenos associados ao acúmulo de espécies reativas de oxigênio (EROs) no meio celular. Figura de autoria própria.

Neste contexto, estratégias de intervenção utilizando antioxidantes nutricionais têm se revelado úteis em aumentar a capacidade antioxidante celular (10-12) principalmente no envelhecimento, onde é observado um enfraquecimento do sistema de defesa antioxidante (13).

Segundo Pisoschi e Pop (14) o sistema antioxidante endógeno pode ser complementado com o uso de antioxidantes exógenos, pela dieta ou por suplementos alimentares provenientes de nutrientes como vitaminas, minerais, ácidos graxos ou aminoácidos que faltam ou não se encontram em quantidades necessárias na dieta. Liu et al. (13) também destacaram que estratégias terapêuticas (à base de antioxidantes) que aumentem a capacidade antioxidante do indivíduo, atrelado a um estilo de vida saudável, possivelmente seja útil para um tratamento a longo prazo.

Frente a essa abordagem, é fato que suplementos antioxidantes podem demonstrar efeitos promissores sobre os danos celulares, e assim, inibir a incidência de doenças. No entanto, ainda apresenta controvérsias quanto às dosagens recomendadas, uma vez que doses muito baixas podem ser ineficazes. Por outro lado, os excessos podem atenuar ou bloquear as respostas adaptativas ao estresse, sabendo também que as EROs em baixos níveis são essenciais para a homeostase celular (13-15).

Visto que um estado mais oxidado é observado nas células envelhecidas e consequentemente, pode contribuir para o desenvolvimento de doenças crônicas degenerativas não transmissíveis, entender os processos que envolvem o estresse oxidativo e o sistema de defesa antioxidante são de extrema importância. Além disso, é importante considerar também que o baixo consumo de alimentos fontes de antioxidantes, possivelmente refletem na formação exacerbada de EROs. Sendo assim, estratégias de intervenção nutricional capazes de minimizar o estresse oxidativo durante o processo de envelhecimento são alternativas fundamentais.

## Estresse oxidativo, espécies reativas de oxigênio e sistema de defesa antioxidante

O estresse oxidativo é um processo responsável por causar danos oxidativos em macromoléculas como carboidratos, proteínas, lipídios e DNA, levando a um comprometimento de sistemas biológicos do organismo (16,17).

Dentre as macromoléculas que podem sofrer os com danos oxidativos, a peroxidação dos lipídeos das membranas é o indicador comumente utilizado em estudos que investigam os danos oxidativos (18-21), tendo em vista que os ácidos graxos poli-insaturados (AGPI) das membranas plasmáticas são mais suscetíveis aos ataques por EROs (22,23).

Em resposta à peroxidação lipídica da membrana, sob concentrações fisiológicas, as células mantêm sua sobrevivência por meio do sistema de defesa antioxidante, resultando em uma resposta adaptativa ao estresse. Por outro lado,

as altas concentrações de peroxidação lipídica alteram a permeabilidade, fluidez e a integridade da membrana, contribuindo fortemente para desenvolvimento de patologias e ao envelhecimento acelerado (23).

Na peroxidação lipídica, a decomposição oxidativa de AGPI formam produtos finais da reação, como o malondialdeído (MDA), o qual apresenta alta toxicidade e reatividade (24). Ademais, é um dos biomarcadores mais confiáveis e utilizados na determinação do estresse oxidativo (23).

Em relação as EROs, essas moléculas são produzidas normalmente pelo metabolismo celular, e incluem principalmente o ânion superóxido ($O_2$-), peróxido de hidrogênio ($H_2O_2$) e radical hidroxila (OH-) (16,17,25).

O $O_2$- pode ser formado pela redução de um elétron do oxigênio molecular, a partir de nicotinamida adenina dinucleotídeo fosfato (NADPH) oxidase, na respiração celular. Entretanto, a maior parte de $O_2$- é dismutado em $H_2O_2$ por uma reação que envolve a atividade de enzimas antioxidantes. O $H_2O_2$, não apresenta elétrons desemparelhados, porém é considerado uma EROs devido a sua capacidade em entrar no citosol e formar o OH-, sendo essa reação conhecida como *reação de Fenton* (17). Já o OH- é considerado o mais reativo das EROs, em virtude da sua alta capacidade de reagir com qualquer molécula biológica, principalmente com os fosfolipídios nas membranas celulares e proteínas, podendo resultar em disfunção e morte celular (16).

Quanto ao sistema de defesa antioxidante, incluem as enzimas endógenas como a superóxido dismutase (SOD), glutationa peroxidase (GPx) e catalase (CAT), considerado a principal linha de defesa do organismo contra EROs (17).

As SODs encontradas no citosol e na mitocôndria, apresentam diferentes íons em seus sítios ativos, como o Cobre (Cu), Zinco (Zn) e Manganês (Mn), podendo ser classificados em CuZn-SOD citosólico, Mn-SOD mitocondrial e SOD extracelular, respectivamente. Já a CAT localiza-se no peroxissomo e a GPx no citoplasma e na parte extracelular dos tecidos do organismo (26, 27).

Essas enzimas, agem interrompendo a cadeia de reação por meio da doação de elétrons, evitando a produção excessiva de EROs, além de retardar processos de peroxidação lipídica, bem como prevenir possíveis danos celulares (26) (Figura 2).

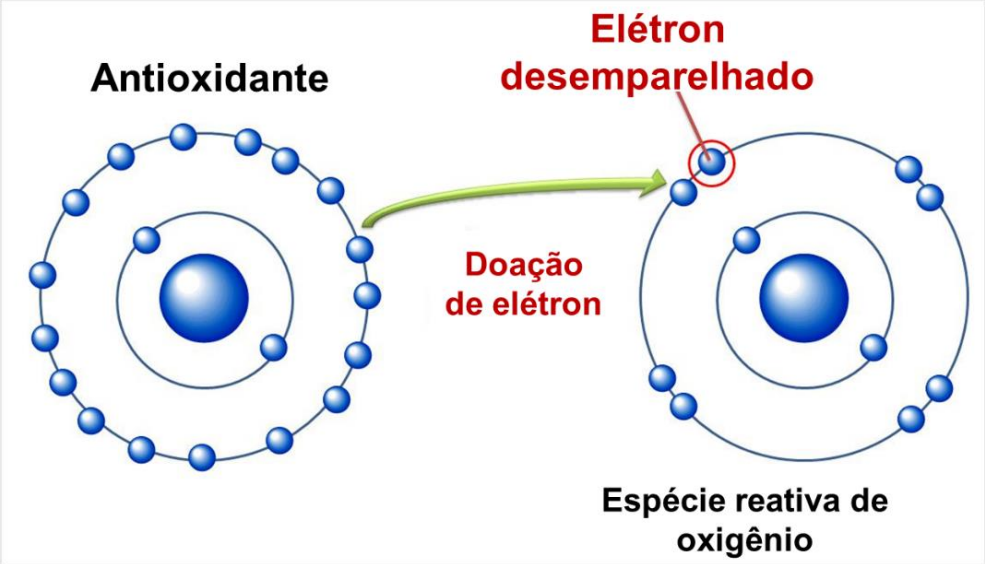


**Figura 2.** Ação de antioxidantes em inibir espécies reativas de oxigênio (EROs) (28) Adaptado.

Além disso, o sistema de defesa antioxidante inclui os antioxidantes não-enzimáticos, especialmente os de origem dietética (exógenos), tais como ácido

ascórbico (vitamina C), α-tocoferol (vitamina E) , β-caroteno, compostos fenólicos e elementos como zinco, selênio e magnésio (14,17).

