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Taurine, a non-proteinous essential amino acid for human body systems: an overview

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Abstract

Purpose – Taurine (2-aminoethane sulfonic acid; C2H7NO3S) is a nonprotein sulfur-containing β-amino acid present in nearly all mammalian tissues and the most ubiquitous free endogenous biomolecule in human cells. Taurine is commonly known as a conditionally essential amino acid because taurine is one of the few amino acids that are not incorporated in protein synthesis. The purpose of this study is to review the existing articles related to taurine and to give an account how useful is taurine to the different body systems. In this thorough overview, taurine is covered in terms of its essentiality, sources, advantages for neonates and the elderly, the effects of taurine deficiency, and the safety and toxicity of taurine supplements.

Design/methodology/approach – This is a narrative review into the subject matter. Published articles were searched on different portals like PubMed, EMBASE, Scopus, Google Scholar, PubChem etc. The authors also evaluated the availability of taurine in commercially available energy drinks.

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Authorship contribution statement

Nadeem Rais: Investigation, Writing – original draft, formal analysis, data curation, writing – review and editing, compiled the figures and tables.

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Mohd. Shadab: Writing – original draft, formal analysis, data curation, writing – review and editing, compiled the figures and tables.

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Mohammad Shahid: Formal analysis, writing – review and editing, data curation validation.

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Findings – This comprehensive review, presents the potential clinical benefits and functional properties of taurine as a conditionally essential amino acid. Energy drinks containing taurine (and their concentration) are also reported in this review.
Originality/value – This is the first data that the authors are aware of that shows taurine content in a variety of energy drinks on the market.

Keywords Taurine, Cysteine sulfinic acid, L-cysteine, L-methionine, β-amino acid, Taurine in energy drinks
Paper type Literature review

Introduction

Leopold Gmelin and Friedrich Tiedemann, two German scientists, were the first to identify the currently recognized taurine derived from the bile of an ox in 1827, and they labeled it Gallen-Asparagin. Afterward, it was given the name taurus, which comes from the Latin word Bos taurus, which means Ox. However, von H. Demarcay was the first to use the current word, taurine, in the literature in 1838. The function of taurine towards homeostasis has captivated the scientific community's interest since 1975 (Baliou *et al.*, 2021). The objective of this study is to evaluate the available taurine-related literature and describe how taurine benefits the various bodily systems. In this comprehensive review, taurine is discussed in terms of its essentiality, sources, health benefits in newborns and elderly, and consequences of its deficiency, as well as safety and toxicity of taurine supplementation. This evaluation also includes information on taurine-containing energy drinks and their concentration.

Taurine is a sulfur-containing amino acid that is connected in a variety of biological and physiological activities in humans. It is nonessential in rodents (such as mice and rats), essential in felines (such as cats) and conditionally essential in humans (Colovic, Vasic, Djuric, & Krstic, 2018). Taurine, unlike real amino acids, is not integrated into proteins and is found in abundance in numerous human tissues, including retina, leukocytes, platelets, skeletal- and cardiac-muscles, as well as the brain (Table 1) (Jacobsen & Smith, 1968). Since, it is one of the conditionally essential amino acids the adult human body can synthesize it. However, it is unknown whether it can make enough amounts to meet its own demands; therefore, we are all likely to rely on dietary taurine. Taurine is found in most mammals, with concentrations

Tissue	μmoles/gm (wet wt.)
Retina	30–40
Leukocytes	20–35
Thrombocytes	16–24
Spleen	11.40
Heart	06
Muscles	02.20–05.40
Kidney	01.40–01.80
Lung	01–05
Brain (fetal/non-fetal)	01.80–05.70/0.8–04.30
Liver (fetal/non-fetal)	02.40/0.30–01.80
Erythrocytes	0.05–0.07
Fluid	**μmoles/ltr (conc.)**
Milk	337
Bile	200
Plasma/serum	25–277
Saliva	16–65
Cerebrospinal fluid	05–10
Sweat	Minute quantity

Note(s): *Table is adopted and modified from Jacobsen and Smith (1968)

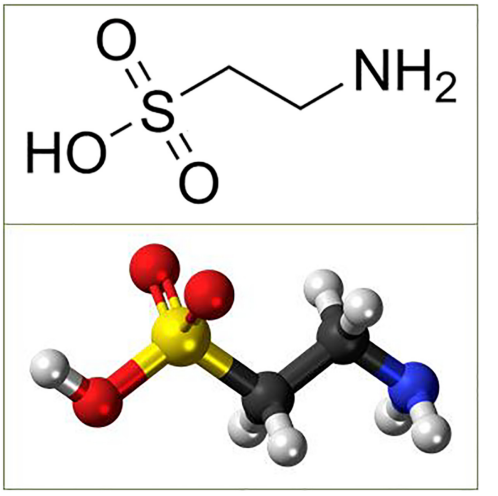
Table 1. Distribution of taurine in humans*

ranging from micro to milli molar. Taurine makes up 0.1% of a normal human's total weight, or 70 g, in a 70 kg person (Chaudhry, Tandon, Gupta, & Gupta, 2018). Several animal and human studies have recently sparked attention of scientists, emphasizing its usefulness in clinical nutrition and as a possible pharmaconutrient (Jacobsen & Smith, 1968; Jong, Sandal, & Schaffer, 2021; Joseph, Varughese, & Daniel, 2021).

According to reports, children from vegan families that consume little to no taurine, have a higher frequency of pediatric problems. As a result, taurine has been introduced to both infant formula and parenteral solutions. Taurine is primarily obtained through the diet in healthy people, while it can also be produced within the body from cysteine and methionine in the presence of vitamin B_6 (Froger *et al.*, 2014). Taurine is found in a variety of foods, especially shellfish and meat. The average daily intake of omnivorous meals was found to be approximately 58 milligrams. Taurine-containing energy beverages, which typically contain about 1 g of taurine, are sold all over the world for the treatment of a variety of ailments, as well as for improving sports performance and general well-being (Jong *et al.*, 2021). Taurine is believed to be involved in a variety of biological processes. Its deficiency is linked to the development of disorders in numerous organs, including eye, heart, kidney, liver and brain, both during infancy and later in life (Antonarakis, 2020; Jong *et al.*, 2021; Joseph *et al.*, 2021; Veeravalli *et al.*, 2020; Wu, 2020).

