*Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.*

# Taurine

**Evidence Summary**

Preclinical data of taurine are compelling. Small clinical trials in humans have shown benefits in some measures of physical, metabolic, and cardiovascular function, but results have been inconsistent.

**Neuroprotective Benefit:** Lower circulating levels of taurine may correlate with higher dementia risk. However, small clinical trials have shown inconsistent effects of taurine on cognitive function in humans. Larger, well-designed trials are needed.

**Aging and related health concerns:** Blood taurine levels decline by 80% with aging. Taurine treatment may improve some measures of physical performance, metabolic function, and cardiovascular health, but results are inconsistent across studies.

**Safety:** Taurine is synthesized in our bodies, and it is also present in many foods. It is proposed that supplementation is safe at up to 3 g/day. Taurine inhibits CYP450 2E1 and may interact with some medications (e.g. antihypertensives), alcohol, and caffeine.

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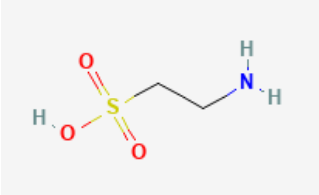
|---|---|---|
| **Availability**: OTC in supplement form; in energy drinks; present in foods | **Dose**: Most clinical trials have tested taurine doses between 1-6 grams, daily, orally. | **Chemical formula:** $C_2H_7NO_3S$<br>**MW**: 125.15<br>  <br>Source: PubChem |
| **Half-life**: plasma elimination half-life between 0.7-1.4 hours | **BBB**: penetrant | |
| **Clinical trials**: The largest meta-analysis of randomized controlled trials included 209 people with diabetes. | **Observational studies**: An observational study of ~12,000 people examined circulating taurine metabolites in relation to age-related diseases. | |

**What is it?**

Taurine is an amino sulfonic acid and is one of the most abundant amino acids found in mammals. Taurine plays a role in various physiological functions, including cardiovascular, metabolic, and muscle function. It is involved in the conjugation of bile acids (e.g., TUDCA), cell membrane stabilization, energy metabolism, anti-oxidation, anti-inflammation, regulation of ER stress and calcium homeostasis (Schaffer and Kim, 2018; Guan and Miao, 2020). In humans, it is a semi-essential micronutrient as we are able to synthesize this in our body from cysteine, which is abundant in high-protein foods. Given its role in metabolic and physiologic processes, taurine has been studied as a potential ergogenic supplement to enhance athletic performance, though the evidence so far is mixed (Ozan et al., 2022).

Blood concentrations of taurine declines significantly with age in mice, monkeys, and humans, and studies have shown that taurine supplementation can extend lifespan and improve healthspan in mice (Singh et al., 2023). Taurine is thought to positively affect several hallmarks of aging, including reduction of cellular senescence, DNA damage, mitochondrial dysfunction, oxidative stress, and inflammation, and protection against telomerase deficiency.

Taurine can be obtained from the diet, such as dark meat, seafood (scallops, clams, octopi, abalone, and fish), dairy products, and seaweed (WebMD.com). Taurine is taken up by cells through taurine transporters. Taurine is also available as a supplement and is often an ingredient in energy drinks and baby formula.

**Neuroprotective Benefit:** Lower circulating levels of taurine may correlate with higher dementia risk. However, small clinical trials have shown inconsistent effects of taurine on cognitive function in humans. Larger, well-designed trials are needed.

*Types of evidence:*

- 4 randomized controlled trials
- 1 prospective controlled trial
- 1 open-label clinical trial
- 1 meta-analysis of CSF and serum/plasma biomarkers for Parkinson's disease
- 1 cohort study evaluating the relationship between amino acid levels and dementia risk
- 1 postmortem study examining brain levels of taurine
- Numerous laboratory studies

***Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function***:

In a pilot double-blind randomized controlled trial of 17 Korean college entrance examinees, taurine jelly (3 g daily) for 2 weeks did not significantly affect measures of learning, but there were some trends for improvement in motivation and self-regulation (p=0.060) compared to before supplementation (Park et al., 2022). It is worth noting that a total of 16 different measures (6 school attitude assessment, 5 college entrance stress, 5 self-regulated learning) were taken before and after intervention without statistical control for multiple comparisons, so statistical trends could possibly have occurred by chance.

In a double-blind randomized controlled trial of 20 elite male boxers (at the national and international level in Turkey), co-ingestion of taurine (3 g) and caffeine (6 mg/kg) significantly improved the neutral reaction time on the Stroop test, compared to taurine alone, caffeine alone, and placebo (Ozan et al., 2022).

In a prospective controlled trial of 48 elderly women (83.58 years old), taurine supplementation (1.5 g/day, dissolved in water; Labor Spirit LTDA, Portugal) alone or combined with exercise for 14 weeks did not significantly alter cognitive function, measured by MoCA (Chupel et al., 2021).

In an open-label clinical study of 26 elderly Koreans (average age, 72.3 years old), supplementation with taurine-containing jelly (3 g; Dong-A Pharmaceutical Co., Ltd) for 4 weeks did not significantly improve cognitive function, as measured by MMSE-dementia screening (MMSE-DS; from 25.9 at baseline to 26.4

after 4 weeks of taurine)(Bae et al., 2022). None of the MMSE-DS subscales (time orientation, place orientation, memory, attention, language, ability to execute, visuospatial constructional ability, and judgement and abstract thinking) showed significant improvements after taurine supplementation compared to baseline. With regards to memory, the total average scores of digit span test-forward (DST-F; but not DST-backward), Korean version of Boston Naming Test (K-BNT), and Korean version of Seoul Verbal Learning Test (K-SVLT) were significantly higher 4 weeks after supplementation (65.7, 51.7, and 17.8 points) than before supplementation (60.6, 46.5, and 15.2 points)($p < 0.01$). The score for subjective memory also was significantly higher 4 weeks after supplementation (3.0 points) than before supplementation (2.6 points)($p < 0.05$). However, because the study was not placebo-controlled or double-blinded, placebo effects and practice effects for these measures cannot be ruled out.