**Taurina: ações fisiológicas e metabolismo**

A taurina é um composto nitrogenado intracelular livre, encontrado em abundância no coração, leucócitos, retina, sistema nervoso central, e no músculo (29). Originalmente, esse composto nitrogenado foi descoberto e isolado na bile de bovinos em meados de 1827, pelos pesquisadores alemãs Friedrich Tiedemann e Leopold Gmelin (30), porém seu reconhecimento em estudos com humanos foi somente em 1975 (31).

Apesar de não participar da síntese proteica, a taurina é referida na literatura como um aminoácido não essencial. Em sua estrutura química há presença de um grupamento sulfônico ao invés de um grupamento de ácido carboxílico (29).

A taurina é sintetizada principalmente pelo fígado, a partir de aminoácidos sulfurados como a metionina e cisteína (32). Em primeiro momento, na via metabólica da taurina, ocorre a reação que envolve a descarboxilação da cisteína a cisteína ácido sulfínico, pela enzima cisteína dioxigenase (CDO). Posteriormente, a cisteína ácido sulfínico é descarboxilada pela cisteína sulfinato descarboxilase (CSAD) e convertida em taurina através da oxidação da hipotaurina, um intermediário da biossíntese da taurina, sendo esta reação dependente da presença de vitamina B6 (33) (Figura 3).

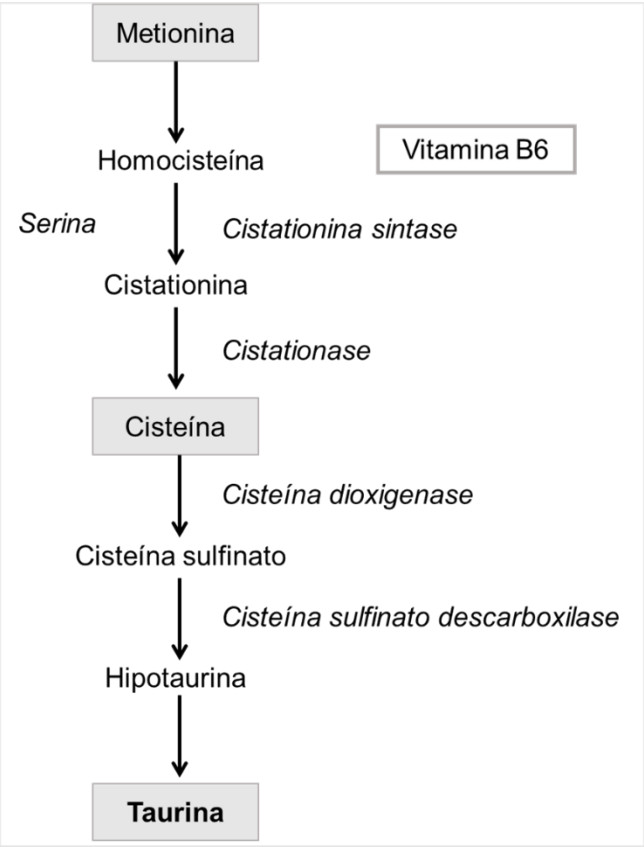


**Figura 3.** Síntese endógena de taurina. Adaptado de Lourenço e Camilo (33).

Entretanto, a sua produção endógena é insuficiente, sendo possivelmente um dos motivos pelos quais é considerada um aminoácido semi-essencial, havendo necessidade do fornecimento dietético, o qual as principais fontes são alimentos de origem marinha e animal (29, 34). Dentre os alimentos de origem marinha, os crustáceos e moluscos contém em média 7000 mg de taurina por quilo de alimento (mg/kg) e pescados contém 1720 mg/kg. Quanto aos alimentos de origem animal, a carne escura do frango contém 2000 mg/kg e peru 3000

mg/kg. Além do mais, alimentos como leite de vaca, nozes e feijão também apresentam concentrações de taurina, porém são concentrações menores (35).

Uma vez obtida pela dieta, é absorvida pelo trato gastrointestinal, particularmente no intestino curto através de seu receptor TAUT (*taurine transporter*), que por sua vez é modulado pelas enzimas proteína quinase C (PKC), responsável pela inibição do transporte, e a proteína quinase A (PKA), enzima responsável por estimular ou inibir o transporte de taurina, dependendo do tecido (34, 36, 37). O conteúdo de taurina absorvido e liberado na corrente sanguínea é então distribuído para diversos tecidos e órgãos através do transporte ativo (34), sendo que o músculo esquelético representa em aproximadamente 70%, a maior reserva de taurina no corpo (38).

Quanto à concentração plasmática de taurina, Ghandforoush-Sattari et al. (39) investigaram o tempo de permanência desse composto nitrogenado no organismo. Os autores constataram que após a ingestão de 4 gramas de taurina, em que jovens saudáveis administram o suplemento, o pico máximo de concentração considerando absorção de taurina foi entre 1 e 2,5 horas, com tempo médio de 1,5 horas (39).

Clinicamente, a taurina tem sido utilizada no tratamento de inúmeras condições patológicas, incluindo, doenças neurodegenerativas como Alzheimer e Parkinson, epilepsia, insuficiência cardíaca, aterosclerose, hipertensão, diabetes (32) e também possui ações importantes no metabolismo lipídico (40), efeitos protetores em processos inflamatórios (29) e atividade antioxidante (32).

**Taurina: funções antioxidante**

Diversos estudos têm demonstrado que a taurina apresenta ações antioxidantes (18-20, 41,42). De acordo com os relatos mencionados na literatura científica, parece que a taurina é incapaz de eliminar diretamente as EROs com destaque para as clássicas, incluindo, ânion superóxido, peróxido de hidrogênio e radical hidroxila (43). Por outro lado, essa molécula provavelmente age de forma indireta, atenuando a toxicidade de EROs ao invés de aumentar as defesas antioxidantes (41, 44).

Além disso, a hipotaurina (precursor da taurina) pode atuar como um carregador de OH- e inibidor da auto-oxidação de íons ferro (Fe2+), podendo prevenir a ocorrência de reações de peroxidação lipídica (45). Klamt e Schacter (46), em estudo com taurina marcada radioativamente em meio de cultura celular, demonstraram que a taurina é captada preferencialmente pelas mitocôndrias. Diante disso, sugere-se que grande parte da taurina intracelular se concentra no interior da mitocôndria, contribuindo na eliminação de EROs e consequentemente em menores níveis de danos celulares.

Zhang et al. (18) investigaram os possíveis efeitos protetores da suplementação de 6 gramas de taurina por sete dias, sobre o estresse oxidativo induzido pelo exercício físico em jovens ciclistas. Os autores constataram aumentos significativos no volume máximo de oxigênio ($VO_2$máx), utilizado pelo organismo, no tempo de exaustão em cicloergômetro e na carga máxima de trabalho, reduzindo a produção de substâncias reativas ao ácido tiobarbitúrico (TBARS), formadas como um subproduto da peroxidação lipídica (18).

Em outro estudo, Silva e colaboradores (42) investigaram os efeitos da suplementação de taurina 300 mg/kg sobre marcadores de estresse oxidativo utilizando método de gavagem por 15 dias, após a realização de exercício extenuante. Foi observado a redução de radicais superóxidos, peroxidação lipídica e carbonilação, atestando o efeito protetor da taurina.

Já no estudo de Carvalho et al. (20) investigaram a eficácia da suplementação de taurina (3 gramas) por meio de um protocolo de 8 semanas, em ciclistas. Como resultado, observou-se níveis aumentados nas concentrações basais de taurina e diminuição dos níveis do biomarcador de estresse oxidativo (MDA), sugerindo que a taurina evitou a peroxidação lipídica. Outros pesquisadores também encontraram resultados similares a essas evidências (19). Foi observado que após a utilização da suplementação de 3 gramas de taurina, associado apenas ao aconselhamento nutricional durante 8 semanas em mulheres obesas, a taurina foi capaz de reduzir os níveis de marcadores da inflamação (proteína C reativa) e peroxidação lipídica (TBARS) (19).