Essentiality of taurine

Taurine ($NH_2CH_2CH_2SO_3H$) (Figure 1) has become more widely recognized as a conditional amino acid for humans, and its supplementation has shown to be benefitting everyone from newborns to the elderly. An "essential" nutrient is one that cannot be generated de novo by the organism from resources normally available to the cells at a rate sufficient to meet the demands of normal development, body maintenance and other physiological processes (Kilb & Fukuda, 2017; Sinha, Manna, & Sil, 2007). There is sufficient evidence available to justify taurine's status as an essential-amino acid in pediatric disorders and a conditionally-essential-amino acid in various adult disorders (Antonarakis, 2020; Jong *et al.*, 2021; Joseph *et al.*, 2021; Veeravalli *et al.*, 2020; Wu, 2020). Experiments in rats, chickens, cats, pigs and



Source(s): Information (2022)

Figure 1.
Chemical structure of an amino sulfonic acid – taurine which is 2-amino derivative of ethanesulfonic acid

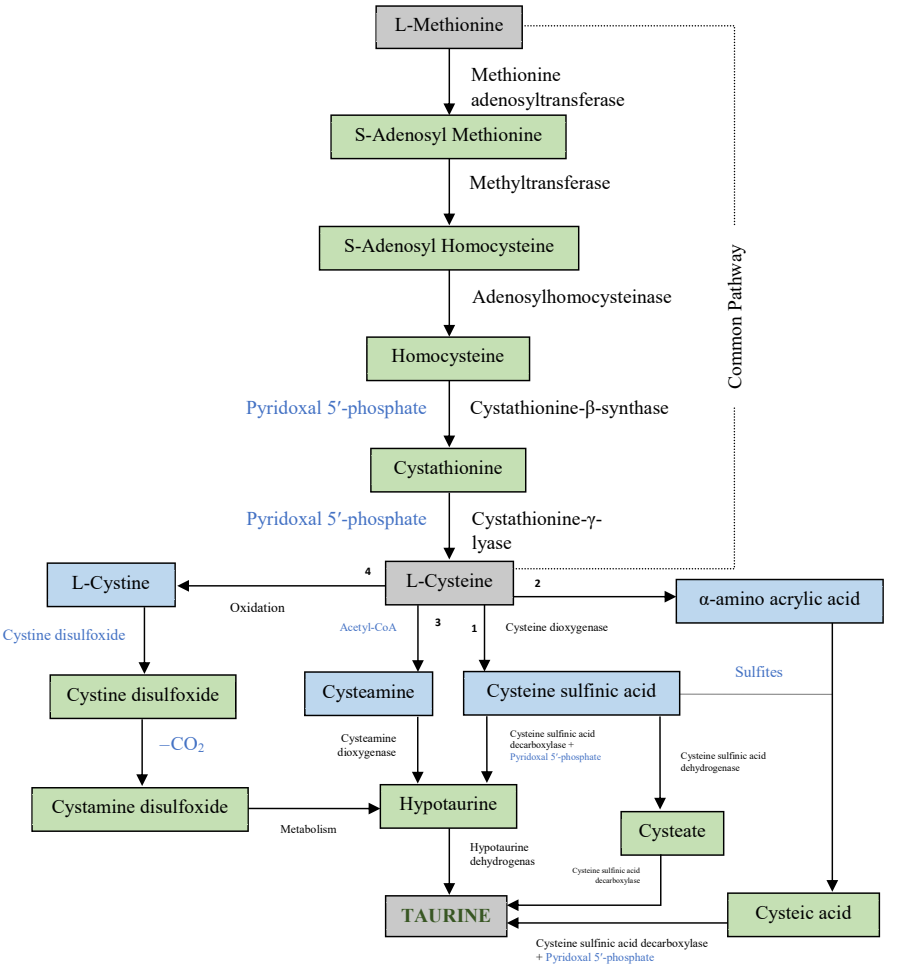
primates have proved that the insufficiency of taurine results in deformities in progression of the central nervous system, retina, cardiovascular system, immunological system, reproductive system and tapetum lucidum (Hayes & Trautwein, 1989; Militante & Lombardini, 2004; Wu, 2020).

Despite the fact that humans are unable to synthesize substantial amounts of taurine, human tissues retain more taurine than cats or foxes. Humans, unlike cats, do not acquire overt indications of taurine deficit, regardless of the fact that parenteral feeding has been linked to taurine deficiency. In obese women, supplementation of taurine has also been associated to a reduce body mass index (BMI) and lower levels of inflammatory markers. As a result, taurine's cytoprotective characteristics aid in the clinical and nutritional well-being of humans (Bouckenooghe, Remacle, & Reusens, 2006; Marcinkiewicz & Kontny, 2014). The antecedents of taurine, methionine and cysteine, are normally available to cells, and de novo production can occur via numerous mechanisms. The pace of synthesis, on the other hand, is controlled not only by the availability of its antecedent methionine and cysteine, but also by the appropriate levels of activity of the essential biosynthetic enzymes (Marcinkiewicz & Kontny, 2014). Enzymatic performances can be influenced by developmental maturity, genetic variability, tissue health at the site of metabolism and availability of cofactors such as pyridoxyl-5-phosphate (P5P). Taurine's roles in a variety of physiological processes, as well as the positive effects of supplementation, have established a foundation for its continued use in patient care. Taurine is important not just in therapy but also as a preventive medicine. There are compelling reports that taurine insufficiency can have adverse clinical consequences (Bouckenooghe *et al.*, 2006; Hayes & Trautwein, 1989; Marcinkiewicz & Kontny, 2014; Militante & Lombardini, 2004).