***Human research to suggest benefits to patients with dementia***:

In an open-label controlled clinical study of 46 elderly women with dementia (50% with Alzheimer's disease, 50% with other dementias), treatment with scorched glutinous rice water supplemented with taurine (3 g; Dong-A Pharmaceutical) for 4 weeks improved the total score of MMSE-dementia screening (MMSE-DS) from 14.2 points to 16.7 points ($p<0.01$)(Bae et al., 2019). The group supplemented with taurine and lotus seeds also improved in MMSE-DS, from 13.8 points to 16.9 points ($p<0.01$). Taurine supplementation also improved judgment and abstract thinking ($p<0.05$) compared to baseline. Taurine and lotus seed supplementation improved place orientation and judgment and abstract thinking ($p<0.05$ for both) compared to baseline. Because this was an open-label study and the scores were not directly compared with those of the control group (receiving the scorched glutinous rice water without any supplementation), the cognitive improvements could be due to placebo effects and/or practice effects.

In the Framingham Offspring Cohort that included 2,067 dementia-free subjects, plasma levels of 217 metabolites were assessed in relation to dementia incidence (Chouraki et al., 2017). Higher levels of plasma taurine levels were associated with lower risk of all-cause dementia (HR=0.74; 95% CI, 0.60 to 0.92) but not with Alzheimer's dementia. The authors suggest that taurine may be acting through vascular pathways to prevent non-Alzheimer's dementia, citing studies reporting improved cerebral blood flow, mitochondrial function, and reduced coagulability in animal models.

In a postmortem study of 4 Alzheimer's brains and 8 normal control brains, concentrations of taurine (along with glutamate and GABA) were significantly lower in Alzheimer's brains than in control brains (Arai et al., 1984). In Alzheimer's disease postmortem brains, taurine levels were at 7.9 nM/mg protein, while in control brains, taurine levels were at 15.01 nM/mg protein.

In a meta-analysis of 32 studies of biomarkers (4 of which measured taurine), Parkinson's disease patients had lower CSF levels of taurine compared to age- and sex-matched controls (Jimenez-Jimenez et al., 2020). There were no significant differences in serum/plasma taurine levels between Parkinson's patients and controls. The study also showed that Parkinson's patients had lower CSF levels of glutamate and higher CSF levels of tyrosine.

***Mechanisms of action for neuroprotection identified from laboratory and clinical research***:

In a prospective controlled trial of 48 elderly women (83.58 years old), taurine supplementation (1.5 g/day, dissolved in water; Labor Spirit LTDA, Portugal) for 14 weeks decreased markers of oxidative stress (MPO) and extracellular matrix degradation (MMP-9)(Chupel et al., 2021). No changes in BDNF levels were observed with taurine alone or combined with exercise training.

In a double-blind randomized controlled trial of 32 patients with traumatic brain injury, taurine treatment (30 mg/kg/day) in addition to Standard Entera Meal for 14 days significantly decreased serum levels of a pro-inflammatory marker, IL-6 ($p=0.04$), improved the Glasgow coma scale ($p=0.03$), reduced weight loss ($p=0.03$), and marginally improved the Acute Physiology and Chronic Health Evaluation II (APACHEII) score ($p=0.05$), compared to patients receiving the Standard Entera Meal alone (Vahdat et al., 2021). There were no effects of taurine treatment on other inflammation biomarkers (IL-10, hs-CRP, and TNF-α) or other functional scores (SOFA and Nutrition Risk in Critically Ill).

In a mouse model of Alzheimer's disease (APP/PS1 mice), oral taurine supplementation (1000 mg/kg/day in drinking water) for 6 weeks rescued cognitive deficits to levels comparable to age-matched wild-type mice on the Y-maze and passive avoidance tests (Kim et al., 2014). In the cortex of APP/PS1 mice, taurine slightly decreased the insoluble fraction of Aβ.

In mice infused with oligomeric Aβ, oral taurine supplementation (250 mg/kg/day in drinking water) for 10 days improved cognitive deficits as measured by Y-maze and passive avoidance tests without altering physical activity (Jan et al., 2017). Additionally, taurine directly bound to Aβ based on surface plasmon resonance analyses.

In a mouse model of Alzheimer's disease (5xFAD mice), taurine treatment started at 2 months of age did not result in differences in amyloid pathology compared to untreated mice, though it increased the mGluR5 (glutamate receptor) binding, based on PET imaging (Oh et al., 2020).

In a rat model of cognitive impairment (induced by intracerebroventricular streptozotocin), taurine treatment (40, 60, and 120 mg/kg, orally) for 28 days attenuated cognitive impairment, while decreasing inflammation (TNF-α, IL-1β) and oxidative stress, and increasing cholinergic activity (decreased cholinesterases, increased ChAT) (Reeta et al., 2017).

In a chick retinal neuronal culture, taurine protected against the neurotoxicity of amyloid and glutamate receptor agonists, through the activation of GABA-A receptors (Louzada et al., 2004).

Other neuroprotective mechanisms of action of taurine include its ability to boost expression of an enzyme, cystathionine beta-synthase that synthesizes H2S, which exerts a variety of neuroprotective effects including anti-oxidative effects and vascular-protective effects (McCarty et al., 2019). Taurine has also been associated with anti-excitotoxic effects, which could lead to neuroprotection in many neurodegenerative diseases.