No entanto, apesar das fortes evidências da suplementação de taurina como potente antioxidante, ainda são poucos os estudos até o presente momento, que retratam as ações terapêuticas desse composto nitrogenado no envelhecimento (47). Além disso, essa linha de investigação por meio de ensaios clínicos com seres humanos, ainda é bastante escassa.

Tendo em vista que os danos celulares resultantes de um estado de estresse oxidativo pode contribuir para o desenvolvimento de doenças crônicas degenerativas não transmissíveis, como exemplo alguns tipos de câncer e

diabetes mellitus, especialmente no processo de envelhecimento, a utilização de terapias farmacológicas se faz necessário para o tratamento, mas muitas vezes são estratégias que geram altos custos e podem resultar em efeitos indesejáveis. Contudo, sabendo que a estratégia de intervenção com taurina (terapia não-farmacológica) tem se mostrado potencialmente capaz de atenuar o estresse oxidativo, este estudo teve como hipótese que, a suplementação de taurina possa minimizar o estresse oxidativo e modular o sistema de defesa antioxidante em mulheres com idade de 55 a 70 anos.

## Objetivos

**Geral:** Avaliar os efeitos da suplementação de taurina sobre biomarcadores de estresse oxidativo em mulheres com idade de 55 a 70 anos.

**Específicos:**

- Avaliar as medidas antropométricas (peso, altura, IMC, CC e CQ), composição corporal e a capacidade funcional antes e após os períodos de suplementação;
- O consumo alimentar antes, durante e após os períodos de suplementação;
- As concentrações plasmáticas de minerais (zinco, selênio, magnésio e cálcio) antes e após os períodos de suplementação;
- As concentrações plasmáticas de taurina antes e após os períodos de suplementação;
- Quantificação de biomarcadores de estresse oxidativo (superóxido dismutase, glutationa redutase e malondialdeído) antes e após os períodos de suplementação.

# ***Capítulo 1.***

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# Taurine as a possible anti-aging therapy? A controlled clinical trial on taurine antioxidant activity in women aged 55 to 70 years

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**Abstract**

*Objective:* Based on taurine's antioxidant effects, capable of controlling oxidative stress in the aging process, we investigated the effects of taurine supplementation on biomarkers of oxidative stress in women aged 55 to 70 years. *Methods:* A double-blind study was conducted with 24 women (61.4±4.2 years, body mass index 31.4±5.1 kg/m²). The participants were randomly assigned to two groups: control group (GC, n = 11), supplemented with placebo (1.5 g of starch); and taurine group (GTAU, n = 13), supplemented with taurine (1.5 g), for 16 weeks. Anthropometry, functional capacity testing, minerals, taurine, and oxidative stress marker levels were determined in plasma samples pre and post intervention. Food consumption was assessed pre, during, and post intervention. The results were analyzed by an ANOVA two-way repeated measures mixed model, with the Sidak post hoc ($p < 0.05$). *Results:* Taurine and superoxide dismutase (SOD, antioxidant enzyme) plasma levels were increased in GTAU, and SOD levels were also higher than GC levels after supplementation. Glutathione reductase (GR) levels decreased regardless of the intervention. Malondialdehyde (MDA) levels increased only in GC when compared to GTAU. *Conclusion:* Taurine supplementation prevented the decrease in the antioxidant enzyme SOD, suggesting taurine as a strategy to control oxidative stress during the aging process.

*Keywords:* Aging, Oxidative Stress, Taurine, Nutritional Supplementation, Therapeutic Strategy.

## Introduction

Aging is a physiological and irreversible process, accompanied by various structural and functional changes at the cellular, tissue, and organ levels [1]. Among the various theories explaining aging, Harman [2], describes the hypothesis that age-related disorders occur due to the cumulative effects of reactive oxygen species (ROS) formation, causing cellular damage over time [3]. ROS exert essential cell signaling functions in the body; however, overproduction of ROS causes a cellular imbalance called oxidative stress [4,3].

Minimizing oxidative damage in cellular structures caused by the excess of ROS could prevent aging-associated diseases such as diabetes, hypertension, cardiovascular disorders, atherosclerosis, and neurodegenerative diseases [3]. Among the strategies that can improve the body's ability to counteract oxidative stress, the use of nutritional antioxidants has been investigated. Taurine (2-aminoethanesulfonic acid) is a "semi-essential" amino acid, also called a nitrogen compound, which has been used as an effective antioxidant due to its ability to neutralize hypochlorous acid, an extremely toxic oxidant produced by leukocytes in the inflammatory process in humans [5,6]. In addition, hypotaurine, a precursor of taurine, can scavenge hydroxyl radicals (OH-) and inhibit the auto-oxidation of iron ions (Fe2+), preventing lipid peroxidation reactions [7].

Oliveira et al. [8] investigated the antioxidant effects of endogenously produced taurine through its respective precursors, methionine and cysteine [9] and observed the ability of taurine to inhibit ROS production and increase the activity of antioxidant enzymes, such as superoxide dismutase (SOD). In addition, taurine can inhibit the exacerbated production of pro-inflammatory oxidants such as superoxide anion ($O_2$-) [10], confirming its participation as an antioxidant agent.

Previous investigations showed anti-oxidant effects of taurine in human [11–13] and animal studies [14]. However, the effects of taurine in individuals aged 55 to 70 years have not yet been explored. Since the aging process is associated with lower antioxidant defense capacity [15] and decreased plasma taurine levels [16], exploring the antioxidant role of taurine supplementation could

provide evidence of possible clinical applicability for individuals in the aging process.

We hypothesized that taurine supplementation in women aged 55 to 70 years may minimize oxidative stress in the aging process by modulating the antioxidant system. Thus, the present study investigated the effects of taurine supplementation with 1.5g/day on biomarkers of oxidative stress.

## Methods

### Study design and subjects

This is a randomized, double-blind clinical trial developed with 24 women (61.4±4.2 years, body mass index (BMI) 31.4±5.1 kg/m²), submitted to taurine or placebo supplementation. The intervention with taurine supplementation or placebo was conducted for 16 weeks and participants were randomly assigned to two groups: control group supplemented with placebo (cornstarch) (GC, n=11) and taurine group supplemented with taurine (GTAU, n= 13).

The recruitment of participants was carried out through dissemination on social networks, on the website of the School of Physical Education and Sports of Ribeirao Preto, University of Sao Paulo, and in the newspapers. To be considered eligible for participation, the subjects attended the inclusion criteria: 55-70 years old, female, post-menopaused, and sedentary (not practicing physical exercise for at least 6 months). Participants with a history of chronic kidney or coronary heart disease, infectious diseases, smokers, and alcoholics were not included.

Initially, 147 volunteers were interested in the study and registered online on the School of Physical Education and Sports of Ribeirao Preto website. Of these 147 eligible subjects, 30 women were selected according to the inclusion and exclusion criteria. The protocol started with 15 participants in each group, but there were six dropouts, four from the GC and two from the GTAU, due to the onset of the COVID-19 pandemic, to other diseases not related to the intervention protocol, and other reasons without justification. The study was approved by the Ethics Committee of the School of Physical Education and Sport of Ribeirao Preto,

University of Sao Paulo (protocol number: nº 29187719.4.0000.5659). All participants signed the consent form prior to the study. The study NCT05149716, was registered on ClinicalTrials.gov.

Figure 1 summarizes the study design.