Biosynthesis pathways of taurine

The precursors of taurine are L-methionine (the essential amino acid) and L-cysteine (the nonessential amino acid); however, synthesis capability varies enormously between species; the maximum human synthesis rate is uncertain. Adults' daily synthesis spans from 0.4 to 1.0 mmol. Synthesis capacity may be impaired under stress; hence some researchers regard taurine to be a conditionally necessary amino acid. Endogenous taurine production takes place mostly in the liver and brain, and involves numerous processes including oxidation of enzymes and cysteine conversion, either straight into taurine or after conversion of methionine into cysteine, then into taurine. The three main enzymes involved are cystathionine-β-synthase, cystathionine-γ-lyase, and cysteine sulfinic acid decarboxylase (CSAD), all of which require pyridoxal 5′-phosphate, the active co-enzyme form of vitamin B_6, as a cofactor. Vitamin B_6 insufficiency has been proven to impede taurine biosynthesis due to low intake, drug antagonism or altered metabolism by one or more diseases (Chen *et al.*, 2021; Stone *et al.*, 2021; Wang, He, Mai, Xu, & Zhou, 2016). The direct synthesis of taurine from L-cysteine can be accomplished in four pathways (Figure 2). The capacity to synthesize taurine is assumed to be reflected by the function of CSAD, an enzyme that transforms cysteine sulfinic acid into hypotaurine and cysteic acid into taurine (Chen *et al.*, 2021; Wang *et al.*, 2016). The quantity of CSAD enzyme has been reported very low in the cat and, low in humans and primates (Baliou *et al.*, 2021; Jacobsen & Smith, 1968).

The main biosynthetic process comprises the catalyzed conversion of cysteine through cysteine dioxygenase enzyme to cysteine sulfinic acid, from which carbon dioxide is removed by CSAD to form hypotaurine, which is subsequently oxidized by hypotaurine dehydrogenase to produce taurine. In the second pathway, the sulfur in cysteine sulfinic acid can be oxidized by cysteine dioxygenase, transformed to cysteic acid with the help of α-amino acrylic acid, and then decarboxylated straight to taurine (Chen *et al.*, 2021; Stone *et al.*, 2021). In the third pathway, cysteamine produces a variety of cystamine intermediates,



Note(s): The first pathway starts from the catalyzed conversion of cysteine to cysteine sulfinic acid, from which carbon dioxide is removed by cysteine sulfinic acid decarboxylase to make hypotaurine, which is then oxidized by hypotaurine dehydrogenase to produce taurine. In the second pathway, the sulfur in cysteine sulfinic acid can be oxidized by cysteine dioxygenase, converted to cysteic acid by α-amino acrylic acid, and then decarboxylated directly to taurine. In the third pathway, cysteine forms a number of cystamine intermediates, which are then transformed to hypotaurine, which is then turned to taurine. The fourth pathway begins with L-cystine, which is an oxidized form of L-cysteine, and proceeds through cystine disulfoxide, cystamine disulfoxide, hypotaurine and finally converted into taurine

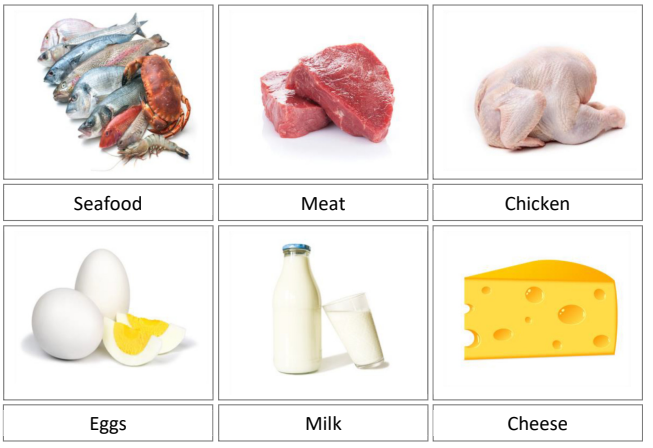
Figure 2.
The biosynthesis steps from L-methionine to L-cysteine are common in all pathways

which are subsequently converted to hypotaurine, which is ultimately converted to taurine. The fourth pathway begins with L-cystine, an oxidized version of L-cysteine, and progresses through cystine disulfoxide, cystamine disulfoxide, hypotaurine and then taurine. Remarkably, taurine's biosynthetic capacity is highest during pregnancy and gradually declines during adulthood, reaching its lowest levels in the elderly and in some pathological

circumstances (sepsis, trauma). As a result, taurine biosynthesis does not produce the amount of taurine required for homeostasis, and exogenous taurine supplementation becomes necessary. Taurine content varies depending on dietary consumption of animal/sea origin, and everyday taurine requirement is expected to range between 40 and 400 mg (Liu, Watson, Place, & Jagus, 2017; Ueki & Stipanuk, 2007; Wang *et al.*, 2016).