***APOE4 interactions***:
Unknown for taurine. Homotaurine (tramiprosate), which is structurally similar to taurine, failed in a phase 3 clinical trial in Alzheimer's patients, but a subgroup analysis showed that it stabilized cognition in APOE4 carriers (Homotaurine report).

**Aging and related health concerns:** Blood taurine levels decline by 80% with aging. Taurine treatment may improve some measures of physical performance, metabolic function, and cardiovascular health, but results are inconsistent across studies.

*Types of evidence:*

- 8 meta-analyses or systematic reviews
- 14 randomized controlled trials
- 3 open-label trials
- Several observational studies
- Numerous laboratory studies

***Lifespan***: BLOOD LEVELS DECLINE WITH AGING; LIFESPAN EXTENDED IN MICE AND WORMS

Serum taurine levels in older people are decreased by more than 80% compared with those in younger people (Singh et al., 2023). Blood levels of taurine also decrease with age in monkeys and mice. In 15-year-old monkeys, serum taurine levels were 85% lower than in 5-year-old monkeys. In wild-type mice, serum taurine concentrations declined from 132.3 ± 14.2 ng/ml at 4 weeks of age to 40.2 ± 7.1 ng/ml at 1 year old.

In middle-aged (14-month-old) wild-type male and female mice (C57Bl/6J), taurine treatment (1,000 mg/kg/day, orally) until end-of-life extended median life span by 10 to 12% and life expectancy at 28 months increased by about 18 to 25% (Singh et al., 2023). This increased lifespan and life expectancy was accompanied by improved functioning of bone, muscle, pancreas, brain, fat, gut, and immune system, indicating an overall increase in health span. Taurine treatment suppressed the age-associated body weight gain by 10% compared with controls, without altering body length or food consumption. Compared to controls, taurine treatment increased bone mass in both the spine and femur, and improved maximal load and stiffness (surrogates of bone quality) in the femur.

Taurine treatment also extended both the median (by 10-23%) and maximum lifespan in *C. elegans* worms in a dose-dependent manner (Singh et al., 2023). But taurine treatment did not affect the replicative lifespan of *Saccharomyces cerevisiae*, a unicellular yeast.

***Physical performance***: SOME STUDIES SHOWED BENEFIT; OTHERS SHOWED LACK OF BENEFIT

A meta-analysis of 10 clinical trials (7 crossover, 3 independent group design) testing taurine treatment (1 to 6 g/day, orally) reported that taurine ingestion improved overall endurance performance (Hedges' g=0.40; p=0.004) and time-to-exhaustion (Hedges' g=0.43, p=0.007)(Waldron et al., 2018). No differences were seen between acute taurine or chronic (up to 14 days) taurine interventions. The dose of taurine did not moderate its effect on endurance performance. The authors speculated that the beneficial effects of taurine may be attributed, in part, to improved metabolic efficiency, anti-oxidative actions, and stabilization of the mitochondrial matrix resulting in efficient ATP turnover. These possibilities require validation in human studies.

In a meta-analysis of clinical studies testing ergogenic aids in female athletes (of which 2 studies tested taurine), taurine treatment improved aerobic tests (measured by end power)(Lopez-Torres et al., 2022). However, the authors noted that further studies are needed.

In a meta-analysis of 25 studies testing dietary supplements (e.g., caffeine, creatine, nitrate, taurine, polyphenols, etc.) in endurance exercisers, taurine treatment had a non-significant positive effect on exercise performance in the heat, which was accompanied by a significant reduction in end core temperature compared to placebo (p=0.035)(Peel et al., 2021). These effects may occur, in part, due to taurine-induced increased sweating and enhanced vasodilation, facilitating evaporative and dry heat transfer during exercise (Sun et al., 2016; Page et al., 2019).

In a double-blind randomized controlled trial of 20 elite male boxers (at the national and international level in Turkey) performing an anaerobic test on a specialized cycle ergometer (Monark 895E, Peak Bike, Vansbro, Sweden), co-ingestion of taurine (3 g) and caffeine (6 mg/kg) taken 60 minutes before the anaerobic test significantly improved peak power, average power, minimum power, time to reach peak power, and the rating of perceived exertion compared to placebo (Ozan et al., 2022). Co-ingestion of taurine and caffeine led to greater peak power and average power compared to taurine or caffeine alone. However, single or combined doses of taurine and caffeine did not affect lactate compared to placebo. The authors speculate that these benefits in anaerobic strength may be attributable, in part, to increased taurine-induced calcium release in the sarcoplasmic reticulum and caffeine-induced activity of the Na+/K+-ATPase channels, together improving the sensitivity of myofilaments that generate force in skeletal muscles.

In a prospective controlled trial of 48 elderly women (83.58 years old), taurine supplementation (1.5 g/day, dissolved in water; Labor Spirit LTDA, Portugal) combined with exercise for 14 weeks improved physical fitness, as measured by the "8 foot-up and go-test" and "2-min step test"(Chupel et al., 2021). However, no effects were observed for the 30-sec chair stand test, 30-sec arm curl test, or hand-grip strength.

In a double-blind randomized controlled trial of 24 women ages 55 to 70, taurine treatment (1.5 g/day) for 16 weeks did not significantly change functional capacity test scores, though the intervention improved palmar grip strength of the left hand compared to the placebo group (1.5 g/day of starch)(Abud et al., 2022).

In a double-blind randomized controlled crossover study of 11 trained male cyclists, a single oral acute dose of taurine (1,000 mg in 500 ml water; Acrōs Organics, Geel, Belgium) 2 hours before three, 4-km time trials did not significantly affect performance or biomarkers such as VO2, lactate, pH, or HCO3- compared to placebo (Ward et al., 2016). This study showed that a pre-exercise dose of taurine (1,000

mg) offers no performance advantage in a cycling time trial, nor does it positively affect blood buffering responses to high intensity exercise.