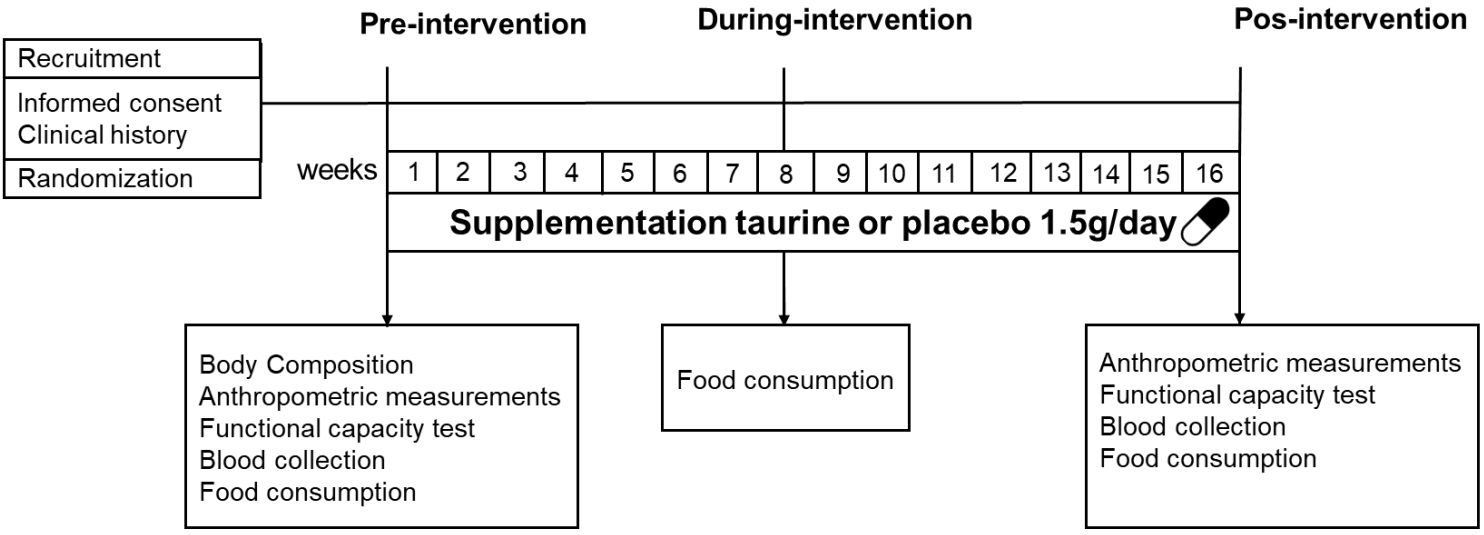



**Figure 1**. Study design.

**Sample size**

For this experiment, 24 individuals were calculated as sufficient to assess the results of the levels of oxidative stress biomarkers in plasma, which were the primary variables of interest. Calculations were performed using GPower (3.1.9.7), based on the method described by Faul et al. [17]. First, the effect size was calculated for the oxidative stress biomarkers. An average effect size of f = 0.98 and SD = 0.53 were obtained. For the calculation, the significance level and statistical power were set at 0.05 and 0.80, respectively. “F tests”, ANOVA test for repeated measures, within–between interactions, and “post hoc” as the type of analysis were selected. Based on these calculations, sufficient statistical power was obtained (a value greater than 0.80).

**Interventions**

Taurine or placebo supplementation

The supplementation of 1.5 grams of taurine (GTAU) was composed of three capsules containing 0.5 grams of pure taurine powder (Aminoethylsulfonic Acid, Ajinomoto®, Sao Paulo, SP) [18]. The placebo supplementation (1.5 grams) was composed of three capsules containing 0.5 grams starch (GC). In order to guarantee the blinding and concealment the capsule containers were similar (same size, shape and color) and a third person not involved in the study was responsible for the supplements allocation.

No dietetic intervention was performed, and participants were instructed to maintain their habitual dietary intake throughout the intervention period and to use the supplement in the morning. Capsule intake was monitored daily by the researchers through phone calls and texts.

**Evaluations**

Anthropometric and body composition assessment

Bodyweight and height were measured using an electronic Filizola™ scale and vertical axis, respectively. Waist and hip circumference were measured with a 200 cm inextensible tape with 0.1 cm markings.

Body composition was initially estimated to characterize the sample. Total body and regional scans measured by iDXA (Lunar GE Medical Systems scanner - Prodigy Advance, Encore software, version 13.6) were performed. The equipment was calibrated every morning before the measurements, always by the same technician, according to the manufacturer's recommendations [19].

Functional Capacity Tests

Agility and dynamic balance

To perform the test, participants were required to get up from a chair and walk around a cone located to the right, walk back 1.5 m, walk 1.8 m to the side of the chair and return as quickly as possible to the sitting position on the chair.

Immediately, the participant lifted her feet off the floor (to ensure completion of the movement) and started the same movement on the opposite side, was considered as completing a cycle. One attempt was adopted as two cycles. The participants were asked to perform two attempts, with the result being the shortest performance time between the two attempts [20].

Strength measurement

To measure the strength, the participants performed a handgrip strength test (HGS), including handgrip strength left (HGSL) and handgrip strength right (HGSR), using the dynamometer (Baseline®). Participants were placed in an orthostatic position, with the elbow flexed to 90◦ and close to the body to perform the test. Participants were familiarized with the device before starting valid attempts. Three attempts were performed for each hand, with a grip duration of 3 s and intervals of 10 s. Of the three attempts, the highest peak force (KGF) was recorded [21].

Dietary intake

All subjects were instructed to complete a three-day food record to verify their nutritional intake before, during, and post-intervention. The values in the table refer to the average consumption listed on the three food records evaluated in each period. Dietwin professional software was used to assess the total intake of energy, macronutrients, and elements (zinc, selenium, magnesium, and calcium) in grams per day (g/day) and in grams per kilogram of weight per day (g/kg/day).

Biochemical measurements

Blood samples were collected 24 hours after the end of the intervention, and plasma was separated by centrifugation and stored at -80ºC until analysis. The collection was performed early in the morning, and participants were 12-h

fasted before the evaluation. Blood samples were collected pre- and post-intervention to quantify minerals, oxidative stress markers, and taurine levels.

Blood minerals measurement

Plasma mineral concentrations were measured by quadrupole inductively coupled plasma mass spectrometry (q-ICP-MS). For the analysis, 100 µL of plasma was used. Prior to analysis, samples were diluted (1:25) in a solution containing 0.01% (v/v) Triton ® X-100 and 0.5% (v/v) nitric acid. In addition, 10 µg $L^{-1}$ of each of the samples contained an internal standard of Rhodium (Rh) and Iridium (Ir). All elements were determined in standard mode by mass spectrometry (q-ICP-MS) according to the method described by [22].

Plasma taurine levels

Plasma taurine was determined by high-performance liquid chromatography (HPLC) (Shimadzu, model LC 10AD). Taurine 99% was used as the standard (Sigma-Aldrich, St. Louis, MO, USA) [23].

Blood oxidative stress marker measurement

The superoxide dismutase (SOD) activity in erythrocytes was evaluated by the spectrophotometric method using the RANSOD kit (RANDOX Laboratories, Ltd.) [24]. Glutathione reductase (GR) activity was determined by the spectrophotometric method at 37 ºC/340nm after the oxidation of NADPH in the presence of oxidized glutathione, according to the method described by Flohe and Gunzler [25]. The measurement of malondialdehyde (MDA) was performed according to the method proposed by Gerard-Monnier et al. [26] with some adaptations.