Source of taurine

Except for protozoans, taurine levels are very high in the animal kingdom. Diet is the primary source of taurine in humans; however, taurine synthesis occurs in the brain and liver endogenously, primarily during developmental stages and to a lesser extent thereafter. Taurine can be obtained from seafood (particularly shellfish such as mussels, clams and oysters), muscular meat and organs (especially the heart and liver) and dark meat of chicken and turkey. Invertebrates, such as marine arthropods and mollusks, have a high taurine content; insects and fish also have a high taurine content. Thus, primary dietary sources of taurine are seafood and meat, and persons who do not consume these items on a regular basis, especially vegetarians, may be at higher risk of taurine insufficiency. Taurine can also be found in milk (fermented goat's milk has 20 times more taurine than cow's milk), cheese and eggs to a smaller level (Figure 3). Taurine is widely distributed in mammals, with significant concentrations seen in platelets and electrically excitable tissues (Jeong & Choi, 2019; Laidlaw, Grosvenor, & Kopple, 1990; Schaffer & Kim, 2018). Because endogenous synthesis is insufficient and insignificant in practice, regulation must maintain a balance between intake and excretion via a process of accumulation, release, absorption, transport and metabolism. Dietary taurine is the most common source of taurine accumulation. Taurine is released by cations, but its absorption is influenced by sodium and temperature. Taurine transporters (TauTs) perform an important role, and a number of TauTs have recently been discovered. Taurine metabolism is slow, but it slows even more when the supply is low. However, with increased dietary taurine supply, excess of taurine simply eliminated through urine. An effective transport and renal reabsorption system are essential to provide an adequate and consistent supply of taurine (Laidlaw *et al.*, 1990; Schaffer & Kim, 2018).



Source(s): Adopted and compiled from https://www.shutterstock.com

Figure 3.
Primary dietary sources of taurine

Taurine in energy drinks

Energy drinks are fortified nonalcoholic beverages with diverse components such as caffeine, taurine, minerals and vitamins that are advertised for their energetic benefits. Energy drinks have become a popular dietary supplement for supplying energy, increasing stamina and improving athletic performance, particularly in the short-term (Schaffer *et al.*, 2014). In mammals, taurine accounts for 50-60% of free amino acids and serves a variety of biological roles. Taurine is found in most energy drinks, and the manufacturers claim that taurine boosts mental performance and provides energy (Gutierrez-Hellin & Varillas-Delgado, 2021). The amounts of taurine in energy drinks range between 30 and 400 mg/100 ml (Table 2). This information is gathered after looking into the ingredient details of the commercial products available in the market.

Health benefits of taurine supplementation

Taurine is a relatively common amino acid that is present in almost every tissue in a mammal's body, and as a result, it plays a variety of important roles throughout the body. Taurine supplementation has the following beneficial effects on newborns and the elderly:

Taurine supplementation in newborns

Taurine is the most ubiquitous free amino acid in embryonic brain and the second most plentiful free amino acid in human breast milk. Long-term parenteral nutrition (PN) can cause neonates to become taurine deficient due to insufficient CSAD activity, resulting in retinal impairment. Furthermore, maternal taurine insufficiency causes neurologic defects in kids and can result in oxidative stress (OS) later in life. Based on the studies indicating that taurine-deficient newborns had defective retinal function, bile acid secretion, fat absorption and hepatic function, the food and drug administration (FDA) approved the addition of taurine in infant formula milk in 1984 (Caine & Geracioti, 2016; Sinha *et al.*, 2007). The quantity and frequency of taurine supplementation needed for premature and low-birth-weight infants is still up for debate as multiple randomized controlled experiments have failed to demonstrate statistically significant developmental impacts. Such conditions have yet to be established in grown neonates (Caine & Geracioti, 2016; Kilb & Fukuda, 2017).

Taurine supplementation in elderly

Current studies have advocated the beneficial effects of taurine supplementation to individuals requiring long-term PN, as well as those with hepatic issues, severe renal failure and a variety of heart ailments. Taurine insufficiency may interfere with the normal development of brain and retina. This could disrupt bile acid conjugation, raising the chances of cholestasis, where taurine supplementation can help. Supplementing with taurine has been shown to help in trauma recovery. Taurine concentration in plasma and blood cells is normalized by a 10 mg/kg taurine supplement (Aerts & Van Assche, 2002; Ahmadian, Dabidi

Table 2.
List of taurine content in energy drinks commonly available in markets

Amount of taurine in energy drinks			
Brand	Taurine per 100 ml	Brand	Taurine per 100ml
Biscon	400 mg	Code Red	30 mg
Monster	80 mg	Cobra	30 mg
Red Bull	400 mg	Royale Ferrari	400 mg
MFP-Hype	400 mg	King Legend	400 mg
Bugzy	30 mg	Power Horse	400 gm

Roshan, & Ashourpore, 2017). Short-bowel syndrome patients do not ordinarily reabsorb bile salts (mainly taurine conjugate), requiring taurine supplementation. If these patients are on PN, taurine supplementation becomes extremely important. Long-term taurine deficiency increases the risk of liver disease in these patients (Ahmadian *et al.*, 2017; Roysommuti & Wyss, 2014). Taurine levels were also found to be below-normal in malnourished postoperative cancer patients, indicating that taurine supplementation can help. Patients with congestive heart failure should consume 2 g of taurine per day, while diabetic patients with additional complications should consume 3 g per day. Taurine deficiency was reported in patients with liver injury or cirrhosis, and taurine supplementation improved the condition (Jong, Azuma, & Schaffer, 2012; Schaffer & Kim, 2018; Sinha *et al.*, 2007).

Taurine's physiological functions

Due to its unique chemical structure, taurine is thought to be engaged in a variety of life processes, suggesting essential physiological functions that are outlined as follows (Table 3):

(1) Taurine as an antioxidant

Taurine is seen in relatively large amounts in tissues exposed to high rates of oxidants, implying that it plays a role in OS reduction. OS is a key cause of tissue destruction in circumstances such as infections, acute/chronic inflammation, aging and cancer. Reactive oxygen species (ROS) produced predominantly by activated leukocytes (macrophages, eosinophils and neutrophils) cause OS at a site of inflammation. ROS help the body defend against infections, but they also cause tissue damage (Baliou *et al.*, 2021; Jong *et al.*, 2012). Antioxidants play a role in preventing oxidant-induced cell damage and reducing oxidative alteration of self-molecules, especially high molecular components like lipids, proteins and Deoxyribonucleic acid (DNA). Taurine has been shown to be an efficient antioxidant in various studies, although the mechanism underlying its antioxidant activity is unknown. Taurine's most well-known antioxidant function is its ability to neutralize hypochlorous acid (HOCl), a very hazardous oxidant produced by the myeloperoxidase (MPO)–halide system. This activity reflects taurine's anti-inflammatory characteristics, as taurine chloramine (Tau-Cl) is generated when it interacts with HOCl. Tau-Cl is a less toxic anti-inflammatory mediator that is more stable (Jong *et al.*, 2012).