In a double-blind crossover study of 11 young physically active male university students, taurine (1 g; My Protein, Manchester, UK) and caffeine (80 mg) cotreatment one hour prior to 10 x 6-second sprints on a cycle ergometer (separated by 24 seconds) resulted in small differences in peak power and intrasprint fatigue (Jeffries et al., 2020). Intrasprint fatigue was slightly greater in the taurine + caffeine cotreatment compared to placebo at sprint 10 and likely also in sprints 6-9. The taurine + caffeine cotreatment had a large effect on increasing heart rate at baseline (140 ± 16 beats/min vs 127 ± 20 beats/min with placebo) and increasing blood lactate concentration after sprints 5 and 10. There was no effect of taurine + caffeine on the rating of perceived exertion. Eight of the 11 subjects showed a trend for a worse maintenance of power in the final sprint of the taurine + caffeine condition compared to placebo, with marginal differences in the remaining 3 subjects. Together, taurine and caffeine administration at doses equivalent to commercial energy drinks failed to improve repeat-sprint cycling performance and may have induced greater fatigue in select sprints, particularly the latter half of the trial. A caveat of this study is despite double-blinding procedures, 5 out of 11 subjects correctly guessed the taurine + caffeine cotreatment, which may have affected their expectations.

In a double-blind randomized controlled trial of 29 young healthy men, taurine treatment (2.0 g, 3 times daily) for 14 days prior to exercise, on the day of exercise (2 sets of 20 maximal-effort eccentric repetitions with the nondominant arm), and 3 days following exercise significantly attenuated the increase in malondialdehyde (MDA) and carotid-femoral pulse wave velocity, measures of oxidative stress and arterial stiffness, respectively (Ra et al., 2016). These findings suggest that taurine may delay the increase in arterial stiffness after exercise.

In a randomized controlled crossover study of 17 healthy young male volunteers, acute taurine treatment (6 g) before exercise did not significantly improve high-intensity running time-to-exhaustion or the "alternative maximal accumulated oxygen deficit" (Milioni et al., 2016). The exercise consisted of 2 bouts of supramaximal treadmill-running at 110% exercise intensity at maximal oxygen uptake until exhaustion.

In male athletes (sprinters, endurance runners, and bodybuilders), a graded cycle exercise test significantly increased (by 1.16-fold) circulating taurine levels ($p<0.05$)(Singh et al., 2023). Levels also tended to be higher after exercise in sedentary subjects, though the change was not statistically significant ($p=0.067$).

In middle-aged (14-month-old) wild-type male and female mice (C57Bl/6J), taurine treatment (1,000 mg/kg/day, orally) increased total hanging time and distance run in the rotarod test (Singh et al., 2023). The latency to fall in the wire hang test was also increased with taurine treatment. Taurine treatment also increased muscle strength as measured by grip strength tests, compared to controls.

***Cardiovascular diseases***: MAY DECREASE BLOOD PRESSURE AND IMPROVE SOME BIOMARKERS

In a meta-analysis of 12 randomized controlled trials in patients with cardiometabolic dysregulation (diabetes, cardiac surgery patients, hepatitis, fatty liver, etc.), taurine treatment (0.5-6 g/day) for a range of duration (15 days to 6 months) decreased systolic blood pressure (weighted mean difference [WMD]=-4.67 mmHg, p=0.04), diastolic blood pressure (WMD=-2.90 mmHg; p<0.001), total cholesterol (WMD=-0.87 mg/dl; p<0.001), and triglycerides (WMD=-13.05 mg/dl; p=0.046)(Guan and Miao, 2020). However, no effects were found on fasting blood glucose, HDL-cholesterol, LDL-cholesterol, BMI, or body weight.

In a meta-analysis of 103 participants of varying age and health statuses (heart failure, borderline hypertensive, liver cirrhosis, healthy, etc.), taurine treatment (1.5-6.0 g/day, orally) for up to 12 weeks reduced systolic and diastolic blood pressure (p<0.0001 for both)(Waldron et al., 2018). These results translated to a mean of 3 mmHg reduction in systolic and diastolic blood pressure.

In a double-blind randomized controlled trial of 120 patients with prehypertension, taurine treatment (1.6 g/day) for 12 weeks significantly decreased the clinic and 24-hour ambulatory blood pressures, especially in people who had high-normal blood pressure (Sun et al., 2016). The mean reductions in clinic systolic and diastolic blood pressures for the taurine group were 7.2 mmHg and 4.7 mmHg, respectively, and for the placebo group were 2.6 mmHg and 1.3 mmHg, respectively. The mean reductions in ambulatory systolic and diastolic blood pressures for the taurine group were 3.8 mmHg and 3.5 mmHg, respectively, and for the placebo group were 0.3 mmHg and 0.6 mmHg, respectively. Additionally, taurine treatment significantly improved endothelium-dependent and endothelium-independent vasodilation and increased plasma H2S and taurine concentrations. In human and mouse mesenteric arteries, taurine upregulated the expression of hydrogen sulfide-synthesizing enzymes and reduced agonist-induced vascular reactivity through the inhibition of transient receptor potential channel subtype 3-mediated calcium influx.