Statistical analysis

Data are presented as mean values and standard deviation. Data normality was verified by the Shapiro-Wilk test. The unpaired t-test was performed for the

characterization of the subjects. Two-way repeated measures ANOVA mixed model and sphericity were used for intra- and inter-group comparisons, followed by the Sidak post-hoc in cases of group*time interaction. For data that did not show homoscedasticity *(Levene)*, a one-way ANOVA test with Welch correction was performed. In cases of non-parametric distribution, the Wilcoxon test was used for comparisons within trials, and the Mann-Whitney test for comparisons between trials. The analysis was performed using SPSS Statistics 20® software, considering a significance level of 5%. The delta shows the percentage change between pre and post evaluation and was calculated, according to the formula, Δ% = Δ (post - pre)*100 / pre. In addition, the Eta squared (η2) was used as a measure of effect size in the ANOVA, using the following formula: η2 = SSeffect / SStotal, where SSeffect is the sum of squares of the effect divided by SStotal, which is the total sum of squares (sum of SSeffect) for all effects, interactions, and errors [27]. Effect size was considered according to the classification: small: 0.10 to 0.29, moderate: 0.30 to 0.49, and large: 0.50 to 1.0.

**Results**

The characteristics of the participants are described in Table 1. The groups were similar at the beginning of the intervention, except for serum triglyceride levels (p=0.012).

**Table 1**. General characteristics of participants at baseline.

| | GC (n=11) | GTAU (n=13) |
|---|---|---|
| Age (years) | 62.0±5.1 | 60.9±3.3 |
| Weight (kg) | 78.4±9.3 | 77.1±15.2 |
| Stature (m) | 1.6±0.1 | 1.6±0.1 |
| BMI (kg/m$^2$) | 31.6±4.3 | 31.2±5.9 |
| Body fat (%) | 48.3±2.9 | 46.6±6.3 |
| Fat-free mass (%) | 50.3±2.6 | 51.8±5.9 |
| Glucose (mg/dL) | 98.6±22.1 | 99.8±33.9 |
| HDL-c (mg/dL) | 43.5±10.3 | 49.7±15.8 |
| LDL-c (mg/dL) | 131.8±36.7 | 144.1±41.1 |
| TC (mg/dL) | 205.4±37.6 | 219.6±33.5 |
| TG (mg/dL) | 150.9±44.5 | 129.2±157.3* |

**BMI:** Body Mass Index, **HDL-C:** High-density lipoprotein cholesterol, **LDL-C:** Low-density lipoprotein cholesterol, **TC:** Total cholesterol, **TG:** Triglycerides. **GC:** control group, **GTAU:** taurine group. Values expressed as mean ± standard deviation. *Differences between groups by unpaired t-test, ($p < 0.05$).

Table 2 shows the anthropometric measurements and functional capacity test results pre and post 16 weeks of intervention. No changes were observed in body weight, BMI, and hip circumference for GC and GTAU. Waist circumference increased only in the GC group (p=0.035).

Functional capacity tests were applied to evaluate the mobility and skeletal muscle function. No changes in the functional capacity tests were observed post intervention in either group. However, the GTAU group presented higher palmar grip strength of the left hand (HGSR) post intervention (p=0.025), when compared to GC.

**Table 2**. Anthropometric measurements and functional capacity tests before and after intervention.

| | GC (n=11) | | | GTAU (n=13) | | |
|---|---|---|---|---|---|---|
| **Variable** | **Pre** | **Post** | **Δ%** | **Pre** | **Post** | **Δ%** |
| Weight (kg) | 78.4±9.3 | 78.5±8.4 | 0.1 | 77.1±15.2 | 78.1±16.1 | 1.3 |
| BMI (kg/m$^2$) | 31.6±4.3 | 31.7±4.2 | 0.3 | 31.2±5.9 | 31.6±6.3 | 1.3 |
| WC (cm) | 99.6±7.1 | 103.5±11.1$^*$ | 3.9 | 99.1±6.4 | 100.5±9.6 | 1.4 |
| HC (cm) | 112.1±9.2 | 113.6±11.0 | 1.3 | 110.1±10.9 | 113.2±12.2 | 2.8 |
| HGSL (kg) | 29.1±4.9 | 27.0±4.4 | -7.2 | 30.8±5.3 | 29.2±4.8 | -5.2 |
| HGSR (kg) | 27.4±5.7 | 25.1±3.3 | -8.4 | 28.8±6.3 | 27.9±5.6$^\#$ | -3.1 |
| AGIL (s) | 28.7±5.1 | 29.4±4.8 | 2.4 | 27.3±4.6 | 28.1±3.4 | 2.9 |

**BMI:** Body Mass Index, **WC:** waist circumference, **HC:** hip circumference, **HGSL:** palmar grip strength of the left hand, **HGSR:** palmar grip strength of the right hand, **AGIL:** Agility and dynamic balance. **GC:** control group, **GTAU:** taurine group. **Δ% (Post-Pre):** variation post to pre supplementation of each group. Values expressed as mean ± standard deviation. $^*$: Difference post vs. pre within group. $^\#$: Difference between groups in the post intervention, by ANOVA *two-way* repeated measures mixed model, ($p < 0.05$).

Food intake was evaluated before, during (eighth week), and post intervention to identify the food consumption profile. It was observed that the intake of macronutrients and elements investigated reached the reference values of nutrient requirements determined by the Dietary Reference Intake (DRIs) for healthy individuals, except for the elements magnesium and calcium. No nutrient exceeded the upper tolerable intake level (UL) [28] (Table 3). Before intervention, the GTAU group showed higher energy intake (p=0.014), as well as higher protein intake considering the intake in grams per day (g/day) (p=<0.001) and the intake in grams per kilogram of weight per day (g/kg/day) (p=<0.001), when compared to GC.

The nutritional assessment performed during the intervention showed that GC presented increased protein intake when considering g/day (p=0.012) and

g/kg/day (p=0.013). Controversially, the GTAU group presented decreased protein intake when considering g/day (p=0.022) and g/kg/day (p=0.012) in the eighth week, which was also lower in the 16-week assessment when considering g/day (p=0.036) and g/kg/day (p=<0.003), when compared to the pre-intervention values.

No changes were observed regarding carbohydrate and lipid intake (g/day) and (g/kg/day) when comparing pre, during, and post intervention. However, lipid intake (g/kg/day) was higher in the GTAU group pre intervention (p=0.032), when compared to GC.

Regarding essential elements intake before intervention, higher intake of zinc (p=0.005), selenium (p=0.018), magnesium (p=0.023), and calcium (p=0.038) was observed in the GTAU group when compared to GC. Additionally, the intake of zinc decreased in the eighth week (p=0.029) and was even lower post intervention (p=0.028) for the GTAU group when compared to the values observed pre intervention. Similar results were observed for calcium intake when comparing pre and post intervention evaluations for GTAU (p=0.023) (Table 3).