(2) Taurine's role in retinal development

In the neurodegenerative process, OS serves a critical role. To prevent OS injury, retinal cells require redox signaling and a balance of ROS and antioxidant scavengers. OS in the eye is increased by aging, gene changes and excessive exposure to external oxidative stressors (e.g. light). Age-related macular degeneration (AMD), diabetic retinopathy (DR), and glaucoma all have OS as a contributing factor in its origin and progression (Castelli *et al.*, 2021; Jacobsen & Smith, 1968). Taurine is the most abundant amino acid in the retina of animals during growth and adulthood. Furthermore, the retina seems to be the richest organ in terms of taurine, with concentrations greater than any other ocular structure or the brain, attaining up to 50 mmol/g tissues in rodents. The retinal pigment epithelium (RPE) and müller progenitor cell (MPC), which accumulate taurine and transmit it to photoreceptor cells, provide retinal taurine. Taurine is ubiquitous in photoreceptor cells, and all retinal cells obtain taurine from the extracellular space. Taurine supplementation has been found to be a preventative and prospective treatment method for retinopathies, such as retinitis pigmentosa, an inherited illness marked by the progressive degeneration of rod photoreceptors. Taurine supplementation reduces OS through a variety of mechanisms, including anti-apoptotic actions; however, the protective actions of taurine against retinal damage are still unknown (Antonarakis, 2020; Castelli *et al.*, 2021).

Physiological functions	Characteristics	Reference No.
Taurine as an antioxidant	• Neutralizes hypochlorous acid (HOCl) • Attenuates endoplasmic reticular (ER) stress • Prevents mitochondrial membrane permeability and apoptosis	Baliou *et al.* (2021), Castelli *et al.* (2021)
Taurine in retinal development	• Exerts neurotrophic effects on the retinal ganglion cells (RGC) • Enhances chloride influx into postsynaptic neurons • Rescue the photoreceptors and ameliorate the visual impairments	Veeravalli *et al.* (2020), Chesney *et al.* (2010)
Renal actions of taurine	• Scavenge ROS (reactive oxygen species) • Osmoregulatory characteristics have a cytoprotective influence • Shows inhibitory effect on the mitogen-activated protein kinase (MAPK) pathways • Suppresses the increased in lipid peroxidation and transforming growth factor-β (TGF-β)	Inam *et al.* (2018), Han and Chesney (2012), Sun *et al.* (2016)
Anti-hypertensive action of taurine	• Sympatholytic action on the central nervous system (CNS) • Block the activation of the renin-angiotensin-aldosterone system (RAAS) • Minimizes the elevation in serum cytokine • Reduces oxygen derived free radical generation	Han and Chesney (2012), Zhao *et al.* (2021), Lourenco and Camilo (2002)
Anti-diabetic action of taurine	• Boosts-up insulin sensitivity and secretion • Reduces mitochondrial calcium overloading • Prevents the production of advanced glycation end products (AGEs) • Stimulates insulin-independent glucose uptake	Han and Chesney (2012), Nakaya *et al.* (2000)
Taurine's role in brain development	• Regulates the hypothalamic-pituitary-adrenal axis • Prevents the impaired calcium handling in sensory neuron • Supports the genesis & survival of neurons in the hippocampus • Reduces pro-inflammatory cytokines in traumatic brain injury	Chung *et al.* (2012), Ito *et al.* (2014)
Cardiovascular actions of taurine	• Modulates Ca^{2+} homeostasis • Reduces the negative effects of norepinephrine • Reduces the development of atherosclerotic lesion • Prevents oxidant-mediated cardiomyocytes apoptosis	Laidlaw *et al.* (1990), Zhao *et al.* (2021), Mousavi *et al.* (2020)
Taurine and aging	• Maintains the excitation-contraction coupling of muscles • Potentiates the rate of sarcoplasmic reticulum (SR) calcium uptake • Reduces the age-related reduction in serum insulin-like growth factor-1 (IGF-1), offering beneficial effect as people got older • Involves in the inhibition of nuclear factor kappa B (NF-κB)	El Idrissi *et al.* (2013), Yoshimur *et al.* (2021), Suarez *et al.* (2016)

Table 3.
Taurine is known to play a pivotal role in a variety of physiological functions in the body and is believed to have considerable impacts on the cardiovascular system, central nervous system, muscular system and endocrine system in addition to other areas of the body

(*continued*)

Physiological functions	Characteristics	Reference No.
Taurine and neonatal development	• Helps infants absorb fat from the gastrointestinal tract • Human milk has a better neurodevelopmental outcome	Heird (2004), Chawla (2018)
Taurine in hair treatment	• Have a role in the preservation of the human hair bulb • Effective in preventing hair loss caused by stress	Collin *et al.* (2006), Kim *et al.* (2013)
Taurine in muscular system	• Increases skeletal muscle performance • Decreases myotonic dystrophy • Promotes glucose uptake and lipolysis • Reduces mitochondrial apoptosis • Decreases age-related sarcopenia	De Luca *et al.* (2015), Spriet and Whitfield (2015), Kurtz *et al.* (2021)

Table 3.