The retina and myocardium have the highest levels of free taurine in the body. Dilated cardiomyopathy is a condition in which the heart chambers enlarge and lose their ability to contract. Taurine has been well-studied in veterinary medicine for the treatment of dilated cardiomyopathy (Pion et al., 1992). In a systematic review of 11 studies in heart failure (case reports, cohort studies, and randomized clinical trials), taurine supplementation (500 mg to 6 g/day, oral delivery method varied across studies) for 2 weeks to 12 months did not significantly improve ejection fraction or stroke volume (McGurk et al., 2022). Studies reported significant improvements in other metrics such as LVEF, exercise capacity, and hemodynamic parameters, but there were not enough studies to perform meta-analyses on these measures. Sample sizes were small for the included studies and a well-designed randomized controlled clinical trial is required to assess whether taurine supplementation is beneficial to patients with heart failure or dilated cardiomyopathy.

***Type 2 diabetes***: MAY IMPROVE SOME METRICS

In a meta-analysis of 5 randomized controlled trials including a total of 209 type 2 diabetes patients, taurine supplementation for 2-16 weeks significantly reduced HbA1c (SMD=-0.41; p=0.01), fasting blood sugar (SMD=-1.28; p=0.03), and HOMA-IR (SMD=-0.64; p=0.03)(Tao et al., 2022). Taurine also showed a tendency to reduce insulin (p=0.06) and triglycerides (p=0.07) but did not reach statistical significance. No changes in serum lipids (HDL, LDL), blood pressure, energy/protein/carbohydrate intake, or body composition (body weight, BMI, waist circumference) were observed.

In a double-blind randomized controlled trial of 46 patients with type 2 diabetes, taurine treatment (3,000 mg/day) for 8 weeks significantly reduced the mean serum levels of fasting blood sugar, HbA1c, insulin, HOMA-IR, total cholesterol, and LDL cholesterol ($p<0.05$)(Esmaeili et al., 2021). This study also reported a significant decrease with taurine in pentosidine and methylglyoxal, measures of advanced glycation end products (AGEs), compared to the placebo group.

In a double-blind randomized controlled trial of 45 patients with type 2 diabetes, taurine treatment (1,000 mg, 3 times daily, orally; Karen Pharma and Food Supplement Co., Iran) for 8 weeks significantly reduced levels of fasting blood sugar (by 7.7% vs 2.0% increase with placebo; p=0.01), insulin (by 5.5% vs 2.7% increase with placebo; p=0.01), HOMA-IR (by 12.6% vs 5.6% increase with placebo; p=0.003), total cholesterol (by 4.8% vs 2.9% increase with placebo; p=0.013), and LDL-cholesterol (by 7.7% vs 3.7% increase with placebo; p=0.041) (Maleki et al., 2020). However, there were no significant effects on HbA1c, triglyceride, HDL-cholesterol, or anthropometric measures (body weight, BMI, waist or hip circumference, or waist-to-hip ratio). Taurine treatment in these same patients increased anti-oxidant

defenses (SOD and catalase), decreased an oxidative stress marker (serum MDA), and decreased inflammation markers (serum hs-CRP and TNF-α) compared to the placebo group ($p<0.05$ for all)(Maleki et al., 2020). No taurine effects were seen in the serum levels of IL-6 or total antioxidant capacity.

In an open-label clinical study of 26 elderly Koreans (average age, 72.3 years old), supplementation with taurine-containing jelly (3 g; Dong-A Pharmaceutical Co., Ltd) for 4 weeks did not alter body weight, blood pressure, or blood glucose levels (Bae et al., 2022). Postprandial glucose was higher after 4 weeks of supplementation in elderly females (138.9 mg/dL) compared to before supplementation (123.6 mg/dL).

In an association analysis of circulating taurine metabolite levels with 50+ clinical risk factors in 11,966 people of the EPIC-Norfolk study, higher levels of taurine metabolites were associated with a lower prevalence of type 2 diabetes and lower glucose levels (Singh et al., 2023).

In aged rhesus monkeys (15 ± 1.5 years old, equivalent to 45 to 50 years old in humans), taurine treatment (250 mg/kg, once daily, orally) for 6 months reduced fasting blood glucose concentrations by 19% (Singh et al., 2023). Taurine-treated monkeys gained 0.75 kg less body weight and their fat percentage tended to be lower compared to controls.

In middle-aged (14-month-old) wild-type male and female mice (C57Bl/6J), taurine treatment (1,000 mg/kg/day, orally) until end-of-life improved insulin sensitivity and these mice metabolized oral glucose more efficiently than control mice (Singh et al., 2023).

***Obesity***: NO CHANGE IN ANTHROPOMETRICS, BUT MAY IMPROVE SOME BIOMARKERS

In a double-blind randomized controlled trial of 38 obese women, taurine treatment (3 g/day, orally) combined with a diet (30% reduction in total energy intake) for 8 weeks significantly lowered total cholesterol ($p=0.03$), LDL-cholesterol ($p=0.03$), leptin ($p=0.006$), total adiponectin ($p=0.04$), and hs-C-reactive protein ($p=0.03$)(Haidari et al., 2020). However, no changes were seen in body weight, BMI, waist circumference, fat mass, fat-free mass, HDL-cholesterol, triglycerides, glycemic indices, and liver enzymes compared to the placebo group (dietary restriction alone).

In a double-blind randomized controlled trial of 24 women ages 55 to 70, taurine treatment (1.5 g/day) for 16 weeks did not significantly change body weight, BMI, or hip circumference (Abud et al., 2022). Waist circumference increased only in the placebo group (1.5 g/day of starch).

In a double-blind randomized controlled trial of 24 obese women, taurine supplementation (3 g daily) alone did not significantly alter anthropometric measures (body weight, BMI, fat-free mass, or fat mass) or mitochondrial markers, though genes related to fat oxidation (ACO2 and ACOX1) were significantly increased in subcutaneous white adipose tissue (de Carvalho et al., 2021). Subjects who were randomized to an exercise intervention or taurine + exercise intervention showed improved subcutaneous white adipose tissue mitochondrial respiratory capacity, increased lipid oxidation rate, and decreased respiratory quotient. No changes were observed for peak lactate levels, total calorie intake, or macronutrient intake.