**Table 3.** Food intake before, during, and post intervention.

| | GC (n= 11) | | | GTAU (n= 13) | | |
|---|---|---|---|---|---|---|
| **Macronutrients** | **Pre** | **During** | **Post** | **Pre** | **During** | **Post** |
| Energy (kcal) | 1233.7±215.6 | 1509.9±445.1 | 1350.5±407.8 | 1624.2±456.2[a] | 1527.6±332.6 | 1486.0±453.2 |
| | [67.7 (11.8)] | [82.9 (24.4)] | [74.1 (22.4)] | [89.4 (25.1)] | [83.9 (18.3)] | [81.4 (24.8)] |
| Protein (g/d) | 45.5±8.7 | 59.8±18.8[*] | 54.1±16.7 | 70.4±15.3[a] | 58.3±12.3[*] | 58.2±14.1[#] |
| | [98.9 (18.9)] | [130.0 (40.9)] | [117.6 (36.10] | [153.0 (33.3)] | [126.7 (26.7)] | [126.5 (30.7)] |
| Carbohydrate (g/d) | 162.4±39.3 | 187.8±44.9 | 180.6±52.2 | 201.9±60.6 | 188.9±46.6 | 188.8±70.7 |
| | [124.9 (30.2)] | [144.5 (34.5)] | [138.9 (40.2)] | [155.3 (46.6)] | [145.3 (35.8)] | [145.2 (37.4)] |
| Lipids (g/d) | 42.1±8.6 | 55.6±24.5 | 44.2±15.0 | 57.8±23.8 | 56.4±19.2 | 51.9±19.1 |
| | ND | ND | ND | ND | ND | ND |
| Protein (g/kg/d) | 0.6±0.1 | 0.8±0.3[*] | 0.7±0.2 | 1.0±0.3[a] | 0.8±0.2[*] | 0.8±0.3[#] |
| | [75.0 (12.5)] | [100.0 (37.5)] | [87.5 (25.0)] | [125.0 (37.5)] | [100.0 (25.0)] | [100.0 (37.5)] |
| Carbohydrate (g/kg/d) | 2.1±0.7 | 2.5±0.8 | 2.3±0.8 | 2.8±1.3 | 2.5±0.8 | 2.6±1.5 |
| | ND | ND | ND | ND | ND | ND |
| Lipids (g/kg/d) | 0.5±0.1 | 0.7± 0.3 | 0.6±0.2 | 0.8±0.3[a] | 0.8±0.3 | 0.7±0.5 |
| | ND | ND | ND | ND | ND | ND |

| **Elements** | | | | | | |
|---|---|---|---|---|---|---|
| Zinc (mg/d) | 6.4±2.2 | 7.4±2.9 | 7.2±2.5 | 9.2±2.2[a] | 7.4±2.0[*#] | 7.3±1.8[#] |
| | [80.0 (27.5)] | [92.5 (36.25)] | [90.0 (31.25)] | [115 (27.5)] | [92.5 (25.0)] | [91.3 (22.5)] |
| Selenium (µg/d) | 39.2±14.9 | 52.5±24.6 | 52.3±17.4 | 69.9±46.7[a] | 63.0±56.8 | 45.6±12.6 |
| | [71.3 (38.0)] | [95.5 (44.7)] | [95.1 (31.6)] | [127.1 (84.9)] | [114.5 (103.3)] | [82.9 (22.9)] |
| Magnesium (mg/d) | 157.7±39.9 | 179.9±51.0 | 174.1±43.0 | 219.5±78.7[a] | 195.4±52.0 | 193.1±60.9 |
| | [49.0 (12.5)] | [56.2 (15.9)] | [54.4 (13.4)] | [69.6 (24.6)] | [61.1 (16.3)] | [60.3 (19.0)] |
| Calcium (mg/d) | 442.6±194.5 | 584.4±339.5 | 482.1±174.1 | 701.3±315.5[a] | 525.5±204.6 | 582.2 ± 441.0[#] |
| | [36.9 (16.2)] | [48.7 (28.3)] | [40.2 (14.5)] | [58.4 (26.3)] | [43.8 (17.1)] | [48.5 (36.8)] |

**GC:** control group, **GTAU:** taurine group, **ND:** Reference value not determined by the RDAs. Values expressed as mean ± standard deviation. and [Percentage of adequacy compared to RDAs or AI (standard deviation)]. **[a]:** Difference pre vs. pre between groups. [*]: Difference during vs. pre within groups. [#]: Difference post vs. pre within groups. Difference before, during, and after by ANOVA two-way repeated measures mixed model with Welch correction for macronutrients and elements, ($p<0.05$).

To complement the mineral evaluation and considering that minerals are key factors in the anti-oxidant system [3,29], levels of zinc, selenium, magnesium, and calcium were quantified in plasma samples. It was observed that the mineral levels decreased in both groups post intervention: zinc GC (p=<0.001), GTAU (p=<0.001); selenium GC (p=0.003), GTAU (p=0.004); magnesium GC (p=<0.001), GTAU (p=<0.001); and calcium GC (p=<0.001), GTAU (p=<0.001).

**Table 4.** Blood minerals before and after intervention.

| Blood minerals | GC (n = 11) | | GTAU (n = 13) | |
|---|---|---|---|---|
| | Pre | Post | Pre | Post |
| Zinc (μg/dL) | 110.4±10.5 | 77.8±8.9* | 110.7±16.7 | 84.4±7.4* |
| Selenium (μg/L) | 81.9±17.9 | 54.2±11.4* | 95.1±30.2 | 66.9±18.3* |
| Magnesium (mg/dL) | 2.1±0.3 | 1.5±0.2* | 2.1±0.3 | 1.6±0.2* |
| Calcium (mg/dL) | 10.0±1.3 | 7.2±0.6* | 10.5±1.5 | 7.6±0.5* |

**GC:** control group, **GTAU:** taurine group. Values expressed as mean ± standard deviation. Reference valuers, plasma minerals: Zinc = 70 – 120 μg/dL [30]; Selenium = 60 – 120 μg /L [31]; Magnesium = 1.7 – 2.2 mg/dL [32]; Calcium = 8.6 – 10.3 mg/dL [33]. *: Difference post vs. pre within groups by ANOVA two-way repeated measures mixed model. Wilcoxon-Mann-Whitney test applied to non-parametric data, ($p < 0.05$).

To verify the effects of taurine supplementation, plasma taurine levels were quantified and shown to be increased in GTAU post supplementation (Pre 50.5±11.3 μmol/L and Post 73.9±16.2 μmol/L, p=<0.001). As expected, no changes were observed in plasma taurine levels in the GC group (Pre 45.3±12.2 μmol/L and Post 45.1±7.1 μmol/L, p=0.967). These results highlight that the supplementation protocol was conducted in a rigorous and controlled manner in the population studied.

Activity of the antioxidant system can be evaluated by antioxidant enzymes such as SOD and GR. At baseline, the levels of SOD and GR were higher in the GC group (p=0.027 and p=<0.001, respectively), when compared to GTAU. However, post supplementation, SOD levels increased in the GTAU group (p=<0.001), and were also higher than the levels in the GC (p=<0.001) (Figure

2A). Regarding GR , lower levels were observed in both groups (GC, p=<0.001; and GTAU, p=<0.001) post intervention (Figure 2B).

Antioxidant system efficiency can also be evaluated by the quantification of lipid peroxidation markers, such as MDA. In the present investigation, it was observed that MDA levels were increased in the GC post intervention (p=0.010), when compared to GTAU. However, no changes were observed in the GTAU group, suggesting that taurine prevented the increase in lipid peroxidation (Figure 2C).