(3) Renal actions of taurine

Taurine has been demonstrated to have an impact on various kidney diseases such as acute kidney injury, glomerulonephritis, renal failure and diabetic nephropathy. In renal cells, taurine is a crucial regulator of various physiologic activities. It has been observed to influence ion re-absorption/secretion, renal blood supply, urine composition, osmoregulation and glomerular filtration in a beneficial way. Taurine has a large nonionic osmolarity capacity in renal cells (Chesney, Han, & Patters, 2010). Taurine's antioxidant and osmoregulatory characteristics have a cytoprotective and multifunctional influence on renal cell homeostasis. In fact, the defensive features of taurine have proven to be useful in animal models of renal diseases, primarily through its osmoregulatory and antioxidant capabilities. Taurine's protective effect against hypertension, which is common in renal disorders, is supported by its inhibitory action on the renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system, as well as its antioxidant, anti-inflammatory and endothelial dysfunction-relieving properties (Chesney *et al.*, 2010; Inam *et al.*, 2018). Moreover, Taurine's anti-diabetic nephropathy benefits are attributed to its antagonistic influence on the mitogen-activated protein kinase (MAPK) networks, as well as its anti-inflammatory and antioxidant characteristics. Despite the fact that taurine has been used in a variety of nephrotoxic animal models, its therapeutic application is limited, allowing for more research into the molecular mechanisms behind its anti-renal-injury properties (Chesney *et al.*, 2010; Han & Chesney, 2012; Inam *et al.*, 2018).

(4) Anti-hypertensive action of taurine

Taurine has identified as a possible therapeutic target for cardiovascular diseases, with the potential to prevent hypertension, stroke and atherosclerosis. Hypertension is a common sign of renal disease, and it is thought to be caused by RAAS deficits, monogenic ion transporter anomalies and acute kidney inflammation. Taurine's hypotensive effect is mostly due to its ability to block the activation of the RAAS by antagonizing angiotensin II (Inam *et al.*, 2018). Prehypertension is a crucial factor in the progression of hypertension. Additionally, prehypertension is linked to stroke, ischemic heart disease and renal impairment as morbidities. Although lifestyle changes and an angiotensin II receptor blocker have been utilized to treat prehypertension, the main therapeutic barriers are poor compliance and anti-hypertensive drug restrictions (Sun *et al.*, 2016; Zhao, Meng, Zhang, Dong, & Zhou, 2021).

In epidemiological investigations, plasma sulfur amino acids have been observed to be decreased in patients with hypertension. Taurine-rich diets have been shown in several clinical investigations to lower cardiovascular risks regardless of ethnicity or genetic background. Furthermore, animal studies have indicated that taurine deficiency speeds up the onset of excessive salt-induced hypertension. Although taurine has been demonstrated to decrease blood pressure in various hypertensive animal models, few rigorous and long-term clinical investigations have validated this beneficial effect in humans (Inam *et al.*, 2018; Sun *et al.*, 2016).

(5) Endocrine and other metabolic actions of taurine

Taurine has been reported to protect against diabetes and insulin resistance through a variety of ways. Taurine is implicated in a number of critical physiological processes, including glucose homeostasis, where it exerts a powerful hypoglycemic effect by lowering OS and inflammation, as well as boosting insulin sensitivity and secretion. Another way that taurine improves diabetic complications is by reducing mitochondrial calcium overloading, which is frequently associated with proper protein folding. Taurine, for example, has been found to attenuate hyperalgesia and improper calcium signaling in diabetic sensory neurons (Inam *et al.*, 2018; Lourenco & Camilo, 2002). In diabetes mellitus, low plasma and platelet taurine levels have been recorded; taurine treatment recovers plasma concentrations and rectifies blood platelet impairment. In this context, a reduced dietary intake of taurine is linked to an increased risk of cardiovascular disease. The fact that these patients have poor intestinal absorption and high renal excretion rates of taurine supports the theory that diabetes is a taurine-deficient condition (Lourenco & Camilo, 2002). Taurine with s-allyl cysteine was reported to have strong antioxidant and anti-diabetic properties in an *in vitro* study, indicating its potential for treating hyperglycemia and its complications (Rais, Ved, Ahmad, Parveen, & Mujeeb, 2021). In a diabetic model of rats, taurine enhanced glucose and lipid metabolism, and also decreased insulin resistance. Taurine supplementation also helps to prevent diabetes complications such as retinopathy, nephropathy, neuropathy, atherosclerosis and cardiomyopathy (Inam *et al.*, 2018; Nakaya *et al.*, 2000).

(6) The importance of taurine in brain growth and function

Taurine plays a prominent role in nervous system disorders, exhibiting protective effects against toxicity in many neurodegenerative condition models such as Alzheimer's, Parkinson's and Huntington's diseases (Kilb & Fukuda, 2017). According to a study, taurine has anti-depressant properties, which may be linked to its role in modulating the hypothalamic-pituitary-adrenal axis and supporting the origination, maintenance and development of neurons in the hippocampus. In fact, taurine augmented neonatal neuron survival, leading in better neurogenesis in the adulthood (Wu *et al.*, 2017). Taurine has a unique physical feature when compared to other neuroactive amino acids: its structure contains sulfonic acid rather than carboxylic acid, making it difficult to penetrate the blood-brain barrier (BBB) (Chung *et al.*, 2012). Several studies have proven the anti-neuroinflammatory properties of taurine (Chung *et al.*, 2012; Su *et al.*, 2014; Wu *et al.*, 2017). Taurine massively improved functional recovery and lowered glial fibrillary acidic protein deposition and water content in the penumbral area in traumatic brain injury (TBI) induced model (Su *et al.*, 2014). The levels of cytokines, such as IL-1α, IL-1β, IL-4, IL-5, tumor necrosis factor-α and interferon-γ, were significantly lowered after a one-week therapy with taurine. Taurine treatment reduced brain edema, astrocyte activity and pro-inflammatory cytokines in TBI patients; and effectively reversed the severity of the injury (Chung *et al.*, 2012; Su *et al.*, 2014).