In another double-blind randomized controlled trial of 22 obese women, high intensity physical training (deep water running, 3 times per week, 50 min per session) combined with taurine treatment (3 g/day, orally) for 8 weeks did not significantly alter body composition, though increased levels of the myokine, irisin (Batitucci et al., 2019). Deep water running increased resting metabolic rate regardless of taurine or placebo (starch) administration.

In an open-label randomized trial of 16 obese women, taurine treatment (3 g/day) increased plasma taurine levels and decreased an inflammation marker, plasma IL-6, but did not alter anthropometric measures (de Carvalho et al., 2021). Taurine treatment combined with exercise training increased anti-inflammatory markers, IL-15 and IL-10 and decreased the gene expression of the inflammatory IL-1β in the subcutaneous white adipose tissue. Gene expression was not altered for adiponectin, leptin, CRP, IL-6, IL-10, IL-15, IFNgamma, MCP1, TNF-α, NFkB, JNK1, PTP1B, and iNOS with taurine alone or combined with exercise. Both taurine-treated and taurine + exercise groups exhibited reduced adipocyte size (by greater than half) and increased connective tissue and multilocular droplets.

In an association analysis of circulating taurine metabolite levels with 50+ clinical risk factors in 11,966 people of the EPIC-Norfolk study, higher blood taurine and hypotaurine levels were associated with lower BMI and waist-to-hip ratio as well as lower abdominal obesity (Singh et al., 2023).

In middle-aged (14-month-old) wild-type male mice (C57Bl/6J), taurine treatment (1,000 mg/kg/day, orally) for 16 weeks did not affect body weight gain but reduced fat-pad weight divided by body weight percentage compared to controls (Singh et al., 2023). This was attributed to the taurine-treated mice consuming more oxygen, generating more carbon dioxide, and having higher respiratory exchange ratios and energy expenditures even though their total activity was decreased compared with that of controls.

***Liver disease***: MAY IMPROVE SYMPTOMS

In a double-blind randomized controlled crossover trial of 39 patients with chronic liver disease (with muscle cramps), taurine treatment (2 g/day, orally) for 4 weeks reduced cramp frequency (7 cramps fewer in 2 weeks, p=0.03), cramp duration (89 minutes less in 2 weeks; p=0.03), and cramp severity (1.4 units less on a Likert scale, p<0.004), compared to placebo treatment (Vidot et al., 2018). Statistically significant effects were not observed with the 1 g/day dose.

Portal hypertension can promote severe (and sometimes fatal) complications of chronic liver disease, including ascites formation, variceal hemorrhage, hepatorenal syndrome, and hepatic encephalopathy. In a randomized controlled trial of 22 cirrhosis patients with portal hypertension, taurine treatment (6 g/day, orally) for 4 weeks significantly reduced hepatic venous pressure gradient (HVPG; measure of portal pressure) from 20 mmHg (±4) at baseline to 18 mmHg (±4)(p=0.0093)(Schwarzer et al., 2018). In the placebo group, the mean HVPG increased from 20 mm Hg (±5) at baseline to 21 mm Hg (±5) after 4 weeks. Taurine treatment significantly increased circulating taurine levels (from 0.56 ng/µL to 7.79 ng/µL), and a significant correlation was found between the magnitude of taurine concentration increase and the magnitude of HVPG drop. These findings suggest that taurine may reduce portal pressure in cirrhotic patients. A caveat to this study includes the limited patient compliance (27% were non-completers), likely due to the severity of liver disease. These initial findings need to be confirmed in larger, double-blind, randomized controlled studies. Currently, non-selective beta-blockers are used to medically reduce portal pressure in patients with esophageal varices, though only 30-60% of patients respond to this treatment.

In a single-arm pilot open-label clinical study of 10 patients with liver cirrhosis, taurine treatment (1 g/50 mL, 3 times daily) for 4 weeks decreased muscle cramp scores (frequency x intensity) in 7 patients (Jan et al., 2021). Compared to the baseline median muscle cramp score of 21, 4 weeks of taurine treatment led to a median score of 6.5 (p=0.126), and this positive trend was sustained at week 8 (median score of 5; p=0.066). Five patients whose baseline plasma taurine levels were below the normal limit showed increased taurine levels at week 4 and 3 of the patients experienced improvements in muscle cramps. Of the remaining 5 patients who had normal or higher taurine levels, 4 of them experienced an improvement in symptoms after 4 weeks of taurine treatment. Given the lack of a placebo control, a placebo effect cannot be ruled out.

In aged rhesus monkeys (15 ± 1.5 years old), taurine treatment (250 mg/kg, once daily, orally) for 6 months reduced the serum concentrations of liver damage markers AST and ALT by ~36 and 20%, respectively (Singh et al., 2023).

***Inflammation/oxidative stress***: IMPROVES INFLAMMATION & OXIDATIVE STRESS BIOMARKERS

In a meta-analysis of 14 controlled studies testing taurine's effects on biomarkers, taurine supplementation (1,500-6000 mg/day, or 50 mg/kg/day) reduced the levels of the oxidative stress marker, MDA (SMD=-1.17 µmol/l; p=0.012), and the inflammation marker, C-reactive protein (CRP; SMD=-1.95 mg/l, p=0.002)(Faghfouri et al., 2022). No effects of taurine treatment were seen for TNF-α and IL-6. Given the limited data, the quality of evidence for these biomarkers were mostly low and need further validation.