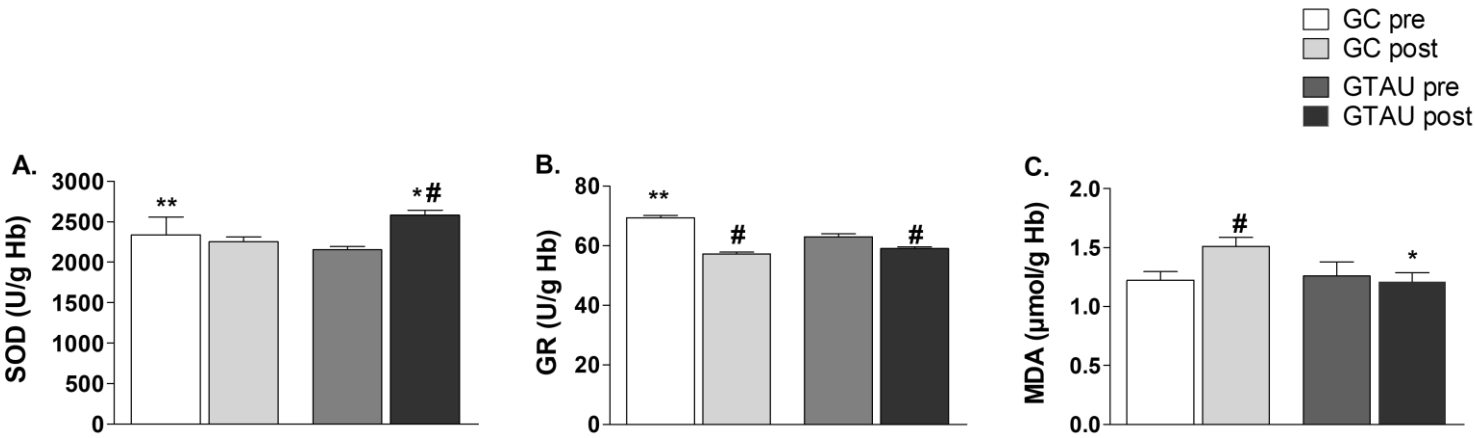



**Figure 2. Levels of oxidative stress markers pre- and post-intervention. GC:** control group; **GTAU:** taurine group. **A.** SOD, superoxide dismutase; **B.** GR, glutathione reductase; **C.** MDA malondialdehyde. Values expressed as mean ± standard deviation. ** Difference between groups pre-intervention . *Difference between groups post-intervention. #Difference within groups post-intervention, by ANOVA two way repeated measures mixed model, ($p < 0.05$). SOD: $\eta^2 = 0.56$; MDA: $\eta^2 = 0.67$.

## Discussion

The purpose of the study was to investigate the effect of taurine supplementation on oxidative stress markers in women aged 55 to 70 years. The results suggest that taurine supplementation for a period of 16 weeks provided considerable benefits to markers of oxidative stress and increased plasma taurine concentration. No changes were observed in the functional capacity post intervention. Although some changes were observed in anthropometric measurements (WC), food intake, and the plasma mineral levels assessed, it is important to consider that the study was performed in a period of intense emotional stress caused by the COVID-19 pandemic.

Regarding taurine supplementation, we observed an increase in the plasma concentration of taurine after 16 weeks of supplementation, but this increase was less expressive than in previous studies carried out by the present research group. It is important to note that the dose used in the other studies was, at least, 2 times higher when compared to the present study and that those studies were carried out with young women with obesity [11,34], and young athletes and healthy adults [12,35]. However, due to the scarcity of data in the literature relating taurine supplementation in women aged 55 through 70 years, we opted for the safe dose of 1.5 g/day previously proposed by Shao and Hathcock [36] and Chupel et al. [13].

Previous studies performed by our research group have indicated that taurine can modulate ROS [11,12]. This function is related to the presence of sulfonic acid in its chemical structure, promoting the conversion of chlorine ions and hypochlorous acid, highly cytotoxic and oxidizing substances, into chloramine taurine (Tau-Cl), a relatively stable substance. Thus, Tau-Cl can decrease the production of inflammatory mediators and inhibit oxidants that cause cell damage [37,38].

Despite the evidence of taurine as a potent antioxidant, there are few studies to date that portray its therapeutic actions in aging, especially with humans [13,18]. Chupel et al. [13] found that taurine supplementation (1.5g/day) plus exercise for 14 weeks in older women showed reductions in myeloperoxidase (MPO), a marker of oxidative stress useful in diagnosing acute coronary syndromes. However, this is the first study to assess the effects of

taurine supplementation on markers such as SOD, GR, and MDA in women aged 55 to 70 years.

In the present study, an increase in plasma concentration of SOD, an antioxidant marker, was observed after taurine supplementation, with an effect size of ($\eta^2 = 0.56$). The plasma levels of zinc were lower in both experimental groups post intervention. This mineral is an essential cofactor for superoxide dismutase enzyme activity, along with copper (Cu/Zn-SOD), which participates in reactions to prevent oxidative damage [29,39,40]. However, knowing that copper is also an essential cofactor of SOD, future studies should evaluate this mineral. SOD is considered the first line of antioxidant defense, promoting the dismutation of superoxide anion ($O_2$-) into hydrogen peroxide ($H_2O_2$) and $O_2$ [29,39]. In a recent study, Kozakiewicz et al. [15] confirmed the occurrence of reduced SOD activity in aging, resulting from increased ROS production. Our results suggest that the antioxidant activity of taurine is possibly related to the "scavenging" action of Tau-Cl, since this compound is able to act as an $O_2$- inhibitor, preventing the decrease in SOD enzyme activity, corroborating with previous studies [8].

As for GR, lower levels were found in both GC and GTAU groups post intervention. This enzyme plays an important role over the glutathione system and is dependent on NADPH to perform its function [29]. After the action of SOD, glutathione peroxidase (GPx) utilizes reduced glutathione (GSH) as a cofactor to reduce hydrogen peroxide ($H_2O_2$) into water ($H_2O$), leading to the formation of oxidized glutathione (GSSG). The enzyme GR catalyzes the conversion of GSSG to GSH and this molecule is used as an antioxidant [29,39,40]. Furthermore, the plasma levels of selenium were lower in GC and GTAU post intervention. This mineral is an important cofactor for glutathione peroxidase (Se-GPx) activity [40]. However, taurine seems to be less efficient against $H_2O_2$ toxicity, according to Oliveira et al. [8]. In addition, lower plasma selenium stocks and a selenium-deficient diet seem to be associated with lower GPx synthesis [41].

Contrary to our findings, previous studies have shown that taurine increased plasma glutathione concentrations in athletes [12], or maintained concentrations stable after taurine treatment in obese women [11], but in both studies the dosage used was 3g/day for 8 weeks, double the dose employed in the present study. However, as previously mentioned, neither of these studies

was conducted with women in the 55 to 70 age group. Furthermore, it is possible that lifestyle, eating habits, time/dose administered, and the period of social isolation due to the COVID-19 pandemic interfered in the results.

Regarding MDA levels, there was a significant increase in the GC, demonstrating a high effect size ($\eta^2 = 0.67$), whereas no changes were observed in the GTAU. These results suggest that taurine supplementation prevented lipid peroxidation. Contradictorily, Yildirim et al. [14] investigated the effects of a single dose of taurine (200 mg/kg/day) for seven days on oxidative stress markers in rodents and found a reduction in the plasma concentration of MDA. Other studies with humans evaluated the effects of taurine supplementation on oxidative stress, using a dose of 6g/day, for seven days [38] and a dose of 3g/day, for 8 weeks [11,12] and observed that taurine reduced levels of lipid peroxidation. Although these investigations demonstrated the antioxidant effects of taurine, we emphasize that none of them were performed with individuals aged 55 to 70 years, and they applied higher taurine doses when compared to the present study.

Magnesium, another important antioxidant mineral, also showed reductions in plasma concentrations in the GC and GTAU. Low levels of this mineral are associated with increased oxidative stress [42], and its deficiency can reduce calcium absorption [32]. In the present study, a significant reduction in plasma calcium concentrations was observed in the GC and GTAU groups. It is important to emphasize that calcium needs are increased in women during the aging process, due to the hormonal changes which are characteristic of the post-menopausal period. Furthermore, its deficiency can lead to bone loss [43].

Although there is no clear evidence of increased oxidative stress in the aging process, it is already known that the antioxidant defenses are not strong enough against oxidative stress [15]. There are several hypotheses about the causes that negatively affect the activity of antioxidant enzymes, including mineral deficiencies resulting from poor eating habits, or even low intestinal absorption, which is common in aging [15]. In general, we observed relatively low consumption of all analyzed minerals, with significant decreases for zinc and calcium in the GTAU. We emphasize that the period of the COVID-19 pandemic was probably a factor that influenced the habits and lifestyle of the participants.