(7) Cardiovascular actions of taurine

Taurine has been licensed for the treatment of congestive heart failure in Japan. Taurine, like other heart failure medications, relieves not just the symptoms of congestive heart failure (such as dyspnea and edema), but also removes or reduces the requirement for additional heart failure medications like digoxin (Schaffer & Kim, 2018). Although taurine has a mild positive inotropic effect on the hypodynamic heart and enhances natriuresis and diuresis, the main therapeutic effect of chronic taurine administration seems to be a decrease in the behavior of angiotensin II and norepinephrine, which are known to reduce myocardial effectiveness by increasing fluid remodeling, afterload pressure and ventricular remodeling (Ito, Schaffer, & Azuma, 2014). Taurine works to reduce the negative effects of norepinephrine by lowering catecholamine overflow (through changes in Ca^{2+} transport) and decreasing cell signaling (by alterations in Ca^{2+} transport, ROS concentration and protein phosphorylation). However current findings have indicated that taurine therapy promotes exercise capacity in heart failure patients, it is still unknown if taurine supplementation lowers the chance of acquiring overt heart failure in the common population. There's reason to assume that taurine could help heart failure patients live longer since it raises the heart's high energy phosphate content, which is a key driver of mortality in individuals with congestive heart failure (Ito *et al.*, 2014; Mousavi *et al.*, 2020; Zhao *et al.*, 2021).

(8) Taurine and Aging

Physical fitness is inversely related to morbidity and mortality from acute to chronic diseases, and these ailments are also responsible for accelerated aging. The utmost important factor in preventing and reversing this tendency is exercise. Amino acid exchange is thought to occur during exercise, as well as an increase in serum taurine level (El Idrissi, Shen, & L'Amoreaux, 2013). In many investigations of physical activities, taurine-containing drinks have been demonstrated to improve cognitive performance, well-being and adaptive potential. Taurine plays a preventive role against the harmful effects of cigarette smoking. It also cuts down on the time it takes to recover from an alcoholic hangover. Dietary taurine supplementation also reduced the age-related decrease in serum insulin-like growth factor-1 (IGF-1), offering beneficial effect as people got older (El Idrissi *et al.*, 2013). Taurine is a plentiful organic osmolyte in epidermal cells and plays a key role in the regulation of cellular water balance and cell volume. Numerous evidences suggest taurine's significance in maintaining the skin's moisture homeostasis (Yoshimura *et al.*, 2021). The majority of neurodegenerative illnesses are caused by increased OS, which produces ROS. Taurine has the ability to scavenge ROS. Taurine appears to play a significant role in immune function modulation. A signal is sent by taurine chloramines which help to suppress the production of cytotoxic cytokines linked to cellular damage. Thus, taurine supplementation with exercise may have a synergistic effect in slowing down the aging process (El Idrissi *et al.*, 2013; Suarez, Munoz, Martin Del Rio, & Solis, 2016).

(9) Neonatal development and taurine

Soon after it was discovered that taurine insufficiency caused retinal degeneration in animals, evidence that taurine may be a conditionally important nutrient for the human neonate began to emerge. The first piece of evidence came from a study which reported that formula-fed infants had lower plasma and urinary taurine concentrations than human-milk-fed infants, but higher plasma and urinary concentrations of all other amino acids (Heird, 2004; Sinha *et al.*, 2007). The presence of taurine in human milk, but not in infant formula milk, was blamed for this. Taurine is extensively distributed in the body and is the most abundant free amino acid in human breast milk. Human milk has an appropriate amount of taurine, and neonates fed

human milk have a better neurodevelopmental outcome than neonates fed formula milk. Thus, taurine was included to most infant formula milk in the early to mid-1980s as a result of these findings. It was also observed that extended taurine-free PN caused retinal degeneration, which could be reversed by supplementing taurine (Caine & Geracioti, 2016; Chawla, 2018; Heird, 2004). Long-term feeding with taurine-deficient formula milk or PN has been associated to retinal degeneration, decreased bile acid secretion, delayed auditory maturation, lower fat absorption and hepatic cholestasis (Chawla, 2018; Kilb & Fukuda, 2017).

(10) Role of taurine in hair treatment

The hair bulb, which is the site of taurine uptake, is a hotbed of cellular activity. It is one of the most active locations in the body, and it is the source of all follicular compartments. This compartment is morphologically and functionally remarkably stable, as isolated hair follicles continue to produce normal hair fibers when grown in a completely defined media. Furthermore, when isolated human hair follicles are cultivated *in vitro* in the presence of taurine, their survival rate improves. These data strongly suggest that taurine may have a role in the preservation of the human hair bulb as an osmolyte or a cysteine and/or calcium metabolism regulator (Collin *et al.*, 2006). Although astressin-B and finasteride are two commonly used medications to treat alopecia, the data in a research suggest that taurine may be more effective than the two anti-alopecia drugs in preventing hair loss caused by stress. This finding strongly indicates that taurine may assist hair root cells to maintain their integrity by alleviating chemical stress (Kim, Chang, & Lee, 2013).

(11) Taurine in muscular system

Taurine is a free-form amino acid found in multiple mammalian tissues, and appropriate taurine levels are required for skeletal muscle performance. The taurine transporter (TauT) activity in skeletal muscle allows it to concentrate the most taurine in the body. Taurine has a variety of physiological effects, including membrane stability, osmoregulation, cytoprotection, antioxidant and anti-inflammatory activity, ion channel activity and calcium concentration modulation (De Luca, Pierno, & Camerino, 2015; Spriet & Whitfield, 2015). Taurine is thought to be involved in the handling of Ca^{2+} from the sarcoplasmic reticulum (SR) in type I and type II muscle fibers, as well as calcium homeostasis regulation. Taurine promotes the release of SR-Ca^{2+} and enhances the sensitivity of contractile myofilaments in both cardiac and skeletal tissue, directly affecting excitation-contraction-relaxation mechanism, resulting in increased muscular force and improved athletic performance (Spriet & Whitfield, 2015). Taurine supplementation may thus be beneficial in restoring the altered levels of myotonic diseases. Taurine's vasodilating characteristics may also help to increase muscle metabolism by counteracting functional ischemia (De Luca *et al.*, 2015). During exercise, taurine may perform a role in PI3K/AKT signaling-pathway, which may help to promote glucose uptake and lipolysis (Kurtz, VanDusseldorp, Doyle, & Otis, 2021). High taurine concentrations in cardiac mitochondria have been shown to act as a mitochondrial buffer, reduce mitochondrial apoptosis and oxidative and endoplasmic reticulum stress. Although the method by which taurine regulates gene expression throughout development is unknown, it appears to be an important element in myogenesis and possibly mitochondrial biogenesis, with implications for tissue development. Age-related sarcopenia, which is characterized by significant changes in the hormonal and metabolic balance of skeletal muscle, is another condition that may benefit from taurine administration. As a result of an increase in proteolysis with age, a significant change