In a double-blind randomized controlled trial of 187 elderly hip fracture patients, taurine treatment (6 g/day) started before surgery and up to 6 days post-surgery did not improve in-hospital morbidity or medical comorbidities during the first year, or mortality during the first year (Van Stijn et al., 2015). However, taurine treatment lowered postoperative oxidative stress, as measured by lower urinary 8-hydroxy-2-deoxyguanosine levels (8OHdG; p=0.04) and there was a trend for lower lactate to pyruvate ratio (p=0.08).

In a double-blind randomized controlled trial of 24 women ages 55 to 70, taurine treatment (1.5 g/day) for 16 weeks significantly increased plasma levels of the antioxidant SOD compared to the placebo group (1.5 g/day of starch)(Abud et al., 2022). Malondialdehyde levels increased only in the placebo group.

In an association analysis of circulating taurine metabolite levels with 50+ clinical risk factors in 11,966 people of the EPIC-Norfolk study, higher blood taurine and hypotaurine levels were associated with lower levels of the inflammation marker CRP (Singh et al., 2023).

In aged rhesus monkeys (15 ± 1.5 years old), taurine treatment (250 mg/kg, once daily, orally) for 6 months reduced the numbers of cells associated with aging-related inflammatory states (white blood cells, monocytes, and granulocytes) by 50% compared to control monkeys (Singh et al., 2023). Taurine treatment also decreased serum markers of oxidative DNA damage (8OHdG), lipid peroxide, and protein carbonyls by 36, 11, and 20%, respectively.

In middle-aged (14-month-old) wild-type male and female mice (C57Bl/6J), taurine treatment (1,000 mg/kg/day, orally) significantly decreased plasma levels proinflammatory markers that are elevated with aging, such as TNFα, IL-17α, RANTES (regulated upon activation, normal T cell expressed and presumably secreted), IL-1α, and granulocyte-macrophage colony-stimulating factor (GM-CSF)(Singh et al., 2023). Taurine treatment also decreased the number of cells associated with aging-related inflammatory states (white blood cells, monocytes, and granulocytes).

With regards to oxidative stress, taurine treatment decreased an oxidative DNA damage biomarker, 8-OHdG, and reactive oxygen species accumulation in mitochondria isolated from mouse muscle (Singh et al., 2023). In the liver, markers of lipid peroxidation and protein carbonylation (markers of oxidative stress-induced molecular damage) showed a decrease by 22 and 11%, respectively, compared to control mice. In brown fat, taurine treatment increased a key regulator of mitochondrial biogenesis (Pgc1α) and uncoupling protein 1, which uncouples mitochondrial fuel oxidation and respiration from ATP production, suggesting that taurine promotes mitochondrial homeostasis.

***Senescent cells***: REDUCED IN MICE

In middle-aged (14-month-old) wild-type male and female mice (C57Bl/6J), taurine treatment (1,000 mg/kg/day, orally) until end-of-life decreased the number of senescent cells in the brain, liver, gut, muscle, and fat, measured by SA β-Gal staining (Singh et al., 2023).

***Autophagy/proteostasis***: IMPROVED IN MICE

In middle-aged wild-type mice (C57Bl/6J), taurine treatment (1,000 mg/kg/day, orally) increased autophagy in the liver, brown fat, and skeletal muscle, as measured by the abundance ratio of isoforms A and B of the light chain 3 (LC3A/B) (Singh et al., 2023).

***Bone health***: IMPROVED IN MONKEYS AND MICE

In aged rhesus monkeys (15 ± 1.5 years old, equivalent to 45 to 50 years old in humans), taurine treatment (250 mg/kg, once daily, orally) for 6 months increased bone density and content (measured by DEXA) in the lumbar spine (L1 to L4) and legs, but not in the head, compared to control monkeys (Singh et al., 2023). Serum markers of bone formation (osteocalcin) increased, whereas those of resorption (C-terminal telopeptide of type 1 collagen) decreased after16 weeks of taurine treatment, and these levels were maintained for the duration of treatment.

In middle-aged wild-type mice (C57Bl/6J), taurine treatment (1,000 mg/kg/day, orally) increased bone mass in both the spine and femur, and improved maximal load and stiffness (surrogates of bone quality) in the femur.

**Safety:** Taurine is synthesized in our bodies, and it is also present in many foods. It is proposed that supplementation is safe at up to 3 g/day. Taurine inhibits CYP450 2E1 and may interact with some medications (e.g. antihypertensives), alcohol, and caffeine.

*Types of evidence:*

- 2 meta-analyses or systematic reviews
- 4 randomized controlled trials
- 1 open-label trial
- 1 editorial
- Several laboratory studies

Taurine is a natural compound synthesized in our body and is present in many foods, such as dark meat, seafood (scallops, clams, octopi, abalone, and fish), dairy products, and seaweed (WebMD.com). Taurine is often added to energy drinks and baby formula. Taurine supplementation is proposed to be safe at up to 3 g/day (Drugs.com).

In a systematic review of 11 studies in heart failure (case reports, cohort studies, and randomized clinical trials), taurine supplementation (500 mg to 6 g/day, oral delivery method varied across studies) for 2 weeks to 12 months did not lead to any significant safety concerns (McGurk et al., 2022). Some subjects experienced nausea, vomiting, or diarrhea, but in these cases, taurine was ingested along with other vitamins and minerals, and the authors found it unlikely that taurine played a causal role in these adverse events. Taurine supplementation did not significantly alter blood chemistry (ALP, ALT, AST) or blood urea nitrogen.