Regarding food intake, although reduced protein intake was observed after 16 weeks of intervention, only the GTAU group remained in accordance with established recommendations - RDA (0.8 g/kg/day) [28]. The results found are possibly related to changes in appetite, food preferences, and protein-based food prices [44,45], among other factors related to the period of social isolation induced by the COVID-19 pandemic [46,47]. Research on aging suggests increasing protein intake with advancing age, which should remain between 1.2 and 2.0 g/kg/day or more, in order to meet nutritional requirements [48,49] and prevent the progressive decline in lean mass, which is a common aging process called sarcopenia [50].

Furthermore, even though there were no changes in energy intake, it is important to consider that the calorie intake was very low, while the participants in both experimental groups showed a prevalence of obesity, that is a BMI higher than 30 kg/m$^2$ according to the WHO classification [51]. These results could be related to underreporting of food intake and possible difficulties in filling out the food records by the participants [52,53].

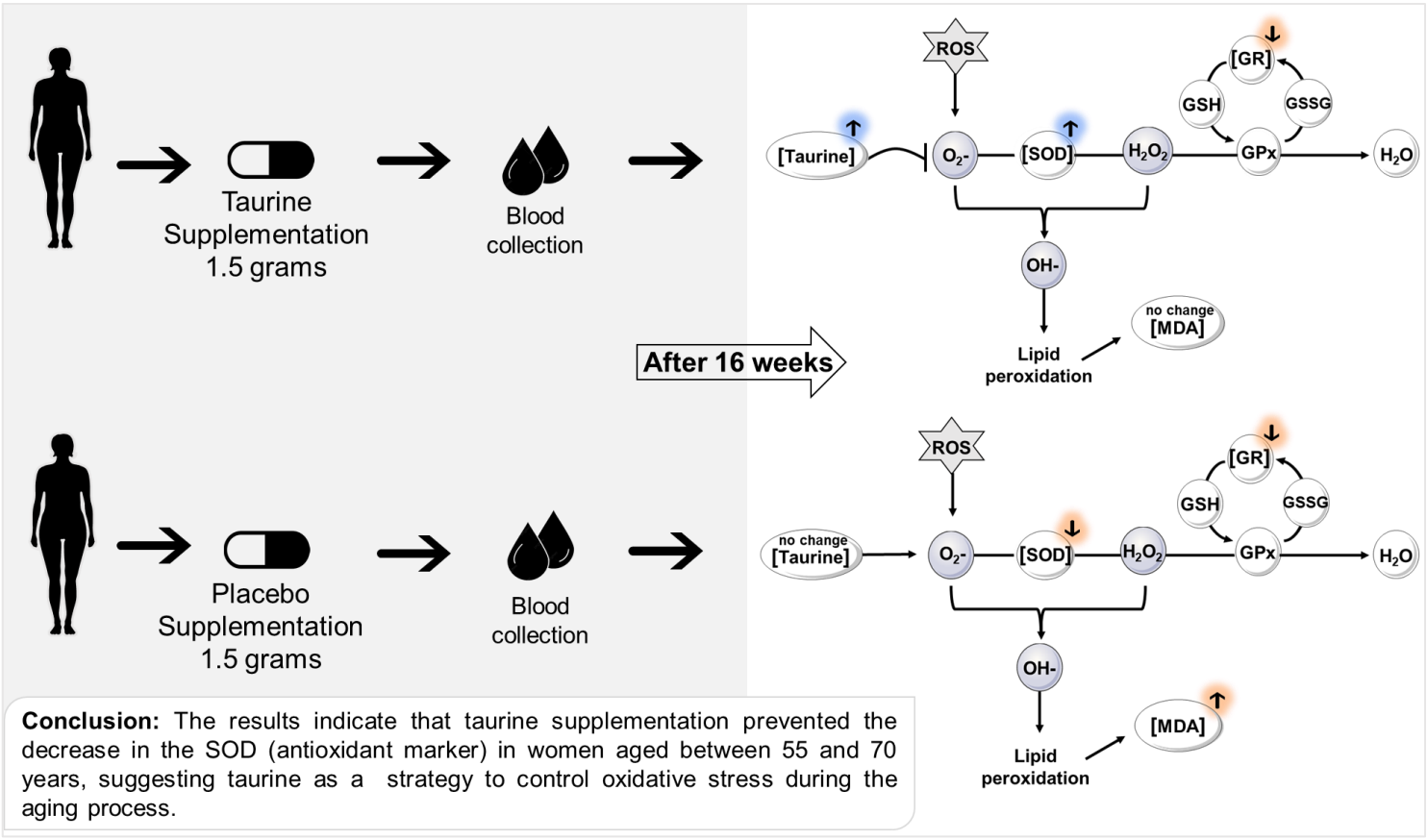
In addition, the increase observed in WC for the GC group was expected because all participants maintained a sedentary pattern, and no nutritional intervention was carried out throughout the intervention, which could impact changes in body weight and anthropometric measurements. It is important to highlight that the BMI and WC values found are associated with an increased risk of metabolic disorders such as hypercholesterolemia, insulin resistance, inflammation, and cardiovascular diseases [54,55].

Functional capacity was accessed pre and post-intervention. In agreement with our findings, a study carried out with individuals over 65 years of age showed greater impairment in the strength and agility variables, especially when associated with a sedentary lifestyle [56]. The slight decline in functional capacity variables was expected since they are not related to taurine supplementation. It is important to highlight that this amino acid does not participate in the protein synthesis process and is not directly associated with muscle strength gain. However, taurine has anti-inflammatory [37] and antioxidant effects [5,57] that could minimize oxidative stress consequences induced by the aging process. It should be considered that the reduction in functional capacity variables in a short

period of time (16 weeks), although not significant, was possibly intensified by the period of social isolation and low activity levels induced by the COVID-19 pandemic, experienced in the present study, which negatively affected the whole body health status of these women [58].

## Conclusion

Overall, the present study indicated a possible protective effect of taurine supplementation through the higher SOD and lower MDA plasma levels observed in the GTAU group post supplementation, when compared to the GC group. Therefore, we believe that taurine supplementation may enhance the antioxidant defense system and could be a viable nutritional strategy to prevent oxidative damage induced by the aging process. Further studies with doses higher than 1.5g/day should be proposed to clarify the potential effects of taurine as an antioxidant agent in aging.




**Conclusion:** The results indicate that taurine supplementation prevented the decrease in the SOD (antioxidant marker) in women aged between 55 and 70 years, suggesting taurine as a strategy to control oxidative stress during the aging process.

**Graphical abstract:** ROS, reactive oxygen species; $O_2$-, superoxide anion; $H_2O_2$, hydrogen peroxide, OH-, hydroxyl radicals; MDA, malondialdehyde; SOD, superoxide dismutase; GPx, glutathione peroxidase; GSSG, oxidized glutathione; GR, glutathione reductase; GSH, reduced glutathione; $H_2O$, water.

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**Conflicts of interest**

The authors declare no conflict of interest.

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## Considerações finais

No que diz respeito sobre a suplementação de taurina em minimizar processos oxidativos a nível celular, ainda é escasso na literatura científica, necessitando de maiores estudos. Porém, nossas observações sustentam a hipótese de que a suplementação de taurina é capaz de modular o sistema de defesa antioxidante e inibir os danos oxidativos, posto que um enfraquecimento das defesas antioxidantes e um estado mais oxidativo é observado no processo de envelhecimento.

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