in the amount of various amino acids occurs in human muscle specimens; at the same time, a significant drop in taurine content has been reported (De Luca *et al.*, 2015; Spriet & Whitfield, 2015).

Consequences of taurine deficiency

Taurine is thought to play a role in a variety of biological processes. Its deficiency is linked to the impairments in numerous organs, including the eye, heart, kidneys and brain, both during development and later in life. Taurine deficiency can be caused by a lack of ability to synthesize or store taurine, as well as an insufficient amount from dietary sources (Basili *et al.*, 2021; De Luca *et al.*, 2015; Duchan, Patel, & Feucht, 2010; El-Batch, Hassan, & Mahmoud, 2011; Guizoni *et al.*, 2021; Mersman, Zaidi, Syed, & Xu, 2020; Miyazaki *et al.*, 2019; Ontiveros *et al.*, 2020; Shao & Hathcock, 2008). In principle, enough methionine or cysteine should ensure adequate synthesis; nevertheless, taurine synthesis can also be constrained by a lack of enough enzymes and vitamin B_6 (Gonzalez-Vazquez *et al.*, 2021; Lourenco & Camilo, 2002). The prominent affected risk groups for taurine deficiency are: preterm newborns, patients on long-term PN and patients with hepatic impairment, chronic renal failure or diabetes (Basili *et al.*, 2021; Lourenco & Camilo, 2002; Ontiveros *et al.*, 2020). It's essential to mention that taurine deficiency in the blood and tissues impact osmolarity, which can affect cell density and membrane stability. These two factors are enough to cause cell dysfunction. Eventually, tissue taurine depletion is linked to the activation of the volume-regulated anion channel, which is involved in taurine efflux (Bkaily *et al.*, 2020; Guizoni *et al.*, 2021). In animal models, taurine depletion has been documented to cause retinal degeneration, dilated cardiomyopathy, high blood pressure, aging and immune function deficiencies (Duchan *et al.*, 2010; Mersman *et al.*, 2020). Tissue taurine depletion caused mitochondrial and endoplasmic reticulum dysfunction, impairing cardiac energy consumption and Ca^{2+}-ATPase activity. In humans, however, such full tissue taurine depletion has never been observed (Guizoni *et al.*, 2021; Lourenco & Camilo, 2002).

Safety and toxicity of taurine supplementation

To date, the literature is scarce regarding potential interactions between taurine and commonly used medications. Although no evidence specifically links taurine with adverse effects when used concurrently with other medications, there may be a link between taurine supplementation and various cytochrome P450 systems responsible for hepatic drug metabolism (El-Batch *et al.*, 2011; Shao & Hathcock, 2008). Specifically, taurine inhibits cytochrome P450 2E1, a highly conserved xenobiotic-metabolizing P450 responsible for the breakdown of more than 70 substrates, including several commonly used anesthetics, analgesics, anti-depressants, anti-bacterials and anti-epileptics. Of note, taurine may contribute to the attenuation of OS in the liver in the presence of alcohol and acetaminophen, two substances frequently used and abused (El-Batch *et al.*, 2011). To date, several studies have involved heavy taurine supplementation without serious adverse effects. While the largest dosage of taurine tested in humans appears to be 10 g/day for 6 months, a number of studies have used 1 to 6 g/day for periods of 1 week to 1 year. However, the assessment of potential acute, sub-acute and chronic adverse effects has not been comprehensive, more research must be done to ensure safety of higher amounts of taurine administration and to define a tolerable upper limit of intake (Caine & Geracioti, 2016; Duchan *et al.*, 2010). Taurine is found in most energy drinks, and the manufacturers claim that taurine boosts mental performance and provides energy (Gutierrez-Hellin & Varillas-Delgado, 2021). A number of recent investigations have looked into the effects of combining energy drinks

with alcohol. Certain studies provide a controlled assessment of the initial consequences of these mixtures, which are commonly consumed by minors and young adults (Curran & Marczinski, 2017).

Conclusions

Taurine, a sulfur-containing amino acid, is by far the most prominent amino acid in retina and leukocytes; and has been associated to a variety of biological and physiological processes. Taurine is not integrated into proteins and is found in its free form, unlike other amino acids. It is an essential amino acid for felines (such as cats) and a conditionally essential amino acid for adult-humans and nonhuman-primates (such as monkeys). In fact, taurine is an essential amino acid for premature neonates, and breast milk provides it. Supplementation is essential for neonates on PN since deficiency seems to have a negative impact on the developing brain and retina. Taurine deficiency is more common in certain groups of persons, such as patients who need long-term PN, those with chronic hepatic impairment and those with heart or renal failure; therefore, taurine supplementation may be beneficial. Taurine is assumed to play a key part in a range of physiological functions in the body, including the cardiovascular system, central nervous system, muscular system and endocrine system, as well as other body systems. Depression, hypertension, diabetes, hypothyroidism, gout, infertility, obesity, kidney failure and other illnesses have been linked to low plasma taurine levels.

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