In a meta-analysis of 103 participants of varying age and health statuses (heart failure, borderline hypertensive, liver cirrhosis, healthy, etc.), taurine treatment (1.5-6.0 g/day, orally) for up to 12 weeks did not result in any adverse events aside from those reported in the control groups (Waldron et al., 2018).

In a double-blind randomized controlled crossover trial of 39 patients with chronic liver disease (with muscle cramps), taurine treatment (2 g/day, orally) for 4 did not result in adverse side effects that were associated with taurine (Vidot et al., 2018).

In a randomized controlled trial of 22 cirrhosis patients with portal hypertension, taurine treatment (6 g/day, orally) for 4 weeks resulted in treatment-related adverse events such as gastrointestinal discomfort and fatigue, and were usually mild and comparable with placebo treatment (Schwarzer et al., 2018). None of the patients had to discontinue the study medication due to treatment-related adverse events. Serious adverse events were observed in 3 patients, which were not considered to be taurine-related. One patient was admitted to a hospital due to hepatorenal syndrome with hyperpotassemia (6.67 mmol/L) on day 6 of placebo treatment. Another patient was admitted for suspected gastrointestinal bleeding, but the bleeding site was not found, and taurine treatment was continued without interruption. There was one patient in the taurine group who stopped treatment on day 2; he died due to septicemia 25 days later. The authors noted that there is no plausible relation between the study medication and the patient's death.

In an open-label phase 3 trial of 10 patients with stroke-like episodes of MELAS (mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes), a rare genetic disorder, no severe adverse events were associated with taurine treatment (Ohsawa et al., 2019). None of the patients discontinued taurine treatment. There were 84 adverse events reported in all 10 patients over 52 weeks of treatment. Six patients experienced adverse events associated with taurine supplementation. Two severe adverse events were reported: serum creatine kinase elevation and acute gastroenteritis. However, these were not considered to be due to taurine supplementation.

It is worth noting that energy drinks that contain taurine may cause a different collection of adverse events as they contain many compounds beyond taurine, such as caffeine. In a randomized controlled crossover trial of 38 young healthy adults, energy drink consumption (Red Bull GmbH, 3-4 cans of 250 ml) led to 79% of the participants experiencing symptoms, though similar percentage of participants experienced symptoms with other study products (control sports drink, Xenofit Competition Citrus-Frucht, Xenofit, GmbH; control sports drink supplemented with energy drink ingredients: 32 mg/100 mL caffeine, or 400 mg/100 mL taurine, or 31 mg/100 mL glucuronolactone)(Basrai et al., 2019). When excluding mild symptoms, 11-37% of participants reported moderate to severe symptoms, with a high percentage of participants reporting 2 or more symptoms after energy drink consumption. One hour after energy drink consumption, there was a significant increase in systolic blood pressure (from 116.9 ± 10.4 to 120.7 ± 10.7 mmHg; $p<0.01$) and a QTc prolongation (from 393.3 ± 20.6 to 400.8 ± 24.1 ms;

p<0.01). Energy drink consumption also significantly accelerated heart rate compared to baseline (p<0.01). Five out of 38 individuals developed severe symptoms, and these occurred only after administration of the energy drink or the control drink + caffeine. After energy drink consumption (1000 mL), 1 participant reported severe nausea, and another participant developed severe tremor. Two individuals experienced severe tremor after administration of the control drink + caffeine (750 mL). Additionally, 1 participant who drank the control drink + caffeine experienced severe restlessness. Cardiac arrhythmia was not detected in any of the participants. All study products decreased serum glucose and increased insulin levels after 1 hour, compared to baseline. The effects of energy drinks could not be attributed to single components (caffeine, taurine, or glucuronolactone).

In a double-blind randomized controlled crossover trial of 24 patients with familial long QT syndrome, energy drink consumption did not reveal a significant change in QTc compared to the control, but systolic and diastolic blood pressure significantly increased (peak systolic change 7±16 mmHg vs 1±16 mmHg, 6% vs 0.8%, p=0.046; peak diastolic change 8±10 mmHg vs 2±9 mmHg, 11% vs 3%, p=0.01). (Gray et al., 2017). There were 3 patients with dangerous QTc prolongation of ≥50 ms following energy drink consumption. Young patients with long QT syndrome should exercise caution when consuming energy drinks.

***Drug interactions***: Taurine may interact with antihypertensive medications such that taurine may strengthen the effects of these drugs (WebMD.com). Taurine inhibits CYP450 2E1; thus any drugs that are substrates of this enzyme may interact with taurine (Drugs.com). Taurine may also interact with alcohol or caffeine.

**Sources and dosing:**

Taurine can be obtained from the diet, such as dark meat, seafood (scallops, clams, octopi, abalone, and fish), dairy products, and seaweed (WebMD.com). Taurine is also available as a supplement and is often an ingredient in energy drinks.

The average daily consumption of taurine in a non-vegetarian diet is about 400 mg per day (WebMD.com). Most clinical trials have tested taurine doses between 1-6 grams, daily, orally. For athletic performance, ingestion 60-120 minutes before exercise may be recommended for peak taurine bioavailability (Examine.com).

**Research underway:**

There are currently 5 clinical trials testing taurine based on ClinicalTrials.gov. Two studies are in sarcopenic obesity, 1 study is in type 2 diabetes, 1 study is in patients with colon cancer risk, and 1 study is in healthy adults.

**Search terms:**

Pubmed, Google: taurine

- + meta-analysis, + clinical trial, + mortality, + Alzheimer, + cognitive, + APOE

Websites visited for taurine:

- Clinicaltrials.gov
- Examine.com
- DrugAge
- Geroprotectors (0)
- Drugs.com
- WebMD.com
- PubChem
- DrugBank.ca
- Labdoor.com (0)
- ConsumerLab.com